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Case Report

Acute Achilles Paratendinopathy following Major Injury of the Crural Fascia in a Professional Soccer Player: A Possible Correlation?

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Background. The anatomy and mechanical properties of the Crural Fascia (CF), the ubiquitous connective tissue of the posterior region of the leg, have recently been investigated. The most important findings are that (i) the CF may suffer structural damage from indirect trauma, (ii) structural changes of the CF may affect the biomechanics of tissues connected to it, causing myofascial pain syndromes, and (iii) the CF is in anatomical continuity with the Achilles paratenon. Consistent with these points, the authors hypothesize that the onset of acute Achilles paratendinopathy may be related to histological and biomechanical changes of the CF. *Case Presentation*. A professional male football player suffered an isolated injury of the CF, interposed between the soleus and medial gastrocnemius (an atypical site of injury) with structural connective integrity of the muscles. After participating in the first official match, two and a half months after the trauma, he has unexpectedly demonstrated the clinical picture of acute Achilles paratendinopathy in the previously injured limb. *Conclusions*. Analysis of this case suggests that the acute Achilles paratendinopathy may be a muscle injury complication from indirect trauma of the calf muscle, if a frank and extensive involvement of the CF were to be ascertained.

1. Introduction

The distal myotendinous junction of the medial gastrocnemius (MG) is the typical site for muscle injuries to the calf. This particular injury is also known as a "tennis leg" calf injury and is widely known and extensively written about in literature [1].

Balius et al. [2] have recently described the injuries of the soleus (SL). The authors emphasise the fact that the rate of accidents against this muscle is likely to be underestimated, due to the anatomical complexity of the muscle and due to the low sensitivity of the ultrasound examination to detect abnormalities [3].

The involvement of the Crural Fascia (CF) is also possibly underestimated. It is the ubiquitous connective tissue of the posterior region of the leg that interfaces and connects the calf muscles. The CF does not integrate into the connective tissues forming the skeletal muscle extracellular matrix [4]. The CF is viewable through the use of ultrasound (Figure 1) and appears as a thick lamina of connective tissue similar to an aponeurosis [5]. The mean thickness of the (superficial) CF is estimated to be 1.1 mm in healthy subjects [6].

The close anatomical relationship of the CF with the Achilles paratenon (AP) has recently been described. The CF and AP join together at about 4 cm proximal to the posterior superior calcaneal tubercle [7, 8]; Webborn et al. [7] were also the first to describe the acute tear of the CF at the attachment to the Achilles tendon, making it an attributing factor to the etiopathogenesis of achillodynia. These new findings have a significant impact in the diagnostic study of calf muscle injury and in the evaluation of their complications.

In this study, the case of a professional football player who suffered a rare and isolated injury to the CF interposed between MG and SL is presented. The case is particularly complex because the football player, at complete sporting recovery, demonstrated the clinical picture of acute

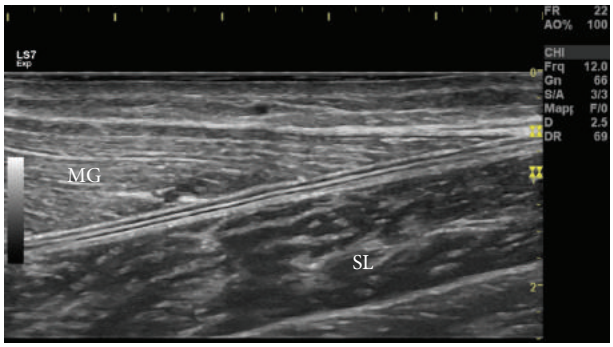

Figure 1: Ultrasound image of Crural Fascia (CF) in a 24-year-old male volunteer. The CF is easily distinguishable by the epimysia of the medial gastrocnemius (MG) and soleus (SL) being between these three structures (hyperechoic) interposed by two layers of hypoechoic connective tissue.

Achilles paratendinopathy in the same leg. Paratendinopathy is defined by inflammation and/or degeneration of the paratenon. Exercise-induced pain and local swelling around the tendon's mid-portion are the most important symptoms [9].

In light of the recent findings above, the hypothesis of the authors is that acute Achilles paratendinopathy may be related to the previous injury of the CF, representing a complication. To the best of the authors' knowledge, this possible correlation has never been presented in literature.

2. Case

2.1. Acute Calf Injury. A male professional football (soccer) player suffered an injury to his right calf muscle during an official match. He described his injury mechanism as a sudden "kick" from the back in his calf during a jump. He had to leave the game. On initial examination, he had localised tenderness at the middle of his right calf. Passive and active movement of the ankle exacerbated the pain. No palpable defect was noted in the gastrocnemius muscle mass. The Achilles tendon was freely movable and Thompson test was negative for Achilles tendon tear. No other injury was reported and the initial clinical diagnosis of gastrocnemius strain was established. After elastic taping in neutral ankle flexion he was sent for an emergency MRI investigation. The MRI reported very generally "gastrocnemius and soleus muscle strain with presence of fluid between the two muscles."

Two days later, an ultrasound examination was performed to assess what structures were actually damaged. All the ultrasound examinations presented in this study were carried out using an ultrasound GE Logiq S7 Expert (GE Healthcare, Milwaukee, WI) with a 50 mm linear footprint matrix probe (5–15 MHz). Contrary to what was expected, the pictures show a rare non-tennis leg calf injury: the epimysia of the MG and of the SL were, in fact, ecostructurally intact. However, a considerable enlargement of the connective component interposed between the muscles was observed, compatible with structural injury and retractions of the CF (Figure 2). The framework was aggravated by the presence of

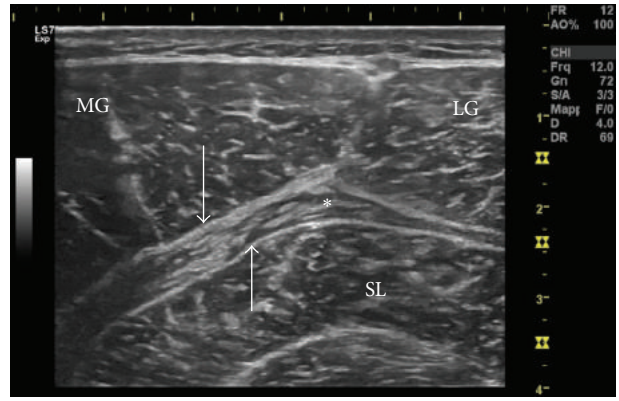

Figure 2: Isolated injury of the Crural Fascia, with considerable thickening of same (*asterisk*). Note the structural integrity of the medial gastrocnemius (MG) epimysium and of the soleus (SL), indicated by the *arrows*, and the absence of intramuscular edema. The muscle belly of the MG and Lateral Gastrocnemius (LG) are observable, a sign that the injury is not at muscle-tendon junction level.

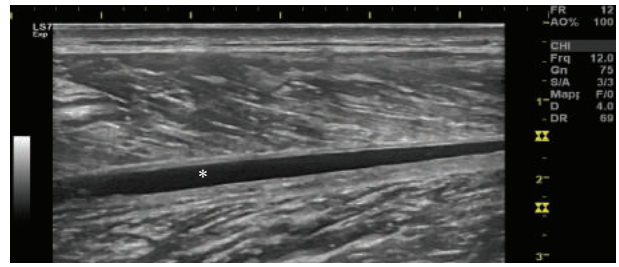

Figure 3: Interfascial blood (*asterisk*), observed at the distal region of the injury.

an extended interfascial spillage, probably blood (Figure 3). The diagnosis of the CF injury was finally made. A second MRI, performed 5 days after the trauma, confirmed "signs of detachment of the area between the SL and MG muscle in distractive outcome, with moderate intrafascial hematoma." Another two MRIs were performed at one month and at two months after the trauma. The report of these does not add anything significant to the diagnostic study of the injury. The MRI examinations were performed using the Hitachi, Open, 2009 (0.4 T) device and interpreted by an operator with considerable experience (nonauthor contributor).

The recovery process is divided into three parts. The proposals of each of the stages are summarised in Table 1. The injury being very rare and its prognosis being unpredictable, we have performed over twenty ultrasound examinations during the recovery process. In such cases it is advisable to monitor the evolution of the healing process as frequently as possible; continuous monitoring has been helpful to better orientate the therapeutic proposals. The player had his first training session with the team two months after the trauma. Despite physiotherapy proposals, the healing process was completed by the formation of a hypertrophic reparative scar tissue; the presence of intrascar liquid still remained modest (Figure 4). The player complains, in particular during the last

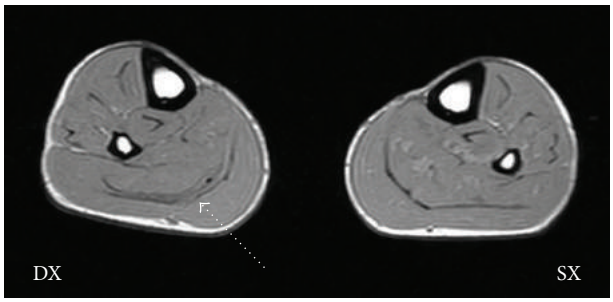

Figure 4: MRI axial section, performed two months after the injury. The *arrow* shows the thickening scar of the right Crural Fascia. Within the scar tissue, intrascar liquid residue, visible as a black dot, is detectable.

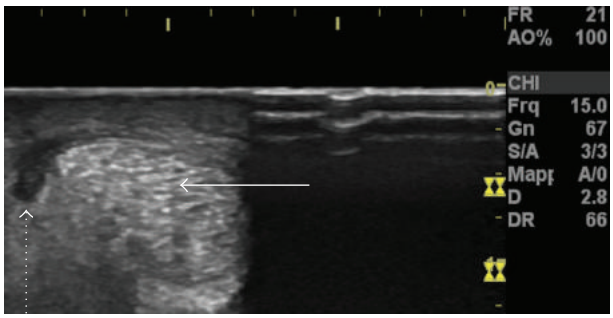

Figure 5: High resolution cross-sectional ultrasound of the Achilles tendon suffering from acute paratendinopathy. Laterally to the body of the Achilles tendon (*filled arrow*), a hypoechoic area is visible (*dotted arrow*), which is compatible with fluid collection between the tendon and the paratenon.

three weeks of recovery, of a feeling of excessive stiffness of the calf and Achilles tendon: sprinting and jumping were the activities of which he complains having more difficulties.

2.2. Acute Achilles Paratendinopathy. Fifteen days after fully returning to sports (see timeline, Table 2), the player has played in his first official match. On the day after, he appeared to be limping. At the interview, the player reported that, during the game, he felt a gradually increasing pain to the right Achilles tendon, so much so as to be forced to "run on his heel" in order to feel less pain. In any case, he played the entire match. He concludes that, on the evening of the game, the tendon felt "stiff and hot," making it difficult to "get to sleep."

On clinical examination, the tendon appeared evidently swollen and sore to the touch, especially when pinching the side surfaces. The swelling was palpable. Consistent with the classification of the Achilles tendon related disorders presented by van Dijk et al. [9], clinical diagnosis of acute Achilles paratendinopathy was made. The picture was confirmed through ultrasound examination (Figure 5). The player suspended activity for only 3 days but therapeutic intervention (manual drainage and cryotherapy; antiinflammatories for a week) lasted for 21 days. The player, 2 months from the onset of the pathology, did not complain of symptoms but moderate swelling of the tendon remained. The follow-up was interrupted when the player was transferred to another club.

2.3. Clinical History. The footballer had already suffered from acute Achilles paratendinopathy 9 months before the injury to the calf (see timeline, Table 2). The pathology had occurred two days after an injection of Betamethasone Disodium Phosphate (unknown dose), given for the treatment of right retrocalcaneal bursitis (whose symptoms lasted in turn for two weeks). Because of the condition the player had suspended activity for only five days but the symptoms resolved themselves after 6 weeks. The footballer did not take any other tendinopathy-inducing drug (quinolones, statins, and aromatase inhibitors) while he was a team member.

The player did not show clinical signs or suspicion of rheumatoid disease and blood levels were normal (routine blood tests have been performed quarterly). Instrumental screen investigations (X-Ray and MRI), performed a year and a half before the injury to the calf, did not show significant anatomical changes at the right knee, ankle, and foot.

2.4. Informed Consent. Written informed consent was obtained from the soccer player for publication of this case report. The subject has explicitly asked to remove personal data and not to include photos that depict him. He has consented, however, to the publication of the instrumental images.

3. Discussion

In this study, the case of a professional football player who suffered a rare and severe isolated CF injury, interposed between MG and SL, is presented. The case is particularly complex because the football player, at complete sporting recovery, demonstrated the clinical picture of acute Achilles paratendinopathy in the same limb.

The football player had resumed activity about two months after the trauma. The healing process was completed by the formation of a hypertrophic scar tissue interposed between MG and SL. The picture corresponds in fact to the net thickened CF, whose biomechanics were believed to be almost certainly altered. On the day after the first official match in which he participated, the clinical picture of acute Achilles paratendinopathy unexpectedly presented itself.

In light of the new findings concerning the anatomy of the CF and, in particular, the close relationship of the same with the AP, it is possible to hypothesize that acute paratendinopathy represents, at least in this specific case, a complication of the CF injury.

The following points support this hypothesis. Stecco et al. [6] observed that "posteriorly (to the Achilles tendon), the CF divided around the tendon to form the paratenon; the CF divides to envelop the tendon, thus forming the tissue usually called paratenon." In the case presented, the structural alteration suffered proximally by the CF has likely also altered the biomechanics of the AP, creating conditions for the onset of paratendinopathy. In addition to this, it should be remembered that the presence of intrascar liquid persists. Consistent with the above, it is likely that this liquid

Table 1: Rehabilitation course for the recovery of the calf muscle injury.

	Sports activity	Physiotherapy	Instrumental tests
Phase 1 (11 days)	Complete suspension of sports activity	Passive: manual drainage and cryopressure therapy. Double session daily Compulsory use of crutches, ankle-foot-orthosis and compression stockings	MRI: 5 days after trauma Ultrasound: daily
Phase 2 (24 days)	Bike (daily). Hydrotherapy (alternate days) Physical training in the gym (alternate days). Exercises without loading the injured calf	As in phase 1. Single session daily 2 times per week: diacutaneous fibrolysis (scar treatment)	MRI: 30 days after trauma Ultrasound: at least 3 times per week
Phase 3 (21 days)	Work on site. Progressive loads. Sports specific technical reeducation from the 45th day after injury	As in phase 2 Once per week: intratissue percutaneous electrolysis (scar treatment)	MRI: 60 days after trauma Ultrasound: at least once per week

Table 2: Timeline. Summary of the relevant player's clinical history.

Time interval	Pathology	Details	Evaluation
2 weeks	Retrocalcaneal bursitis	Resolution of the condition through local corticosteroid injection	Ultrasound examination
6 weeks	Acute Achilles paratendinopathy	Clinical picture manifested itself 2 days after injection into the bursa	Clinical assessment and ultrasound examination
9 months		The footballer trains and plays regularly	
2 months	Injury to the Crural Fascia (rehabilitation course, described in Table 1)	Crural Fascia injury result: hypertrophic scar tissue	See Table 1
2 weeks		The footballer trains and plays regularly	
3 weeks	Acute Achilles paratendinopathy	Clinical picture manifested itself 1 day after the first official match in which he participated	Clinical assessment and ultrasound examination

component will be progressively "accumulated" at AP level, triggering the symptoms at the time of maximum functional load (an official match). The AP was, in fact, the only region to which the intrascar liquid had direct access; the epimysium of the muscles was intact so that the liquid could not accumulate either subcutaneously (a situation not uncommon in case of "tennis leg" injuries) or deeply, with respect to the Achilles tendon. Other authors have already described the implication of the histological and biomechanical changes of the CF in the etiopathogenesis of overuse injuries in the leg, in particular of the Medial Tibial Stress Syndrome [10] and of the accessory superficial peroneal sensory nerve entrapment [11]. Thickening of the fascia and interfascial fibrosis are in fact considered a risk factor for the development of myofascial disorders and overuse injuries.

A variable to be considered in the analysis of this case, however, is the fact that the player had already suffered from acute paratendinopathy before the injury to the calf. This manifested itself shortly after use of corticosteroids in the treatment of the deep retrocalcaneal bursitis. Consistent with the work of Turmo-Garuz et al. [12], it is possible that the medication has spread to the Achilles tendon and connected

structures, in particular to the AP. If this possibility were indeed real, it would be justified to say that the injection brought on, as a complication, the paratendinopathy, potentially altering in a definitive way the histological properties. The same authors, in fact, conclude by saying that the "risk-benefit has to be taken into account when corticosteroid injections are prescribed to professional and high-level athletes" [12].

Therefore, it would be possible to hypothesize that acute paratendinopathy suffered after the calf injury is not dependent on the latter but is rather derived from previously occurring histological alteration (or even that it is an independent event). The opinion of these authors is that this view is potentially discredited by two considerations. The first is that, in the resolution of the (plausible) corticosteroid-induced paratendinopathy, the footballer has never actually presented the clinical picture and prepathological signs were not detected. The second consideration is that, being past nine months, one might have expected a clinical pattern of chronic paratendinopathy. However, none of the major clinical and instrumental characteristics of this disease [9] have been observed. For these reasons, the possibility that the paratendinopathy, suffered by the footballer after the calf injury, is connected to this (cause-effect relationship) seems more plausible than the other. Not in conflict with this, it is well-known that preexisting inflammation or degeneration is implicated as a major risk factor for tendon disorders. Therefore, despite the elimination of paratendinopathy symptoms, the footballer remained exposed to a relevant possibility of exacerbation in terms of his clinical profile.

This study has some limitations: (i) to better guarantee the anonymity of the professional footballer and his request of same, the authors have purposely omitted the basic data (age, height, BMI, and nationality) and the sports-specific data (role, dominant foot). The authors do not believe that this information is, in any case, relevant in the analysis of the case; (ii) the distinction between acute and chronic paratendinopathy can be assured only through histopathological examination. The diagnoses made in this study are only clinical or instrumental; (iii) the magnetic resonance equipment used does not offer high-quality images. This may have made the diagnosis difficult in spite of the examiner's experience: minor SL injuries may have remained undetected, in particular.

4. Conclusion

The analysis of the case suggests that the acute Achilles paratendinopathy may be a complication of calf muscle injury when there is decisive involvement of the CF. This possible correlation has not yet been hypothesized and verified in literature, probably because CF injuries do not generally come into consideration. The opinion of the authors is that the CF may have a role in the onset of painful syndromes and overuse injuries whose etiopathogenesis is still unclear today.

Competing Interests

The authors declare that they have no competing interests.

Acknowledgments

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A Molecular Mechanisms of Regeneration in Chronic Tendinopathy Using Ultrasound-Guided Intratissue Percutaneous Electrolysis (EPI®)

Keywords: Chronic tendon injury; Clinical symptoms; Non-tendon cells; Tendon stem cells; Electrolysis

Abbreviations: SP: Substance P; PRP: Platelet Rich Plasma; ECM: Extracellular Matrix; VEGFR-2: Vascular Endothelial Growth Factor Receptor 2; TSCs: Tendon Stem Cells; MMPs: Matrix Metalloproteinase; PPAR-γ: Peroxisome Proliferator-Activated Receptor Gamma; VISA-P: Victorian Institute of Sport Assessment-Patella; MMP-3: Matrix Metalloproteinase-3

Review Article

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Review Article

Chronic tendon injury, or tendinopathy, refers to the clinical symptoms including pain, focal tendon tenderness, decreased strength and movement in affected tendons. Approximately 30% of general practice consultations for musculoskeletal pain are related to tendon disorders [1]. Tendon injury can affect people of all ages, and can impair the activity of young and old adults in their work environment or sports activities. In summary, tendon disorders are common, have a substantial effect on quality of life and represent an important economic burden on healthcare systems [2].

Tendinopathy can be identified by the following histological characteristics: collagen fibril disorganization, increased proteoglycan and glycosaminoglycan content and increased non-collagenous ECM, hypercellularity and neovascularization [3].

These cellular and molecular changes modify the mechanical properties of tendon and cause pain. Because the pathogenesis of tendinopathy is not fully understood, different hypotheses have been proposed, including degeneration and failed healing [4]. Tendinopathies are in the main accompanied by an excessive nociceptive signalling from the tendon, causing pain and restricted mobility. Mechanisms driving these structural and neurological changes are not fully understood. A more recent theory ascribes part of the tendinosis changes to an increased production of biochemical agents, such as substance P (SP) and NMDAR1 glutamate receptor [5].

Chronic tendon injuries are facilitated by many extrinsic and intrinsic factors. Common intrinsic risk factors for tendon disorders include sex, age and diseases such as type 2 diabetes mellitus and obesity. Genetic predisposition might also influence risk of tendon injuries [6]. The main recognized extrinsic factor for tendon injury is abnormal loading on tendons, which is linked to physiological exercise, sport and specific work settings. Tendinopathy is thought to result from repetitive abnormal mechanical loading, whereas acute tendon injury often results after one isolated overloading event [7]. Aberrant mechanical stimulation induces the production of biological factors, including metalloproteinases, growth factors and prostaglandins, which can all lead to extracellular matrix (ECM) remodelling defects [8]. Moreover, excessive mechanical loading has been proposed to cause aberrant differentiation of Tendon stem cells (TSCs) into nontendon cells [9].

The primary goal of tendinopathy treatment is to reduce pain, mainly through the use of topical or systemic antiinflammatory drugs, whereas surgical techniques aim to repair ruptured tendons [10]. Independently of surgical procedures or nonsurgical management of tendon injury, rerupture often occurs because scarring results in weakened tendon tissue [11]. For both chronic and acute tendon injuries, exercisebased rehabilitation is indicated [12]. The use of autologous growth factors is another therapeutic approach that is gaining in popularity for the treatment of tendon injury. Plateletrich plasma (PRP) is a blood derivative containing high levels of growth factors, known to promote tissue healing [13]. Extracorporeal shockwave therapy has demonstrated some efficacy but only in calcified tendinitis of the shoulder; less-conventional procedures, such as phonophoresis, therapeutic ultrasonography or lowlevel laser therapy, are other options for the treatment of tendon injury [14].

In recent years, the intratissue percutaneous electrolysis (EPI®) technique has become more relevant in the scientific literature given the good results yielded in the treatment of patellar degenerative tendinopathy in comparison to other previous conservative treatments. This technique (Figure 1), created by Sánchez-Ibáñez and who have over 15 years' experience in its use, uses a flow of cathodic current directed exclusively to the area of degenerated tendon through an ultrasound-guided needle that brings about an organic reaction that leads to rapid regeneration of the degenerated tendón. The application of ultrasound-guided EPI® technique produces a non-thermal electrochemical reaction centered on degenerated tissue (tendinosis). This leads to a controlled local inflammatory reaction that leads to the regeneration of damaged tissue [15-18].

In experimental studies with human tendon injury, there has been a disproportionate expression of certain cytokines and matrix metalloproteinase (MMPs), prostaglandin E2 (PGE2), interleukin-6 (IL-6) and interleukin-1b (IL-1b). IL-1b in turn increases the production of matrix metalloproteinase-1 (MMP-1), matrix metalloproteinase-3 (MMP-3) and prostaglandin E2 (PGE-2) [19]. A recent experimental study by Sánchez-Ibáñez JM and co-wokers (2014) showed that with the use of EPI® technique in patellar tendinopathy increase of anti-inflammatory proteins, like peroxisome proliferator-activated receptor gamma (PPAR-γ). These proteins play a key role in the inhibition of expression of proinflammatory molecules secreted by macrophages, such as tumor necrosis factor alpha (TNF-α), IL-6 and IL-1β, thus producing in the treated tissue a highly beneficial molecular response during degenerative tendinopathy. This, in turn, results in an increase of the expression of vascular endothelial growth factor (VEGF) and vascular endothelial growth factor receptor 2 (VEGFR-2), mediators responsible for angiogenesis anti-inflammatory response. The EPI® technique makes for the activation of molecular and cellular mechanisms of the tendon responsible for phagocytosis and the regeneration of degenerated tissue [20]. A study of patellar tendinopathy in humans directed by Sánchez-Ibáñez JM [18] to evaluate the therapeutic effects of EPI® technique on the patellar tendinopathy. The results documented were good and stable with the Victorian Institute of Sport Assessment-Patella (VISA-P) score, Tegner scores and Roles and Maudsley score, and terms of clinical and functional improvement in patellar tendinopathy and providing a follow-up of 10 year [21].

The EPI® technique achieves a much localized organic reaction in the clinical focus by using a specially designed device (Figure 2) for this purpose (EPI Advanced Medicine, Barcelona, Spain), which leads to the rapid regeneration of degenerated tissue. This leads to the production of new immature collagen fibers that become mature by means of optimal mechanical stimulus, thereby obtaining good results in the short and long-term in terms of pain and function.

EPI® technique which leads to the rapid regeneration of degenerated tissue (Figure 3). This leads to the production of new immature collagen fibers, thereby obtaining good results in the short and long-term in terms of pain and function.

Figure 1: Treatment of tendinopathy with EPI® device (EPI Advanced S.L. Barcelona, Spain).

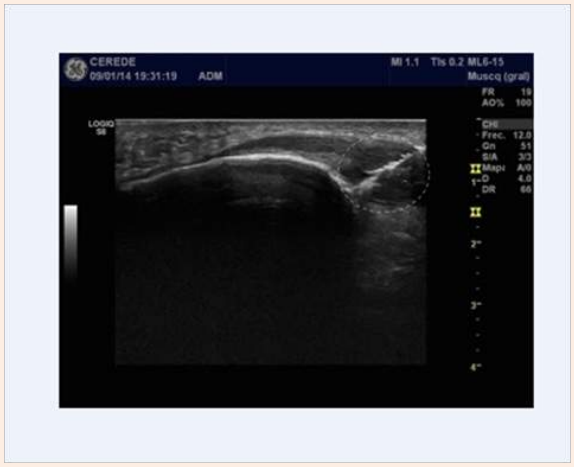

Figure 2: Hyperecoic image produced by the EPI® needle of 0,30mm in the degenerative area of the tendon. This hiperecoic image corresponse to a gas density produced by the electrochemical response of the catodic flow (CF) in the degenerative extracelular matrix. Note the electrochemical reaction (white area) produced on the tip of the needle, just in the area of damaged tissue.

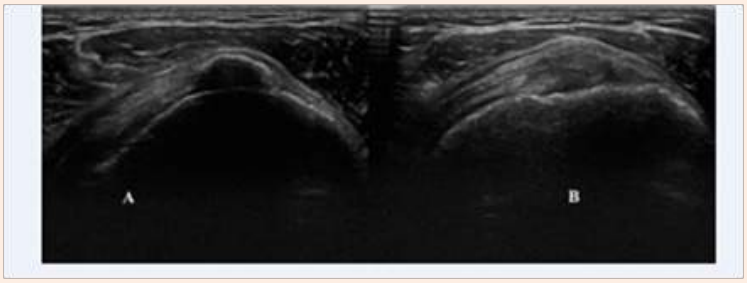

Figure 3: A) Ultrasound image in longitudinal view: Calcific tendinosis of the supraspinatus tendon with calcification; B) Three week after the EPI® technique treatment. It is observed the degenerated area of the tendon that is substituted by a new connective tissue and disappearance of calcification.

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Distiquiasis canina

Tratamiento con la técnica EPI®

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El término distiquiasis hace referencia al **crecimiento ectópico de las pestañas** en zonas no habituales del borde palpebral, con una dirección anómala, asomando dichos pelos por el borde libre del párpado **a través del conducto excretor de las glándulas de Meibomio**, en un número variable, que puede ir de uno solo a múltiples pelos (Stades, 2007). El folículo suele estar a 4-6 mm de distancia del borde libre del párpado en el aspecto distal de la superficie posterior del tarso, o cerca de la base de las glándulas de Meibomio. Las glándulas de Meibomio son glándulas sebáceas constituidas por acinis holocrinos dispuestos verticalmente para abrirse en un conducto central; cuando crece uno o varios pelos en su interior resulta la distiquiasis (Raimond-Letron *et al*., 2012) (figura **1**).

La sintomatología depende del tipo de pelos y su dirección. Si van dirigidos el exterior del ojo pueden no tener ninguna repercusión clínica; sin embargo, si van dirigidos hacia la córnea pueden causar desde irritación (prurito ocular y epífora) hasta una lesión corneal (úlcera) (Gellatt, 2003).

No es un proceso frecuente y tiene mayor incidencia en la especie canina, en la que se han realizado estudios acerca de la heredabilidad del proceso (Kaufhold *et al*., 2007; Petersen *et al*., 2015). Aunque es raro en otras especies, también se ha descrito en gatos (Reinstein *et al*., 2011), hurones (Verboven *et al*., 2014) y caballos frisones (Hermans *et al*., 2014).

Las razas caninas en las que aparece este proceso con mayor frecuencia son: Staffordshire bull terrier, bulldog inglés, cocker spaniel, spaniel tibetano, shih-tzu y lhasa-apso, así como las braquiocefálicas (Gellatt, 2003); sin embargo, también se ha descrito en otras como el carlino (Krecny *et al*., 2015) y el Elo dog (Kaufhold *et al*., 2007).

La bibliografía consultada no refleja ningún tratamiento sencillo que garantice la resolución del proceso, siendo la recidiva habitual, por lo que debe informarse a los propietarios del pronóstico (Gellatt, 2003).

Tratamiento

El tratamiento más económico y simple de la distiquiasis consiste en la **depilación manual**, si bien con esta técnica el porcentaje de recidiva o reaparición de los cilios resulta inaceptablemente elevado, con el agravante de que los nuevos pelos ocasionarán una distiquiasis más grave, debido a que crecen más cortos y son menos flexibles que los iniciales. Por tanto, dicha técnica únicamente se recomienda en aquellos casos leves en que el animal tiene solamente dos o tres cilios problemáticos, o bien como técnica diagnóstica encaminada a confirmar o descartar que los pelos son la verdadera causa del problema ocular del paciente (Petersen-Jones, 2007).

En el pasado, se llegaron a desarrollar algunas **técnicas quirúrgicas** para la eliminación de los folículos desde los que se origina la distiquiasis, consistentes en la escisión palpebral, en la ablación tarsal parcial o plastias encaminadas a modificar la dirección de los cilios. Entre ellas se incluyen la escisión parcial de la meseta tarsal (Bedford, 1973), la eliminación de una tira tarsoconjuntival (Spreull, 1982) o la técnica de Hotz-Celsus para evertir el párpado y dirigir los pelos en dirección opuesta a la córnea. Estos métodos, que suponen una grave alteración anatómica y funcional del párpado, se encuentran en la actualidad prácticamente abandonados por sus múltiples inconvenientes. Entre los severos efectos secundarios, se describe la posibilidad de inducir cicatrices significativas, de provocar la distorsión de los párpados y de ocasionar lesiones en las glándulas de Meibomio incluso en pacientes con párpados gruesos, pudiendo causar, cualquiera de ellas, inestabilidad de la película lacrimal y dar lugar a problemas más

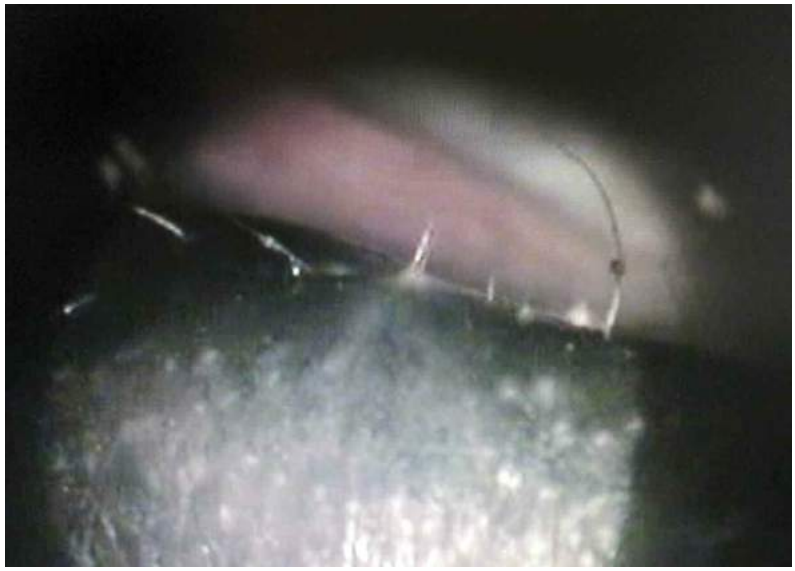


Figura 1
Distiquiasis de párpado superior.

serios aún que los causados por la propia distiquiasis (Peña *et al*., 1999; Petersen-Jones S, 2007).

En la actualidad, los tratamientos más utilizados son la criodepilación, la electrodepilación y la fotodepilación.

La **criodepilación** se lleva a cabo mediante la aplicación de una pequeña sonda de óxido nitroso o de nitrógeno líquido que se apoya sobre la conjuntiva en la zona en la que se sospecha que está el folículo del pelo ectópico. Al activar la sonda se congela la zona afectada del párpado durante algunos segundos, hasta que la bola de hielo que se forma alcanza el borde palpebral. Antes de retirar la sonda, es necesario esperar a la descongelación lenta de la misma para evitar arrancar el tejido congelado. El procedimiento se repite individualmente en cada pelo a tratar. Con esta técnica, los párpados sometidos al tratamiento se inflaman, lo que hace necesaria la administración sistémica de antinflamatorios no esteroideos, así como la aplicación, durante varios días, de diversos tratamientos locales que combinen antibióticos y corticoides. Tras la criodepilación, es común la despigmentación del párpado y del pelo, que puede llegar a ser permanente. La posibilidad de recidivas con esta técnica no es muy elevada, y los nuevos cilios no siempre precisan tratamiento, ya que suelen aparecer en un número reducido y ser más finos (Petersen-Jones S, 2007).

La **electrodepilación** se realiza, normalmente, con una unidad comercial de corriente continua diseñada al efecto, dotada de una placa ánodo, que debe sostenerse en la lengua de los pacientes, ganando así contacto eléctrico. Para llevarla a cabo, tras introducir el electrodo cátodo en forma de aguja en el párpado, a lo largo de la trayectoria del cilio y a varios milímetros de profundidad, se activa a una intensidad de 2-5 mA durante 5-10 segundos hasta que el pelo se suelte fácilmente. Se observa habitualmente la salida de secreción de las glándulas de Meibonio y burbujas de hidrógeno. Con este procedimiento, las recidivas son frecuentes, siendo necesario repetir la intervención. En cuanto a la utilización de corriente alterna de alta frecuencia, proporcionada por las unidades electroquirúrgicas, no está recomendada para la depilación, ya que puede producir necrosis y reacciones cicatriciales graves; además, se necesita de más tiempo y también suele ser necesario repetir la intervención (Petersen-Jones S, 2007). No obstante, Reinstein *et al*. (2011) documentan el tratamiento exitoso de la distiquiasis en un gato mediante la electrocauterización transconjuntival.

Figura 2
Equipo para técnica EPI®.

La **fotodepilación** o depilación por medio del láser, utilizada desde hace décadas en medicina humana, se ha introducido más recientemente en medicina veterinaria. Mediante un haz de luz monocromática, se transporta una gran cantidad de energía a través de la melanina del pelo, hasta su raíz. Cuando el haz de luz, con una determinada longitud de onda e intensidad, interacciona con el vello, la energía lumínica aplicada es absorbida por la melanina, transformándose en calor. Esto es lo que se conoce como fototermolisis selectiva, que provoca la destrucción del bulbo piloso sin afectar a los tejidos adyacentes. Entre las ventajas de esta técnica se encuentran la rapidez de actuación, realmente notable en las técnicas con escaneo (aplicadas generalmente en medicina humana) y menor en las técnicas de aplicación pelo a pelo (más utilizadas en veterinaria), su carácter indoloro y la larga duración de la depilación así obtenida. Como inconvenientes, se pueden citar el elevado coste de la técnica, la necesidad de varias sesiones para que resulte efectiva, la irradiación de toda la piel circundante en cada una de las sesiones, que puede dar lugar a efectos indeseados por la afectación de los melanocitos, y la considerable variabilidad de su eficacia en función de la pigmentación de los cilios del paciente, pues, al actuar el láser únicamente sobre las zonas ricas en melanina (oscuras), no resulta eficaz para el pelo blanco o muy claro (Campbell, 1990; Liew, 2002).

En el caso de la distiquiasis, el inconveniente más importante radica en el riesgo de daño ocular que podría generar su aplicación, ya que la retina tiene una gran concentración de melanocitos (Zaragoza, J.R, 1999; Parver, 2006; Spiess, 2012).

Los autores plantean una propuesta alternativa para el tratamiento de este proceso patológico mediante la **técnica EPI®** (electrólisis percutánea intratisular) aplicada a cada folículo piloso mal orientado.

Esta técnica, desarrollada en animales de experimentación y ampliamente aplicada, con éxito, en pacientes humanos para el tratamiento de lesiones musculoesqueléticas, aún no es muy conocida en veterinaria y, por lo tanto, no se está utilizando de manera rutinaria. Sin embargo, el equipo al que pertenecen los autores lleva tiempo trabajando en la adaptación de la técnica EPI® para su uso en la clíni-

ca veterinaria, considerando que es una técnica mínimamente invasiva con un gran futuro (Sánchez *et al*., 2011; 2015 Alonso *et al*., 2016).

La técnica EPI® produce la ablación electroquímica no térmica, por flujo catódico, de una determinada estructura orgánica en la que se ha insertado el electrodo cátodo. La EPI® produce una disociación del agua, las sales y los aminoácidos de la matriz extracelular, creando nuevas moléculas a través de una inestabilidad iónica. La reacción orgánica que se produce en la aguja catódica causa una inflamación aguda muy localizada, única y exclusivamente en el punto que se está tratando, lo que permite la activación inmediata de una respuesta inflamatoria breve, facilitando la fagocitosis de la zona (Sánchez-Ibáñez *et al*., 2005; 2008; 2010; 2013).

La depilación mediante la técnica EPI® consiste en la aplicación, auxiliados por la visión magnificada de un microscopio quirúrgico, de corriente continua a través de una aguja de acupuntura insertada en cada folículo piloso, que actúa como electrodo negativo (cátodo) y que va a provocar una reacción electroquímica en el folículo, facilitando su degeneración, su posterior reabsorción y, por lo tanto, su desaparición (figura **2**). Además, presenta la ventaja con respecto a otras técnicas que se utilizan actualmente del bajo coste del tratamiento (Alonso *et al*., 2015).

Estudio clínico

Se realiza un estudio con el objetivo de aumentar la eficacia del arsenal terapéutico actualmente empleado para el tratamiento de las distiquiasis y los cilios ectópicos en la clínica veterinaria, utilizando la técnica EPI®. Como segundo objetivo, se busca ajustar los protocolos y dosis de la dicha técnica para llegar a un tratamiento eficaz del citado proceso patológico.

Los casos estudiados corresponden a dos pacientes caninos con distiquiasis palpebral bilateral: el caso 1 es de raza shih-tzu, hembra, de 5 años de edad; el caso 2, un samoyedo de 2 años, macho. Ambos presentaban prurito ocular, blefaroespasmo notorio y epífora bilateral, así como úlcera corneal recurrente.

El caso 2, durante el año anterior y tras confirmar mediante depilación ordinaria que el origen del marcado blefarospasmo radicaba en la distiquiasis, había sido sometido a un tratamiento de electrodepilación con bisturí eléctrico monopolar mediado por pinza (10 meses antes) y, posteriormente, a electrodepilación ordinaria (4 meses antes), sin que ninguno de los procedimientos diera resultados positivos.

En ambos casos se realizó una exploración con biomicroscopio (figura **3**), observando los cilios a lo largo de toda la extensión de los bordes palpebrales superiores e inferiores de ambos ojos, que habían causado úlceras corneales de diversa consideración. En el caso 1 el proceso de distiquiasis, dado el número de cilios ectópicos, el grosor de los mismos y la magnitud de las lesiones corneales y conjuntivales, fue calificado de grave, mientras que en el caso 2, que tenía un muy elevado número de pelos y apenas era capaz de abrir los ojos, de muy grave (figura **4**).

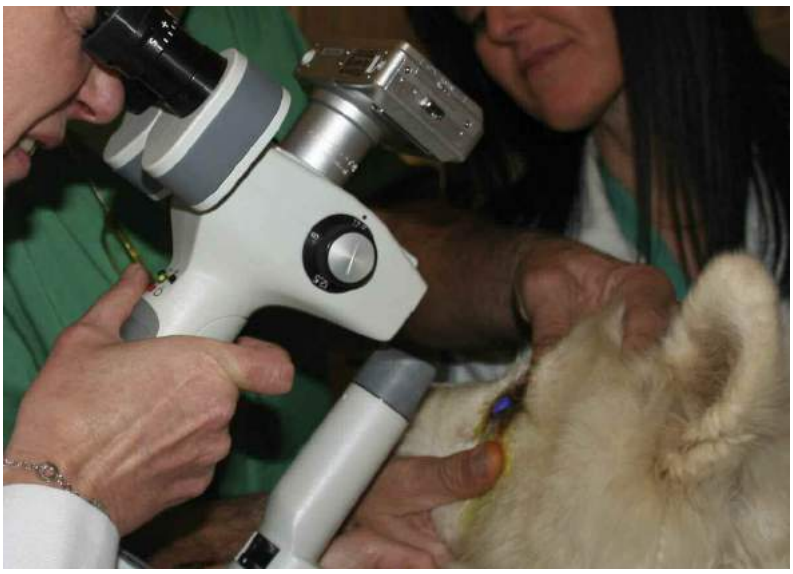


Figura 3
Diagnóstico de distiquisis mediante biomicroscopía.

Figura 4: Aspecto de los ojos del perro del samoyedo, evaluado como muy grave, antes del inicio del tratamiento con EPI®.

Una vez iniciado el tratamiento de las úlceras corneales, se comenzó con las sesiones de EPI®, que se realizaron a intervalos aproximados de 30-60 días, en función de la recurrencia de los signos y las lesiones iniciales y de la gravedad de los mismos.

Para llevar a cabo el tratamiento de EPI®, los pacientes, en todas las ocasiones, fueron anestesiados mediante un protocolo convencional de anestesia general inhalatoria equilibrada, para evitar las molestias que ocasionan las punciones y las descargas en los párpados, así como los movimientos consecuentes que estas darían lugar, dificultando o imposibilitando su aplicación, o bien predisponiendo a la aparición de lesiones iatrogénicas en los ojos.

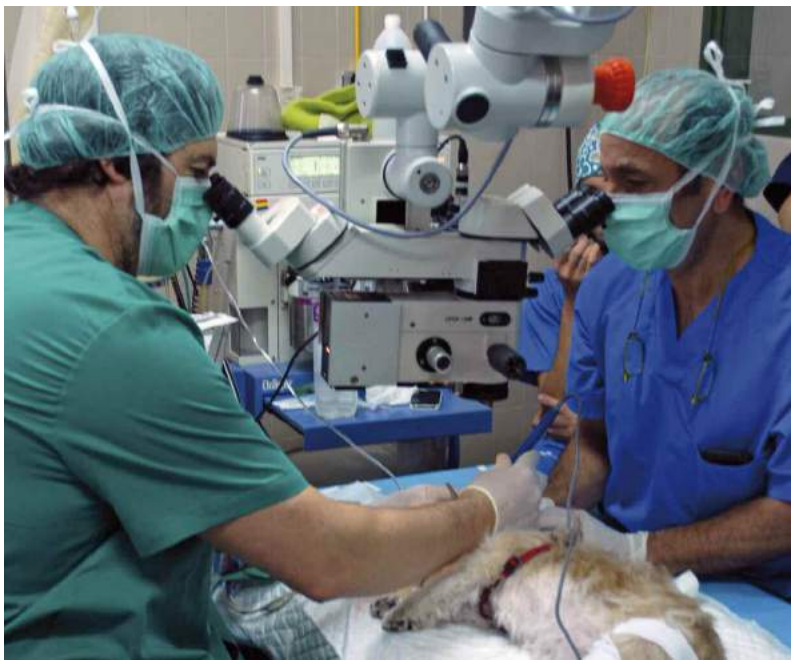
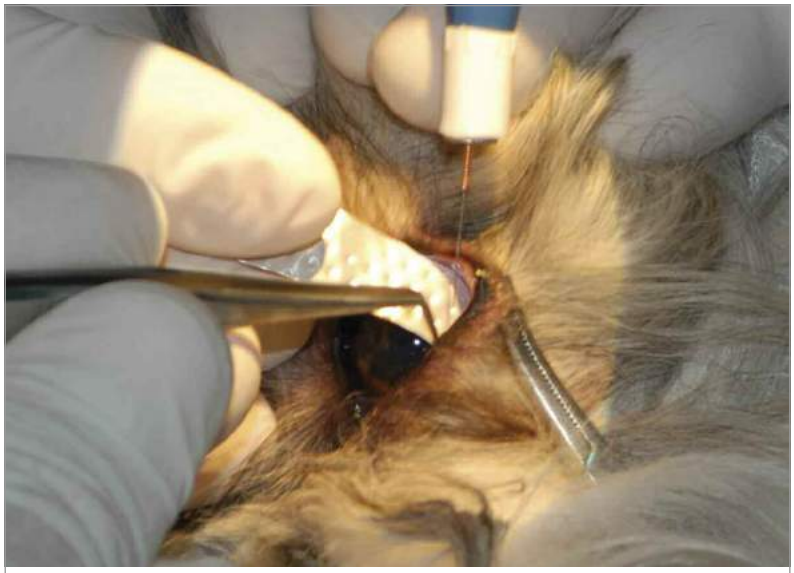
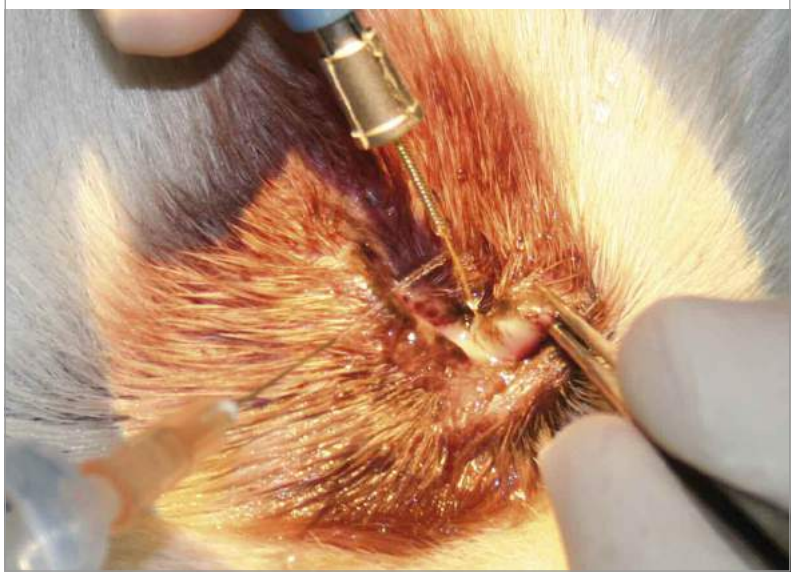


Figura 5
Durante las sesiones se empleó un microscopio quirúrgico.





Figuras 6 y 7: Aplicación de EPI®.
En la imagen inferior se observa la irrigación con suero salino fisiológico.

El **protocolo anestésico** utilizado en ambos casos fue el siguiente:

- Sedación: dexmedetomidina a 2,5 µg/kg y midazolam a 0,3 mg/kg, ambas por vía intramuscular (IM).
- Analgesia: butorfanol IM a 0,3 mg/kg.
- Inducción: propofol 4 mg/kg vía intravenosa (IV).
- Mantenimiento: anestesia inhalatoria con isofluorano mediante un circuito semicerrado circular con absorción de anhídrido carbónico en el caso 2, y mediante un circuito T de Ayre en el caso 1, mantenidos ambos pacientes siempre en respiración espontánea.

Para magnificar la visión y asegurar la correcta punción de los folículos ectópicos, se utilizó el microscopio quirúrgico modelo Wild Microscope®, con un objetivo Leica M690 y un ocular Leica 10445170 10X/21B, (figura **5**) con capacidad de conexión a cámara fotográfica, a monitor de visión y a grabadora informática.

La preparación del campo consistió en el lavado palpebral y ocular con suero salino fisiológico (SSF) estéril.

En ambos casos, se utilizó para el tratamiento un electroestimulador de cuatro salidas EPI® que constituye una fuente de corriente continua monopolar.

Las sesiones de técnica EPI® se realizaron colocando, en el polo cátodo del equipo, agujas de acupuntura estériles de acero inoxidable, que fueron variando a medida que aparecieron dificultades hasta dar con la más adecuada. En la primera ocasión, se utilizaron agujas de 0,18x13 mm y de 0,25x25 mm; en las dos siguientes de 0,25x25 mm; a partir de la tercera sesión, de acero recubiertas de oro de 0,40x15 mm.

El electrodo ánodo no modificado se ubicó en la región inguinal del paciente, envuelto en papel secante empapado con SSF, con el fin de aumentar la conductividad.

Para llevar a cabo la depilación, se insertó la aguja en el folículo piloso y se realizaron descargas en cada uno de ellos (figuras **6** y **7**). En las tres primeras ocasiones, se utilizó una dosis de 8 mA durante 2 segundos (a una media de 21,36 V y 0,339 J) y, a partir de la cuarta, dado que la extracción de los cilios con descargas de 2 segundos no siempre resultaba satisfactoria, de 8 mA durante 3 segundos (a una media de 14,04 V y 0,302 J). Durante las descargas, se observó la salida de secreción y burbujas, procediendo posteriormente a la extracción de los pelos mediante una pinza de mano. En el caso de que hubiera resistencia a la extracción manual o se rompiese el pelo como consecuencia de su desarrollo o grosor, se repetía una o dos veces más la descarga en el mismo folículo hasta que la extracción no ofreció dificultad alguna. Durante los impactos, se aplicaba, mediante goteo, SSF sobre el punto de entrada la aguja para facilitar la conducción eléctrica y, por lo tanto, activar la reacción química de la electrolisis.

Una vez finalizada la sesión, cuando se hubieron extraído todos los pelos visibles, se hizo un nuevo lavado ocular con SSF y se administraron dos gotas de colirio de diclofenaco sódico (Voltarén®) y pomada con gentamicina sulfato, metionina y retinol (Óculos epitelizante®) en cada ojo, cada 12 horas, durante los dos días posteriores a la intervención.

En las primeras ocasiones, para el postoperatorio inmediato, se colocó un collar isabelino como barrera física para evitar el rascado; no obstante, dado que los animales no mostraron apenas molestias y en ningún caso intentaron rascarse después de la intervención, en las siguientes sesiones no se aplicó dicha medida preventiva.

A la paciente del caso 1 se le realizaron tres sesiones de EPI® y en el caso 2, cinco sesiones.

Resultados y discusión

Uno de los principales problemas de la distiquiasis palpebral es el crecimiento de los cilios dirigidos hacia la córnea, ocasionando prurito ocular y úlcera corneal que, generalmente, se agrava con la automutilación por parte del animal al rascarse.

Según el conocimiento de los autores, no existe un tratamiento que, a la vez, sea eficaz y poco agresivo con los párpados y con otras estructuras del ojo y sus anejos.

La utilización de la técnica EPI® sobre los folículos pilosos ectópicos de los dos perros ha resultado muy satisfactoria, tanto en cuanto a la disminución de los cilios posteriormente a cada sesión, como en cuanto a los escasos efectos secundarios que se hallaron.

En ambos casos, la mejoría clínica fue muy ostensible ya a las pocas horas de cada tratamiento, pudiendo comprobarse que desaparece la fotofobia y el blefarospasmo.

• Caso 1

En la primera sesión, se comenzó con una única descarga eléctrica por folículo; sin embargo, se observó que los cilios más fuertes no se desprendían con facilidad o se quebraban al tirar de ellos con la pinza de mano. Por ello, se optó por aplicar dos descargas de 8 mA y 2 segundos por folículo, lo que resolvió el problema en la mayor parte de los pelos sin causar daños adicionales visibles en el canto palpebral.

Al utilizar para el electrodo cátodo las agujas de acupuntura de 0,18x13 mm, se encontró que se doblaban con facilidad y que no trasmitían adecuadamente la corriente eléctrica, por lo que se sustituyeron por otras de calibre 0,25x25 mm, que permitieron terminar la sesión (**tabla I**).

Tras 30 días, se realizó una revisión mediante biomicroscopía, hallando una reducción drástica del número de cilios sobre los cuatro párpados, cilios que además eran mucho más finos y aislados. El procedimiento de aplicación de la técnica EPI®, en esta segunda sesión, fue el mismo que para la primera.

Tabla I

Datos del caso 1 (shih-tzu)

	Día 0	Día 30	Día 60
Clínica	Prurito Blefarospasmo Epífora Fotofobia	Menos: Blefarospasmo Epífora Fotofobia	Apenas: Blefarospasmo Epífora Fotofobia
Test Schirmer	OD 20 OI 23	OD 23 OI 20	OD 26 OI 19
Exudado	Mucoso	Sin exudado	Sin exudado
Pelos	OD S: 3 OD I: 5 OI S: 5 OI I: 5 Gruesos	OD S: 2 OD I: 3 OI S: 3 OI I: 3 Más finos y aislados	OD S: 0 OD I: 2 OI S: 0 OI I: 2 Poco desarrollados
Hiperemia conjuntival	Palpebral + Bulbar +	Menos: Palpebral + Bulbar +	Menos aún: Palpebral + Bulbar +
Córnea	OD: queratitis; úlcera OI: NO	OD: NO OI: queratitis	OD: NO OI: NO
Borde palpebral	Normal	Normal	Normal
Valores EPI®	8 mA, 2 segundos	8 mA, 2 segundos	8 mA, 2 segundos
Aguja	0,25x25 mm	0,25x25 mm	0,25x25 mm
Descargas/pelo	2	2	2
Resultado inmediato (0-48 h)	Sin clínica	Sin clínica	Sin clínica

OI: Ojo izquierdo; OD: ojo derecho; S: párpado superior; I: párpado inferior.

Transcurridos dos meses, se realizó de nuevo una exploración ocular en la que, si bien aún se constató la presencia de algunos pelos ectópicos, resultaba obvia su disminución en cantidad y desarrollo. Se realizó un tercer tratamiento idéntico a los anteriores.

La presencia de estos cilios puede ser atribuida a que, en alguno de los folículos, la técnica EPI® no hubiera dado el resultado esperado con una o dos sesiones, o bien a que, en el momento del tratamiento, dichos cilios no fueran aún visibles.

En este primer caso, el resultado general fue sumamente satisfactorio, dada la marcada mejoría clínica que presentaba el paciente desde inmediatamente después de la primera intervención y en los días siguientes, ya que era capaz de abrir los ojos con normalidad, y no manifestaba fotofobia, blefaroespasmo, conjuntivitis ni cualquier otro efecto secundario. Sin embargo, debido a la imposibilidad de los clientes de continuar, el paciente no ha vuelto a revisión y no se ha podido completar el seguimiento del caso.

• Caso 2

Al perro de raza samoyedo del caso 2 se le habían realizado varios tratamientos médicos sintomáticos y dos quirúrgicos (uno mediante bisturí eléctrico monopolar y otro con electrodepilación convencional), ambos con resultados no satisfactorios.

Se le aplicaron cinco sesiones de EPI ®, consistentes en descargas de 8 mA durante 3 segundos, sin que en ninguna de ellas se presentara ningún tipo de problema, salvo que, dado que desde la primera

ocasión se constató que las agujas de 0,25x25 mm se doblaban con cierta facilidad, estas fueron sustituidas por otras de acero recubiertas de oro de 0,40x15 mm, cuya utilidad fue sumamente satisfactoria en todas las sesiones.

Tras las dos primeras sesiones, el número de pelos se redujo sensiblemente, pero, dado su ingente cantidad y su gran desarrollo, no fue hasta la tercera sesión cuando se constató una reducción drástica del número de pelos y de su grosor, evidenciándose una franca mejoría clínica (**tabla II**).

Durante la cuarta sesión, el tejido del borde palpebral, quizá por la proximidad temporal entre las anteriores sesiones, ofrecía una resistencia ligeramente mayor de lo habitual, lo que dificultó, en pequeña medida, la introducción de la aguja de acupuntura en el borde palpebral; aun así, el tratamiento se llevó a cabo sin mayores complicaciones.

En la revisión previa a la quinta sesión, la mejoría clínica fue ostensible en lo relativo a la conjuntivitis, la queratitis, la fotofobia y el blefarospasmo, que eran casi inapreciables, y los escasos pelos presentes eran mucho más finos. Durante la intervención, el tejido del borde palpebral no estaba indurado en absoluto ni ofrecía resistencia adicional a la penetración de la aguja y, después de cada impacto, los pelos se extrajeron con facilidad. Una vez desaparecidos los efectos de la anestesia, también desapareció el blefaroespasmo.

Dos meses después, en la última revisión oftalmológica del paciente, este apenas manifestaba sintomatología clínica, presentándose con ambos ojos completamente abiertos, sin epífora ni exudado, y sin conjuntivitis bulbar ni lesiones corneales, observándose únicamente dos pelos en un ojo, uno en cada párpado, y tres pelos en el otro ojo, dos en un párpado y uno en el otro, todos ellos muy finos y pequeños. Por esta razón, se decidió no realizar la intervención y proceder a una nueva valoración clínica más adelante (figura **8**).

A los 15 meses de la quita sesión, mediante la exploración con biomicroscopio, no se evidencia crecimiento de pelos ectópicos en los bordes palpebrales.

Conclusiones

El trabajo expuesto arroja las siguientes conclusiones:

❶ Para abordar con ciertas garantías de éxito el tratamiento de la distiquiasis palpebral y de sus consecuencias, haciendo uso de la técnica EPI®, es imprescindible un **diagnóstico oftalmológico** lo más certero y específico posible.

❷ El manejo clínico de la técnica EPI® a nivel palpebral es delicado, dado que es necesaria la punción exacta de los folículos y la aplicación de descargas sumamente precisas en los mismos, sin afectar al ojo ni a las estructuras altamente sensibles que lo rodean, por lo que se hace imprescindible un buen protocolo de anestesia general equilibrada.

❸ Los detalles aportados para la aplicación de la técnica EPI® en los párpados (microscopía quirúrgica, humectación del cilindro ánodo, irrigación de las agujas con SSF durante las descargas, valores de la longitud y grosor de las mismas, dosis y tiempos de aplicación, etc.) se han mostrado altamente eficaces a la hora de tratar los cilios ectópicos en oftalmología veterinaria.

Tabla II

Datos del caso 2 (samoyedo)

	Día 0	Día 30	Día 60	Día 90	Día 150	Día 210
Clínica	Prurito, blefarospasmo, epífora, fotofobia	Prurito, blefarospasmo, epífora, fotofobia	Clara mejoría, pero: prurito, blefarospasmo epífora, fotofobia	Clara mejoría menos: prurito, blefarospasmo epífora, fotofobia	Mejoría ostensible: blefarospasmo. Casi sin síntomas	Sín clínica
Test Schirmer	OD 23 OI 20	OD 23 OI 20	OD 21 OI 24	OD 25 OI 23	OD 18 OI 20	OD 18 OI 23
Exudado	Sin exudado	Sin exudado	Sin exudado	Sin exudado	Sin exudado	Sin exudado
Pelos	En ambos ojos y ambos párpados. Abundantes, gruesos y duros	Menos cantidad OD S: 6 OD I: 3 OI S: 8 OI I: 9	Menos gruesos OD S: 5 OD I: 2 OI S: 7 OI I: 8	Menos gruesos OD S: 4 OD I: 2 OI S: 6 OI I: 7	Muy finos OD S: 2 OD I: 2 OI S: 5 OI I: 3	Muy finos OD S: 1 OD I: 1 OI S: 2 OI I: 1
Hiperemia conjuntival	En ambos ojos Palpebral ++ Bulbar ++	En ambos ojos: Palpebral + Bulbar +	En ambos ojos: Palpebral ++ Bulbar ++	En ambos ojos Palpebral +	En ambos ojos Palpebral +	No
Córnea	Normal	Normal	Normal	Normal	Normal	Normal
Borde palpebral	Normal	Normal	Normal	Normal	Normal	Normal
Valores EPI®	8 mA, 3 segundos	8 mA, 3 segundos	8 mA, 3 segundos	8 mA, 3 segundos	8 mA, 3 segundos	-
Aguja	0,40x15 mm	0,40x15 mm	0,40x15 mm	0,40x15 mm	0,40x15 mm	-
Descargas/pelo	2-3	2-3	2-3	2-3	2-3	-
Resultado inmediato (0-48 h)	Sin clínica	Sin clínica	Sin clínica	Sin clínica	Sin clínica	-

OI: Ojo izquierdo; OD: ojo derecho; S: párpado superior; I: párpado inferior.

❹ La técnica EPI® es un procedimiento mínimamente invasivo que manifiesta una ausencia prácticamente absoluta de molestias y complicaciones secundarias para el paciente, lo que facilita enormemente su manejo postoperatorio; estos hechos sugieren una gran proyección de futuro para esta técnica en la clínica oftalmológica veterinaria.

❺ Dados los alentadores resultados de estas primeras experiencias con la aplicación de la técnica EPI® para la eliminación de folículos pilosos palpebrales y la ausencia de efectos secundarios de ningún tipo a corto, medio o largo plazo, comparada con otras técnicas de depilación existentes en el mercado y en la bibliografía revisada, consideramos que el procedimiento descrito podría hacerse extensivo a cualquier proceso que requiera eliminación definitiva del pelo para su solución.

Figura 8: Aspecto de los ojos de paciente del caso 2 tras la finalización del tratamiento.

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Clinical results after ultrasound-guided intratissue percutaneous electrolysis (EPI®) and eccentric exercise in the treatment of patellar tendinopathy

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Abstract
Purpose To investigate the outcome of ultrasound (US)-guided intratissue percutaneous electrolysis (EPI®) and eccentric exercise in the treatment of patellar tendinopathy during a long-term follow-up.
Methods Forty patients with patellar tendinopathy were prospectively evaluated over a 10-year follow-up period. Pain and function were evaluated before treatment, at 3 months and at 2, 5 and 10 years using the Victorian Institute of Sport Assessment–Patella (VISA-P) score, the Tegner score and Blazina's classification. According to VISA-P score at baseline, patients were also dichotomized into Group 1 (<50 points) and Group 2 (≥50 points). There were 21 patients in Group 1 and 19 in Group 2. Patient satisfaction was measured according to the Roles and Maudsley score.
Results The VISA-P score improved globally by 41.2 points ($p < 0.01$) after a mean 4.1 procedures. In Group 1, VISA-P score improved from 33.1 ± 13 to 78.9 ± 14.4 at 3-month and to 88.8 ± 10.1 at 10-year follow-up ($p < 0.001$). In Group 2, VISA-P score improved from 69.3 ± 10.5 to 84.9 ± 9 at 3-month and to 96.0 ± 4.3 at 10-year follow-up ($p < 0.001$). After 10 years, 91.2 % of the patients had a VISA-P score >80 points. The same level (80 % of patients) or the Tegner score at no more than one level lower (20 % of patients) was restored, and 97.5 % of the patients were satisfied with the procedure.
Conclusion Treatment with the US-guided EPI® technique and eccentric exercises in patellar tendinopathy resulted in a great improvement in knee function and a rapid return to the previous level of activity after few sessions. The procedure has proved to be safe with no recurrences on a long-term basis.
Level of evidence Therapeutic study, Level IV.

Keywords Intratissue percutaneous electrolysis · EPI · Eccentric exercises

Introduction

Patellar tendinopathy or jumper's knee is a frequent condition that most commonly affects the tendon's origin on the inferior pole of the patella [2, 4, 10]. Once considered an inflammatory condition, it is currently considered a degenerative process due to the presence of myxoid degeneration, the disruption of the collagen fibres and signs of hypoxia in tenocytes and resident macrophages [6, 17].

The overall prevalence of patellar tendinopathy is around 14 % in the sports population [3, 16], but may be as high as 40 % in highly demanding athletes [8]. The tendon's overuse in sports that involve running, jumping or rapid change in direction is considered the main risk factor for developing the said condition [16].

Current treatment options include eccentric training [15, 18, 29], open or arthroscopic surgery, extracorporeal shockwave therapy [25], ultrasound (US)-guided sclerosis [12], non-steroidal anti-inflammatory drugs, platelet-rich

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plasma injection [30] and aprotinin [1]. These studies have also suggested that, in general, patients with a worse functional status before treatment obtain inferior final outcomes. However, due to the limited evidence-based therapies, there are still several controversies regarding the real efficacy of these treatment modalities [1].

Intratissue percutaneous electrolysis (EPI®) treatment is a pioneering US-guided technique developed by one of the authors. It leads to a non-thermal electrochemical ablation through a cathodic flow directly at the clinical focus of degeneration. EPI® causes an organic reaction leading to a highly localized inflammation, exclusively at the region of treatment that conduces to a rapid regeneration of the injured tendon [26].

The present study provides the first analysis of the results of EPI® in the treatment of patellar tendinopathy at 10 years follow-up. This study could be clinically relevant given the lack of effective techniques in the treatment of patellar tendinopathy.

The aim of this study was to investigate the outcome of the US-guided EPI® technique in terms of pain, function and the return to the previous level of activity in patients with patellar tendinopathy. The mean follow-up of 10 years provides information on safety and the rate of recurrence. The main hypothesis was that the US-guided EPI® technique would quickly improve the outcome in patients with patellar tendinopathy and that this improvement would be maintained over a long period of time. The second hypothesis was that good outcomes would be obtained regardless of the initial degree of functional impairment. It was also hypothesized that the patients would be restored to their pre-injury activity level.

Materials and methods

From January 2002 to October 2002, 41 patients with patellar tendinopathy were included in the investigation. Demographic data and patient information (age, gender, affected and dominant side, kind of sport or activity level) were recorded.

The inclusion criteria were a history of patellar tendon pain, tenderness upon palpation, functional limitation directly related to the studied tendon and sonographic confirmation of tendon degeneration. A tendon injury located at the inferior pole of the patella was considered a requisite. Other inclusion criteria were more than 4 weeks of symptoms and an age of <60 years old. Patients were classified according to Blazina's scale [22]. Exclusion criteria were pain at the proximal pole of the patella (frequently included in jumper's knee), chronic articular disease, a concomitant knee pathology, contraindications to the EPI® technique and the concomitant administration of certain drugs (at least 2 weeks before receiving treatment). The inclusion and exclusion criteria are summarized in Table 1.

Ultrasound examination

All the patients went through an exhaustive US examination of the tendon and adjacent structures using a high-resolution greyscale US (Fig. 1) with Doppler power and linear multi-frequency probe (6–15 MHz). The injured and the contralateral knees were studied in all patient. The US efficacy for the proper diagnosis of patellar tendinopathy was previously reported [11, 36, 37].

Intratissue percutaneous electrolysis (EPI®) protocol

The EPI® technique was applied using a specifically developed medically certified (Directive 93/42/EEC) device (EPI Advanced Medicine, Barcelona, Spain), which produces modulated galvanic electricity through the negative electrode cathodic flow. This is applied using a modified electrosurgical scalpel that uses acupuncture needles (0.3 mm in diameter) with different lengths. The intensity can be adjusted by changing the duration or the milliamps of the device. Conversely, the polarity of the machine is fixed (i.e. only the cathodic flow is usable). During the procedure, performed by the same experienced operator, the patients are supine so as to minimize any potential vagal reaction.

Isopropyl alcohol was used to prepare the skin despite the bacteriostatic action of the EPI® system. Polyvidone iodine was avoided to prevent a tattoo effect of the

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
<60 years old	Chronic articular disease
History of patellar tendon pain >4 weeks	Concomitant knee pathology (e.g. cruciate ligament injury of meniscal tear)
Tenderness to palpation	Contraindications of EPI® technique (i.e. pregnancy, knee prosthesis, osteosynthesis, cardiac disease, malign tumour or coagulopathy)
Functional limitation directly related to the tendon injury	Concomitant administration of drug (i.e. fluoroquinolones, anticoagulants, corticosteroids or non-steroidal anti-inflammatory
Sonographic confirmation of tendon degeneration	
Injury located at the inferior pole of the patella	
Blazina's classification ≥grade I	

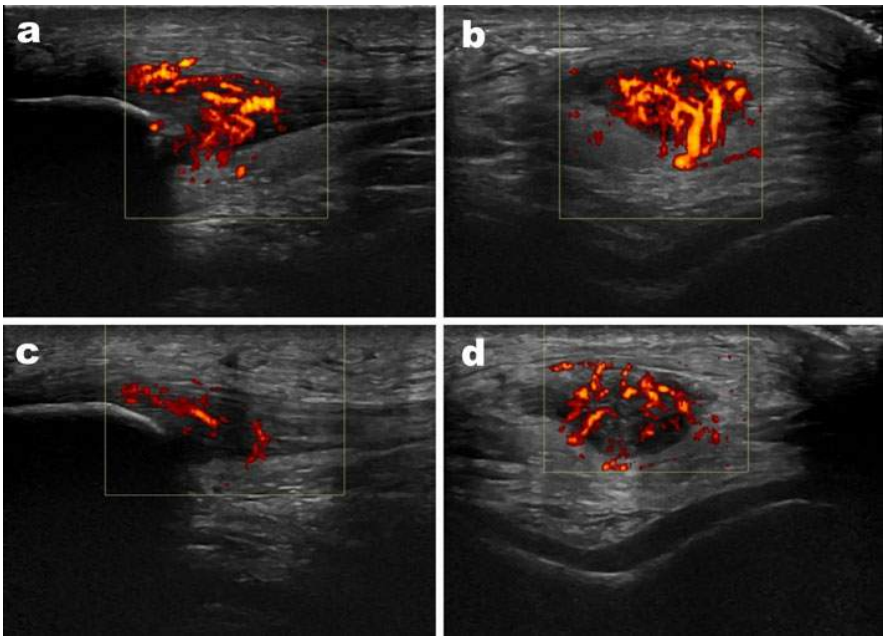

Fig. 1 High-resolution colour Doppler ultrasound of patellar tendinopathy. **a** Longitudinal and **b** transversal views of the involved tendon showing a high degree of neovascularization before the EPI® treatment. The same patient 3 months after initiation of the EPI® procedures had a remarkable decrease in the vascularization of the patellar tendon clearly seen in these longitudinal (**c**) and transversal (**d**) views

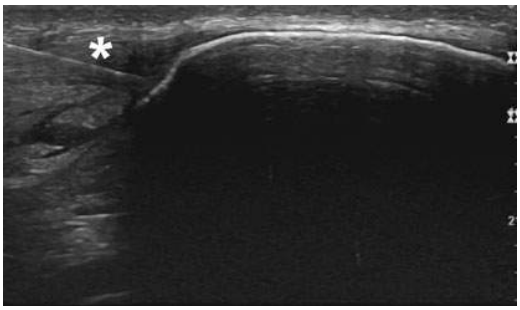

Fig. 2 Intratissue percutaneous electrolysis (EPI®) procedure. The 0.3-mm needle (*Asterisks*) is being guided by high-resolution greyscale ultrasound to puncture the injured region of the tendon

cathodic flow. Finally, three US-guided precise punctures at 3 mA (Fig. 2) were performed until a complete debridement of the treated area was obtained. The debridement was assessed with the sonographic images. After the first EPI® treatment, the patients underwent consecutive sessions of EPI® every 2 weeks and 2 weekly sessions of an eccentric exercise training using the resistance isoinertial leg-press machine (YoYo™ Technology AB, Stockholm, Sweden). Eccentric exercises were performed in three sets of ten repetitions twice a week in order to obtain maturation of collagen fibres [24, 31]. Each repetition was performed with the concentric phase with both extremities, whereas the eccentric phase was only performed with the affected limb at a maximum of 60° of knee flexion.

Patients received US-guided EPI® treatment up to a maximum of ten sessions. The treatment finished either when the patients were symptom free or if there was no improvement in terms of pain or function after those ten sessions.

Treatment evaluation

All the patients were evaluated before treatment and prospectively when their treatments were finished (at the third month), at 2-year, at 5-year and at 10-year follow-up.

The primary outcome measure was knee function using the Victorian Institute of Sport Assessment–Patella (VISA-P) score, a specific validated questionnaire to quantify pain and knee function and ability to play sport in patients with patellar tendinopathy [9, 34]. The VISA-P score ranged from a maximum of 100 in asymptomatic patients to the theoretical minimum of 0. The authors of the score suggested that a score between 80 and 100 points might be considered as the optimal outcome category. Functional evaluation was further assessed with Blazina's classification [22]. This classification categorizes the symptomatic patients as in *phase I* (pain only after activity), *phase II* (discomfort during activity), *phase III* (pain during activity that interferes with participation) and *phase IV* (complete tendon disruption). The Tegner score was also used to assess the influence of the treatment in terms of restoring the previous sports activity level. All the written questionnaires were personally filled out by all patient before treatment, at the end of the treatment (at 3-month) and at the 2-year follow-up. The questionnaires corresponding to the 5- and 10-year follow-up evaluations were all filled out through a telephone interview. Patient satisfaction was

measured according to the Roles and Maudsley score [23]. In this score, patients are classified as *Excellent* (no pain, full movement and full activity), *Good* (occasional discomfort, full movement and full activity), *Fair* (some discomfort after prolonged activity) or *Poor* (pain limiting activities).

All those patients that scored <50 points with the VISA-P questionnaire at baseline were denominated Group 1, whereas the remaining patients scoring equal to or higher than 50 points were denominated Group 2. This classification allows to display the results in different degrees of injury of the patellar tendon: more (VISA-P < 50 points) or less affected (VISA-P > 50 points).

The Clinical Research Ethics Committee of ICATME-Institut Universitari Dexeus, University of Barcelona, approved the study (09/06/0049). All the patients signed informed consent to participate in the study as well as for the evaluation and publication of their results.

Statistical analysis

Categorical variables are presented as number of cases and percentages. Continuous variables are presented as mean ± SD (range). The relationships between categorical variables were described using contingency tables, and inference was studied using the chi-square test or Fisher's exact test. The relation between the VISA-P score and dichotomous variables was assessed using the Mann–Whitney test, showing the median value. Analysis of variance (ANOVA) was used to compare the evolution between groups. Statistical significance was set at 0.05 two-sided. Statistical analysis was performed using SPSS 19 (SPSS Inc., Chicago, IL, USA).

Results

One patient was lost during the first 3 months of follow-up. The remaining 40 patients were available at the 3-month and at the 2-year evaluations. At the 5-year evaluation, another three patients were lost (37 patients available, 90.2 % of the cases) and another three patients at the 10-year assessment (34 patients available, 82.9 % of the cases).

Patient description

Twenty-one patients (52.5 %) were included in Group 1 and the remaining 19 (47.5 %) in Group 2. Both groups were comparable in terms of age, gender, side and functional scores at baseline (Table 2). Sports involvement is summarized in Table 3. No relation (n.s.) between the injured tendon and the dominant extremity, the type of sport, the age of the patient and gender, and the VISA-P values obtained after the treatments was observed.

The mean duration of symptoms prior to the treatment was 69.4 ± 65.6 weeks (range 4–288 weeks). The athletes were off sports activities due to their patellar tendinopathy for a mean time of 40.6 ± 50.9 weeks (range 0–192 weeks). Treatment duration averaged 7.5 ± 2.6 weeks (range 1–10 weeks), and the patients required a mean of 4.1 ± 2.6 EPI® procedures (range 1–10). According to Blazina's classification, one patient (2.5 %) was of stage I at baseline, seven patients (17.5 %) stage II and the remaining 32 patients (80 %) stage III. At the 3-month evaluation, once all the treatments were finished, five patients (12.5 %) were classified as of stage I and six patients (15 %) stage II. All the remaining 30 cases (72.5 %) were considered completely cured (less than Blazina's stage I). At the 2-year follow-up evaluation, 31 cases (77.5 %) were asymptomatic (less than Blazina's stage I) and nine (22.5 %) were in stage I. Analysis

Table 2 Patient characteristics at baseline

	Group 1 $n = 21$ (52.5 %)	Group 2 $n = 19$ (47.5 %)	p value
Age (years)			
Mean ± SD	26.0 ± 8.49	25.7 ± 8.12	n.s.
Gender % (n)			
Male	81.0 (17)	94.7 (18)	n.s.
Female	19.0 (4)	5.3 (1)	
Dominant extremity % (n)			
Right	81.0 (17)	89.5 (17)	n.s.
Left	19.0 (4)	10.5 (2)	
Injured knee % (n)			
Right	38.1 (8)	15.8 (3)	n.s.
Left	47.6 (10)	68.4 (13)	
Bilateral	14.3 (3)	15.8 (3)	
Baseline VISA-P			
Mean ± SD	32.5 ± 12	69.5 ± 10.05	<0.001

Values expressed as mean ± SD or frequencies and percentages

Table 3 Patient sports involvement at baseline

	Series $n = 40$
Blazina's stage	
Median (range)	3 (2–3)
Sports type % (n)	
Soccer	60 (24)
Other	40 (16)
Sports level % (n)	
Professional (first division)	12.5 (5)
Semi-professional (second division or similar)	67.5 (27)
Recreational	20 (8)

Values expressed as mean ± SD or frequencies and percentages

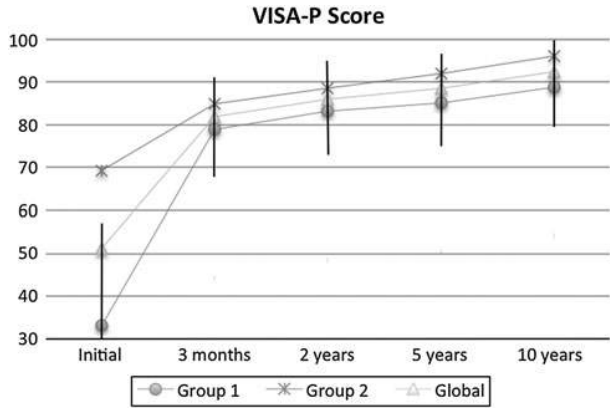

Fig. 3 Linear diagram of the mean Victorian Institute of Sport Assessment–Patella (VISA-P) scores for Group 1, Group 2 and all the patients (*Global*) at baseline (*Initial*), at 3 months and at 2, 5 and 10 years

of the patients using the Blazina's classification remained unchanged throughout the remaining follow-up evaluations of the period studied (n.s.).

Clinical outcomes over time

The VISA-P (Fig. 3) and Tegner scores before treatment, at 3 months and at 2, 5 and 10 years of follow-up are summarized in Table 4. Group 1 improved by 45.8 points ($p < 0.001$) at 3 months to obtain a mean VISA-P score of 78.9 ± 14.4. In Group 2, the mean improvement in VISA-P score at 3 months was 15.6 points at 3 months ($p < 0.001$). The Tegner level did not drop over the 10 years of the study period, and no differences between the intermediate evaluations (n.s.) were observed either.

According to the Roles and Maudsley score, patient satisfaction at 3 months of follow-up was considered *Excellent* in 32 cases (80 %), *Good* in seven cases (17.5 %) and *Fair* in one case (2.5 %). These values persisted without significant differences throughout the period studied. No recurrences, adverse episodes or any additional modality of treatments were reported after the 10 years of follow-up.

At the 3-month follow-up evaluation, 32 (80 %) patients restored their previous activity level according to Tegner scale (n.s.). In eight patients (20 %), there was a decrease in only one single level on the same scale. These values were maintained over the remaining period studied (n.s.).

Discussion

Treatment with EPI® in combination with eccentric exercises has been shown to effectively improve the symptoms of patellar tendinopathy quickly and steadily for at least 10 years. It confirmed the first hypothesis. This improvement in patients that had different severities of VISA-P scores at baseline was equally obtained in terms of symptomatology, knee function and return to sports activity, which is also in concordance with the second hypothesis. The results observed in the first study reporting on the clinical use of EPI® are encouraging [26]. Its effects are based on a local and non-thermal electrochemical therapy that induces a localized short inflammatory response through an electrolytic reaction produced by a cathodic flow. Consequently, this causes an organic reaction leading to the regeneration of the injured tendon [26].

Conservative treatment was traditionally considered the first option of treatment of tendinopathies. Many different techniques were used [1, 8], such as modification of activity, eccentric physical training, patellar straps, cold and heat compression transfriction massage and stretching for quadriceps, hamstrings and patellar tendons. Despite some good results reported with eccentric programmes [18, 28], it is still unclear as to the more effective exercise protocol, its frequency, load and dosage. While Zwerver et al. [37], in a recent randomized clinical trial, concluded that no benefit came of extracorporeal high-energy shock-wave therapy during competition, Rompe et al. [25] reported, at 4-month follow-up, that eccentric loading

Table 4 Victorian Institute of Sport Assessment–Patella (VISA-P) values during follow-up

Time	VISA-P score			Tegner score		
	Group 1	Group 2	Global	Group 1	Group 2	Global
Baseline ($n = 40$)	33.1 (±13)	69.3 (±10.5)	51.2 (±21.7)	8.1 (6–10)	7.8 (4–9)	7.9 (4–10)
3 months ($n = 40$)	78.9* (±14.4)	84.9* (±9)	81.9* (±12.2)	7.7 (4–10)	7.6 (3–9)	7.7 (3–10)
2 years ($n = 40$)	83.2 (±13.6)	88.6 (±7.4)	85.9 (±11.1)	8.1 (5–10)	7.7 (4–9)	7.8 (4–10)
5 years ($n = 37$)	85.2 (±12.2)	91.9 (±5.6)	88.6 (±10)	7.9 (5–10)	7.6 (4–9)	7.8 (4–10)
10 years ($n = 34$)	88.8 (±10.1)	96.0 (±4.3)	92.4 (±8.5)	7.7 (5–10)	7.3 (4–9)	7.5 (4–10)

Victorian Institute of Sport Assessment–Patella (VISA-P) values expressed as mean (±SD). Tegner values are expressed as median (range)

* $p < 0.001$. No statistically significant differences were observed in the results between any intermediate outcome measurements other than from baseline

alone was less effective when compared with a combination of eccentric loading and repetitive low-energy shockwave treatment. Similarly, low-intensity US is not currently considered a reliable method for the treatment of patellar tendinopathy [14, 15, 35].

Different injection treatments for patellar tendinopathy have been proposed. While some studies on the effect of dry needling, autologous blood and high volume have been put forward as providing functional improvements, steroid treatment has shown a relapse of symptoms after few months, not to mention the deleterious effect on the tendon histology [32]. Recent investigations have observed slightly better outcomes after treatment with platelet-rich plasma injections in association with an eccentric training programme than an eccentric training programme alone in short-term studies [7, 30, 32]. Some authors had initially reported pain relief after sclerosing injections of polidocanol [10], but recent studies have shown contradictory results [33]. Hoksrud et al. reported their results with US-guided sclerosis of neovessels in 29 patients with 44 months of follow-up [12] and in 101 patients with 24 months of follow-up [13]. The patients needed several injections over 8 months of treatment, and only a moderate improvement in knee function was observed. One-third of their patients obtained a VISA-P score <50 points, and only few patients were completely cured. Conversely, in the present investigation with short- and long-term reported outcomes, even the patients with lowest VISA-P score (<50 points) at baseline significantly improved to around 80 points at 3 months and to around 90 points at 10 years. These final outcomes were comparable with those obtained by the patients with better VISA-P scores before treatment. This is of considerable relevance because the professional sports patients included in this series started from lower VISA-P values and they still obtained excellent scores. Overall, 80 % ($n = 32$) of the treated patients returned to the same level of sports activity at 3 months, and the remaining eight patients only decreased a single level in the Tegner score.

Regarding surgical treatment of patellar tendinopathy, some open [5, 21] and arthroscopic [5, 20, 27] techniques have also been recommended when conservative treatment fails. However, surgery usually provides unpredictable and inconsistent results [4, 15], which is often no more effective than an isolated eccentric exercise programme [2], and it does not allow the athletes to resume their previous sports at the same level, at least within the first year of treatment [19].

The main strengths of the current study are that, as far as we know, it is the first investigation reporting on any treatment modality for patellar tendinopathy over the course of 10 years. Few patients were lost during this long follow-up period. In addition, it is also the first study reporting on the clinical outcome using the EPI® technique in the treatment of tendinopathy at long term follow-up. The promising results obtained with the EPI® procedure showed excellent functional results assessed with the VISA-P score as well as with the Blazina's classification in around 80 % of the patients at 3 months and over 90 % at 10 years. It also allowed a full recovery to the previous activity level in most patients. This outcome's improvement with the use of EPI® in the treatment of patellar tendinopathy was achieved after a short period of time (mean 7.5 weeks) and with a few number of treatment sessions (mean 4.1 EPI® treatments).

Besides the low sample size, one of the most relevant limitations of the current study is the lack of a control group. Comparison with a placebo-treated group of patients would have made for much stronger conclusions. However, most of our patients were professional or semi-professional athletes referred by other physicians after failure of conservative therapy. It seems highly unlikely that this sort of patients would be willing to accept placebo treatment for a long enough period. Another weakness might be that the combination of treatment with eccentric exercises might have positively affected the results attributed to the EPI® technique. Although this could more logically affect the results during the first months of follow-up, it does not seem that it should have had any influence in the long-term results. Regardless of the aforementioned limitations, this study provides the first analysis of the EPI® technique on the treatment of patellar tendinopathy, with promising results after a long follow-up period.

The clinical relevance of the reported results was that EPI® technique brought about a major improvement in pain and function in comparison with the so far known techniques and offers a good treatment option in patellar tendinopathy.

Conclusion

Treatment with the US-guided EPI® technique and eccentric exercises in patellar tendinopathy resulted in a great improvement in knee function and a rapid return to the previous level of activity after few sessions. The procedure has proved to be safe with no recurrences on a long-term basis.

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Randomized, double-blind study comparing percutaneous electrolysis and dry needling for the management of temporomandibular myofascial pain

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Abstract

Background: To assess whether the techniques of percutaneous needle electrolysis (PNE) and deep dry needling (DDN) used on trigger points (TrP) of lateral pterygoid muscle (LPM) can significantly reduce pain and improve function in patients with myofascial pain syndrome (MPS) compared to a control group treated with a sham needling procedure (SNP).

Material and Methods: Sixty patients diagnosed with MPS in the LPM were selected and randomly assigned to one of three groups. The PNE group received electrolysis to the LPM via transcutaneous puncture. The DDN group received a deep puncture to the TrP without the introduction of any substance. In the SNP group, pressure was applied to the skin without penetration. Procedures were performed once per week for 3 consecutive weeks. Clinical evaluation was performed before treatment, and on days 28, 42 and 70 after treatment.

Results: Statistically significant differences (p <0.01) were measured for the PNE and DDN groups with respect to pain reduction at rest, during chewing, and for maximum interincisal opening (MIO). Values for the PNE group showed significantly earlier improvement. Differences for PNE and DDN groups with respect to SNP group were significant (p <0.05) up to day 70. Evaluation of efficacy as reported by the patient and observer was better for PNE and DDN groups. No adverse events were observed for either of the techniques.

Conclusions: PNE and DDN of the LPM showed greater pain reduction efficacy and improved MIO compared to SNP. Improvement was noted earlier in the PNE group than in the DDN group.

Key words: *Myofascial pain syndrome, myofascial trigger points, percutaneous needle electrolysis, deep dry needling, lateral pterygoid muscle.*

Introduction

Myofascial pain syndrome (MPS) is a complex disorder of the musculoskeletal system, with multifactorial involvement, which has several clinical presentations in multiple areas of the body. One of these is the orofacial region, affecting the masticatory muscles and the temporomandibular joint (TMJ). MPS should be suspected in patients with pain and dysfunction of the masticatory muscles, together with the existence of trigger points (TrP) on palpation (1). TrPs are bands of muscle whose activation triggers tension and a deep and constant pain that can cause central excitation. The pain can be local or referred, and is characterized by its tendency to become chronic, limiting interincisal opening and causing muscle weakness as valid diagnostic criteria to differentiate myofascial temporomandibular disease from properly intra-articular disorders (1-3). It has been observed that the masseter and temporal muscles along with the lateral pterygoid muscle (LPM) are the muscles most frequently involved in active TrP in patients with temporomandibular disorders of myofascial origin (4).

In the temporomandibular area, TrPs associated with MPS usually do not resolve without treatment (4). Management can include the control of parafunctional habits, use of a mouth guard, and analgesic-anti-inflammatory therapy. This can be in conjunction with inactivation of TrPs by non-invasive methods, such as massages, ultrasound, muscle stretching with application of cold spray, and magnetic or electrical stimulation. Other mechanical treatments such as acupuncture or the direct application of medication to TrPs may be considered (5-7). To date, several minimally invasive methods have been described (8,9), with deep dry needling (DDN) being one of the techniques used to inactivate TrPs (1). Several studies in the literature have reported on its safety, efficacy and low cost in the management of MPS with LPM involvement (4,10,11).

Percutaneous needle electrolysis (PNE) consists in the application of a low intensity galvanic current through an acupuncture needle to accelerate tissue regeneration (12). It has been used successfully in various musculoskeletal pathologies, such as for the treatment of patellar tendinitis, tennis elbow, osteitis pubis and acute whiplash syndrome (13-16). However, to the best of our knowledge, no previous study has investigated the effect of PNE on TrPs of the masticatory muscles. The aim of the present study was to investigate if the PNE technique in LPM could reduce pain and improve mandibular mobility compared to DDN and a sham needling procedure (SNP). Secondary objectives were to assess the level of improvement in the general condition of the TMJ, as well as to assess the patient's tolerance to the treatments performed and to side effects.

Material and Methods

-Subjects:

A randomized, double-blind, single-centre clinical trial was carried out in the outpatient clinic of the Department of Oral and Maxillofacial Surgery of the Virgen del Rocío University Hospital, Seville (Spain), from June 2015 to June 2016.

The following diagnostic inclusion criteria were evaluated: a) age between 18 and 65 years, b) myogenic pain in the temporo-mandibular area of at least 6 months' duration, c) moderately limited mandibular movement (interincisal opening limited to <40 mm and requiring passive stretching to increase opening by > 5 mm), according to Group I criteria of the RDC/TMD Consortium (17), and d) criteria satisfied for active TrPs in the LMP (pain upon intraoral palpation, limited range of movement, painful chin protrusion against resistance, lateralization of the contralateral side with mouth opening, and pain in the ipsilateral TMJ) according to the protocol used previously (1), following confirmation according to magnetic resonance study and panoramic radiography to rule out the presence of other conditions.

Exclusion criteria were: a) the presence of TrPs in any other masticatory or cervical muscle, b) intra-articular pathology according to diagnostic criteria for temporomandibular disorders (17), c) dentofacial deformities, d) facial paralysis, e) vascular diseases, f) tension headache or migraine, g) previous infectious-inflammatory diseases of dental origin, h) belonephobia, i) fibromyalgia, j) depression or k) other medical comorbidities (diabetes, hypo- or hyperthyroidism).

The study was approved by the Hospital Ethics Committee (approval number 2014PI/083). All patients provided their informed consent prior to inclusion.

-Study design:

Patients were randomly assigned by Epidat 4.0 software to one of the three groups. The principal investigator and patients were all blinded to the assigned group until completion of the statistical analysis. The clinical evaluation of the patients was performed prior to treatment,

and on days 28, 42 and 70 after treatment. Data was collected at each visit by the same observer.

The PNE group received a transcutaneous puncture in the LPM, according to the technique described by Koole *et al*. (18). Sterile stainless-steel needles (length 40 mm/ caliber 0.25 mm, with a cylindrical plastic guide, Agu-punt ®, Barcelona, Spain) were used for the muscle puncture. The puncture needles were connected to an electrosurgical device, and the electrotherapy equipment (EPI® Advanced Medicine, Barcelona, Spain) produced a continuous galvanic current of 2 mA for 3 seconds, three times through the cathode (electrosurgical scalpel), while the patient held the anode (hand electrode).

The puncture technique used for the DDN group was performed as previously described (2,11). A deep intramuscular puncture of the TPs was carried out without the introduction of any substance (dry puncture) (19). The objective was to provoke a jump reaction or local twitch response when the needle was inserted in a TrP (8). During the procedure, the operator used the volume of the electrotherapy equipment as a guide, simulating the EPI® technique. For the SNP group, the needle was pressed against the skin with its plastic protective tube, simulating a puncture, with the same noise reproduced with the EPI® equipment.

In all cases, the preauricular area was cleaned with alcohol 90% prior to the procedure, and the unilateral upper and lower bellies of the LPM were located manually intra- and extraorally. The procedures were performed once per week, for 3 consecutive weeks. Two weeks after each procedure, all subjects were instructed to perform concentric exercises with the masticatory muscles.

-Measures:

The main parameters evaluated were: a) pain at rest and with mastication according to a visual analogue scale (VAS), ranging from 0 (without pain) to 10 (worst pain imaginable), b) maximum interincisal opening (MIO) without causing pain or discomfort, using a jaw motion ruler to evaluate the distance between the upper and lower incisor in millimetres (Therabite® System ruler), and c) involvement of the TMJ, assessed by a 100-point questionnaire (0 worst case, 100 optimal) based on pain in daily activities (maximum 40 points), function (45 points) and mastication (15 points). Secondary efficacy results were the overall efficacy scores evaluated by the patients and the observer using a 5-point scale, ranging from 0 worst-possible outcome to the optimum outcome of 4. Tolerability to the treatment was evaluated by the patient and the observer using a 5-point scale, ranging from 0-very bad to 4-excellent. The type and frequency of adverse events were recorded at each visit.

-Statistical analysis:

Data were analysed with SPSS statistical software (IBM Statistics 19.0). Pre- and post-intervention comparisons of the variables in each group were performed with the Friedman test, while variations within each group were analysed with the Wilcoxon signed-rank test (with Bonferroni correction). Comparisons between the study groups were made with the Kruskal-Wallis test for each time point. If differences were detected between groups, the Mann-Whitney U test was used to detect where the difference was. Values of $p < 0.05$ were considered to indicate statistical significance. When the Bonferroni correction was applied, the statistical significance was $p<0.016$.

Results

Sixty patients were included in the study and randomly assigned to one of the three groups (20 patients in each group), from June 2015 to June 2016. The three groups had similar number of patients, and similar age distributions (median age of 39, range 18 to 62). Table 1 shows the demographic characteristics and pain descriptions for the 60 participants. No significant differences were found between the 3 groups. Two patients from the DDN group and one patient from the SNP group dropped out of the trial. When performing the statistical analysis,

Table 1: Demographic characteristics and pain description of all participants.

	PNE	DDN	SNP	Significance (P)
Age (y), median (range)	38.5 (18-57)	36 (19-58)	42 (25-62)	0.3247
Gender Male/Female (n)	5 / 15	2 / 18	1 / 19	0.5273
Pain (VAS), Me (IQR) At rest Mastication	 6 (5-6.75) 7 (6-8.375)	 6 (5-7) 8 (7-8)	 5.5 (4-7) 7 (5-8.5)	 0.929 0.670
MIO, Me (IQR)	34.5 (29.5-36.75)	34 (30-35.5)	34 (25-39)	0.765
TMJ functionality test, Me (IQR)	38.5 (21.25-51.5)	45 (20-52.5)	35 (20-42)	0.312

VAS= visual analogue scale. Me= median. IQR= interquartile range. MIO= maximum interincisal opening. PNE= percutaneous needle electrolysis. DDN= deep dry needling. SNP= sham needling procedure. TMJ= temporo-mandibular joint.

the intention-to-treat analysis and the per-protocol analysis yielded identical results for all parameter measures; therefore, only the analysis per-protocol will be used to describe the results.

The reduction in pain at rest from day 0 to day 70 was statistically significant in the PNE and DDN groups (p <0.001) (Table 2). In the PNE group, this difference was first evident on day 28 (p<0.0001), while in the DDN

Table 2: Pain at rest and pain on mastication, as measured on a 10-cm VAS.

	Pain at rest: Intragroup analysis							
	Day 0	Day 28	Day 42	Day 70		Δ 0-28	Δ 28-42	Δ 42-70
	Me (IQR)	Me (IQR)	Me (IQR)	Me (IQR)	Significance (*P*) [1]	Significance (*P*) [2]	Significance (*P*) [2]	Significance (*P*) [2]
PNE group	6 (5-6.75)	1.5 (0.2-4)	1.25 (0-3)	1.5 (0-2	0.001*	<0,0001*	0.454	0.497
DDN group	6 (5-7)	5 (3.5-5)	3 (2-4)	2 (2-3.5)	0.001*	0.004*	0.008*	0.014*
SNP group	5.5 (4-7)	5 (3-7)	5 (4-7)	5 (3-6)	0.776			
	Pain at rest: Intergroup analysis							
	Day 0	Day 28	Day 42	Day 70				
Significance (*P*) [3]	0.929	0.002*	0.001*	<0.0001*				
PNE vs DDN Significance (*P*) [4]		0.007*	0.012*	0.033				
PNE vs SNP Significance (*P*) [4]		0.002*	0.001*	<0.0001*				
DDN vs SNP Significance (*P*) [4]		0.308	0.023	0.010 *				

p

	Pain on mastication: Intragroup analysis							
	Day 0	Day 28	Day 42	Day 70		Δ 0-28	Δ 28-42	Δ 42-70
	Me (IQR)	Me (IQR)	Me (IQR)	Me (IQR)	Significance (*P*) [1]	Significance (*P*) [2]	Significance (*P*) [2]	Significance (*P*) [2]
PNE group	7 (6-8.3)	4 (2-5)	2.7 (1-5.1)	2 (1-4)	<0.0001*	0.001*	0.077	0.351
DDN group	8 (7-8)	5 (4.5-6)	3 (3-5.5)	3 (2-5)	<0.0001*	<0.0001*	0.046	0.046
SNP group	7 (5-8.5)	6 (4-9)	8 (4-9)	3 (3-8)	0.303			
	Pain on mastication: Intergroup analysis							
	Day 0	Day 28	Day 42	Day 70				
Significance (P) [3]	0.670	0.016*	0.004*	0.004*				
PNE vs DDN Significance (P) [4]		0.173	0.161	0.279				
PNE vs SNP Significance (P) [4]		0.008*	0.005*	0.002*				
DDN vs SNP Significance (P) [4]		0.073	0.011*	0.016*				

Data from the tables are the median of the differences between the different days. VAS=visual analogue scale. Me=median. IQR=interquartile range. PNE=percutaneous needle electrolysis. DDN=deep dry needling. SNP=sham needling.
Significance (P)(1) = Friedman test for intragroup comparative analysis at each visit. * Results considered significant (p<0.05).
Significance (P)(2) = Wilcoxon test for the intragroup comparative analysis of VAS increase every two visits consecutive * Results considered significant (p<0.016).
Significance (P)(3) = Kruskal-Wallis test for intergroup comparative analysis at each visit. * Results considered significant (p<0.05).
Significance (P)(4) = Mann-Whitney U test for intergroup comparative analysis at each visit. * Results considered significant (p<0.016).

group it was significant at all time points (p= 0.004, p= 0.008 and p= 0.014). When comparing among the three groups, differences were statistically significant at all time-points in the study (p<0.001). Differences between the PNE and SNP groups were found for all three days in which data was collected (p = 0.002, p = 0.001 and p <0.001). Differences between the PNE and DDN groups were found between days 28 (p = 0.07) and 42 (p = 0.12), and between DDN and SNP at day 70 (p = 0.01). From day 0 to day 70, a significant reduction in pain with mastication was seen for the PNE and DDN groups (p <0.001) on day 28 (p = 0.001 and p <0.0001) (Table 2). When comparing between the three groups, significant differences were seen at all time-points of the study (p = 0.016, p = 0.004 and p = 0.004). Differences between the PNE and SNP groups were significant at all time-points (p = 0.08, p = 0.05 and p = 0.02), while between the DDN and SNP groups differences were found on days 42 and 70 (p = 0.011 and p = 0.016). MIO values improved significantly from day 0 to day 70 in both the PNE and DDN groups (p <0.001) (Table 3), with a significant reduction also seen for both groups on day 28 (p <0.0001 and p = 0.001). When comparing between the three groups, differences were obtained on all three days of the study in which data was collected (p <0.001, p = 0.002 and p = 0.001). For the PNE group, the increase in MIO was higher than in both the DDN group (p = 0.001, p = 0.007 and p = 0.003) and the SNP group (p <0.001, p = 0.002 and p = 0.001) at all times.

Values obtained in the 100-point questionnaire improved significantly between day 0 and day 70 in the three groups (p <0.001) (Table 4). Significant differences were also found on day 28 for the PNE and DDN groups (p <0.0001 and p = 0.001). Again, when the three groups were compared, differences were significant on each of the three days in which data were recorded (p = 0.009, p = 0.004 and p <0.001). Values for the PNE group were higher than those for the SNP group on all three days (p = 0.006, 0 = 0.003 and p <0.001), and higher than the DDN group on day 70 (p = 0.001).

The only reported adverse effect was a self-limiting hematoma in one patient in the PNE group. No statistically significant differences in treatment tolerance were found between the three groups (Table 4). The evaluation of the efficacy outcomes among the three groups was statistically significant both for the patient (p <0.0001) and the observer. When comparing between the three groups, this difference was greater for the PNE group than in the DDN and SNP groups, and in

Table 3: Maximal interincisal opening (MIO), as measured using a jaw motion ruler.

	Intragroup analysis							
	Day 0	Day 28	Day 42	Day 70		Δ 0-28	Δ 28-42	Δ 42-70
	Me (IQR)	Me (IQR)	Me (IQR)	Me (IQR)	Significance (P) (1)	Significance (P) (2)	Significance (P) (2)	Significance (P) (2)
PNE group	34.5 (29.5-36.75)	40 (38-45)	40 (36-45)	40 (38-45)	<0.0001*	<0.0001*	0.291	0.360
DDN group	34 (30-35.5)	37 (35-40)	37 (35-38)	37 (35-38.5)	<0.0001*	0.001*	0.811	0.020
SNP group	34 (25-39)	35 (28-40)	33 (26-40)	35 (28-40)	0.95			
	Intergroup analysis							
	Day 0	Day 28	Day 42	Day 70				
Significance (P) (3)	0.765	<0.0001*	0.002*	0.001*				
PNE vs DDN Significance (P) (4)		0.001*	0.007*	0.003*				
PNE vs SNP Significance (P) (4)		<0.0001*	0.002*	0.001*				
DDN vs SNP Significance (P) (4)		0.078	0.244	0.132				

Data from the tables are the median of the differences between the different days. Me = median. IQR = interquartile range. PNE = percutaneous needle electrolysis. DDN = deep dry needling. SNP = sham needling procedure.
Significance (P) (1) = Friedman test for intragroup comparative analysis at each visit. * Results considered significant (p<0.05).
Significance (P) (2) = Wilcoxon test for the intragroup comparative analysis of VAS increase every two visits. * Results considered significant (p<0.016).
Significance (P) (3) = Kruskal-Wallis test for intergroup comparative analysis at each visit. * Results considered significant (p<0.05).
Significance (P) (4) = Mann-Whitney U test for intergroup comparative analysis at each visit. * Results considered significant (p<0.016).

Table 4: Functionality of the TMJ, measured by the 100-point test, and tolerance to treatment and subjective evaluation, measured by the 5-point test.

A) Functionality of the TMJ, measured by the 100-point test:

	Intragroup analysis							
	Day 0	Day 28	Day 42	Day 70		Δ 0-28	Δ 28-42	Δ 42-70
	Me (IQR)	Me (IQR)	Me (IQR)	Me (IQR)	Significance (*P*) [1]	Significance (*P*) [2]	Significance (*P*) [2]	Significance (*P*) [2]
PNE group	38.5 (21.25-51.5)	75 (51.25-83.75)	75 (56.25-93.75)	82.5 (60-90)	<0.0001*	<0.0001*	0.529	0.028
DDN group	45 (20-52.5)	57 (52.5-70)	57 (53.5-70)	60 (52.5-70)	<0.0001*	0.001*	0.595	0.713
SNP group	35 (20-42)	45 (15-70)	37 (15-65)	37 (25-67)	<0.0001*	0.035	0.408	0.422
	Intergroup analysis							
	Day 0	Day 28	Day 42	Day 70				
Significance (*P*) [3]	0.312	0.009*	0.004*	<0.0001*				
PNE vs DDN Significance (*P*) [4]		0.064	0.022	0.001*				
PNE vs SNP Significance (*P*) [4]		0.006*	0.003*	<0.0001*				
DDN vs SNP Significance (*P*) [4]		0.087	0.109	0.244				

Data from the tables are the median of the differences between the different days.
Me = median. IQR = interquartile range. PNE = percutaneous needle electrolysis. DDN = deep dry needling. SNP = sham needling procedure.
Significance (P) [1] = Friedman test for intragroup comparative analysis at each visit. * Results considered significant (p<0.05).
Significance (P) [2] = Wilcoxon test for the intragroup comparative analysis of VAS increase every two visits. * Results considered significant (p<0.016).
Significance (P) [3] = Kruskal-Wallis test for intergroup comparative analysis at each visit. * Results considered significant (p<0.05).
Significance (P) [4] = Mann-Whitney U test for intergroup comparative analysis at each visit. * Results considered significant (p<0.016).

B) Tolerance to treatment and subjective evaluation, measured by the 5-point test:

	Tolerance to treatment at day 28		Subjective evaluation of improvement at day 70	
	Me (IQR)		Me (IQR)	
	Patient	Observer	Patient	Observer
PNE group	4 (3-4)	4 (3-4)	4 (3-4)	4 (4-4)
DDN group	4 (3-4)	4 (3-4)	3 (3-3)	3 (2,5-3)
SNP group	4 (4-4)	4 (4-4)	2 (1-2)	2 (1-2)
Significance (*P*) [1]	0,238	0,390	<0,0001*	<0,0001*
PNE vs DDN Significance (*P*) [2]			0.02088*	0.041*
PNE vs SNP Significance (*P*) [2]			<0.0001*	<0.0001*
DDN vs SNP Significance (*P*) [2]			0.00012*	0.0104*

Data from the tables are the median of the differences.
Me = median. IQR = interquartile range. PNE = percutaneous needle electrolysis. DDN = deep dry needling. SNP = sham needling procedure.
Significance (P) [1] = Kruskal-Wallis test for intergroup comparative analysis. * Results considered significant (p<0.05).
Significance (P) [2] = Mann-Whitney U test for intergroup comparative analysis. * Results considered significant (p<0.016).

turn greater in the DDN group than in the SNP group, in terms of both patient and observer perception.

Discussion

The objective of the present study was to evaluate the efficacy of PNE and DDN, two minimally-invasive techniques, applied three times to the LPM (once per week for three consecutive weeks). To do this, an analysis was made of the pain intensity at rest and with mastication, together with the measurements of the MIO ranges. The main findings can be outlined as follows: Compared to baseline values prior to treatment, PNE and DDN serve as effective treatments for MPS located in the LPM, improving pain, mandibular mobility and involvement of the TMJ ($p < 0.01$). Both techniques immediate pain relief, and provided a stable outcome throughout the follow-up period as evidenced by significant improvements maintained until day 70 ($p < 0.05$). It would seem that this effect was achieved earlier with PNE than with DDN. Pain reduction values were proportionately higher compared to those of improvements in MIO. And finally, when comparing these results with the SNP group, significant differences were generally obtained on all of the study days in which evaluations were made.

The therapeutic management of MPS should be based on a multidisciplinary approach where TrP inactivation is the fundamental objective. While various puncture methods have been described in the literature that attempt to inactivate myofascial TrPs (9,11), the principal difference between the different techniques consists of the injection, or not, of a substance into the TrP (dry puncture or wet puncture). No significant differences were reported in the literature between the use of DDN and the injection of any substance in the muscle belly (9).

DDN involves inactivation of TrPs via the insertion of an acupuncture needle without the administration of any substance. The mechanism of underlying the inactivation is not known, but the technique has been shown to provide effective pain relief and short-term functional recovery of muscles (20). The most accepted hypothesis of the technique's mechanism of action is that the needle damages the motor endplate, which in turn causes denervation of the distal axon, and interruption of the central pain circuit (21). To ensure the success of the procedure, the local twitch response that occurs when the needle enters the TrP seems to be the best indicator to establish the diagnosis (8), although occasionally, identification of the local twitch response can be extremely difficult. The local twitch response corresponds to a spinal reflex with a momentary contraction of the fibers that make up the taut band of muscle. The patient describes it as a cramp or tingling at the time of the puncture.

A limited number of studies have investigated the use of DDN to treat TrP in the orofacial area. Fernandez-Carnero *et al.* (4) studied the use of DDN of the masseter muscle. Gonzalez-Perez *et al.* (11) compared DDN with analgesic medication for MPS by treating TrPs in the LPM, with pain relief achieved almost immediately in the DDN group. Recently, Blasco-Bonora & Martín-Pintado-Zugasti (3) used DDN on the temporal and masseter muscles. Taken together, these studies have reported statistically and clinically significant results in reducing both pain and dysfunction.

PNE is an emerging, minimally invasive physiotherapeutic technique that involves the application of direct current (galvanic) through a puncture needle such that used in DDN, which acts as a negative electrode and induces an electrochemical reaction in the area to which it is applied. Cell necrosis is caused by this reaction, which results in a local inflammatory process in the soft tissue, inducing phagocytosis and repair of the affected tissue (12). Tissue regeneration induced by PNE can restore function to the muscle, which is usually structurally damaged. PNE has been used to the present time to treat pathologies of the muscles and tendons, particularly in the lower limbs (13-16). To the best of our knowledge, no study has provided data on its use in orofacial pain as in our clinical trial. The paucity of other studies means that we are not available to compare our findings with others, making it difficult to arrive at definitive conclusions.

When comparing PNE with DDN in the present study, it was found that pain at rest and upon mastication decreased earlier in the PNE group. This was possibly because the technique combines both mechanical (needle) and electrical (galvanic current) stimulation (14). This effect could be explained by the inactivation of TrPs and by the acceleration of the regeneration of the damaged muscle with PNE. Three punctures were performed (one per week for three weeks) with application of a low intensity galvanic discharge in the LPM, with the aim of inactivating the TrPs. The slower improvement in the DDN group could have been due to the effect of the SNP and the blinding of the patients. In general, patients in the PNE group reported less post-puncture pain than in the DDN group. Improvements in MIO and in the 100-point test score were similar in the PNE and DDN groups, generating an improvement in the perceived quality of life of patients owing to the larger variety of foods they could eat.

The diagnosis of the presence of a TrP in the LPM is difficult due to its deep location. Painful intraoral palpation or limited mandibular opening are two common indirect clinical signs. The most reliable clinical test seems to be the painful protrusion against resistance (1,11,18,19). Exact localization of the TrP before the puncture can be achieved by palpation, ultrasound or

electromyography, although their use is complex and not validated (22-25). In general, the precise puncture of the LPM is a simple, reliable and validated technique (11,18) achieved via a transcutaneous approach, with the two muscle bellies easily reached (26).

Tolerance to the treatment was the same in the three groups. The overall evaluation by the patients and observer of the effectiveness of the treatment, and the patients' evaluation of treatment tolerance, were better for PNE and DDN than for SNP. Similarly, the overall efficacy evaluated both by patients and the observer was better for the PNE and DDN groups. No adverse reactions were detected with DDN, whereas in the PNE group a self-limiting hematoma was detected in one patient. As for any minimally invasive technique, both PNE and DDN were well tolerated without significant contraindications or costs (16). The strengths of the present trial lie in the fact that it was randomized, blinded and controlled, comparing two active interventions. Furthermore, data collection at standardized time-points during the postoperative period facilitated comparisons with the pre-operative baseline status.

This study has some limitations. Maintaining the blinding of patients in a clinical trial based on an intervention involving a muscle puncture is challenging. This type of effect makes it extremely difficult to conduct studies with a SNP in which participants are truly blinded. In the SNP group of this study, a superficial puncture of the skin was performed with the plastic protection applied (sham dry needling). In this way, the influence of the placebo effect of the procedure and / or the natural evolution of the TMD was controlled throughout the study. Tekin *et al.* (27) blinded participants by applying gentle pressure to the skin with the plastic protection; they described a mild effect in the first days after treatment, which was attributed to the stimulation of superficial cutaneous receptors. To achieve a true placebo effect, Mayoral *et al.* (28) conducted a study in which patients were placed under general anesthesia, and therefore had no way of knowing afterwards what procedure they had been subjected to. Another of the limitations identified here was the infrequently identified, exclusive affectation of the LPM, since disorders of the LPM usually coexist with the involvement of other masticatory muscles such as the masseter or the temporal muscle (29). The evaluation was limited only to the effects observed in the short- and medium-term. To improve the validity of the study it would be important to increase the number of subjects, the time of follow-up, and the inclusion of patients in whom other masticatory muscles are affected. In addition, it would be interesting to assess the treatment in patients with fibromyalgia or depression (30), which in this study were excluded. The use of EMG in the diagnostic work-up, and as a treatment support for puncture of the LPM, could also be studied.

Conclusions

In comparison with SNP, PNE and DDN of the LPM showed greater efficacy in relieving pain and improving MIO in patients with MPS in that muscle. The improvement was seen earlier in the PNE group than in the DDN group. No serious adverse events were observed with respect to any of the techniques used. Future studies should aim for greater validity by enrolling more patients and patients with other disorders of the temporomandibular region, to determine the true role of PNE in the management of MPS in the orofacial area.

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Conflicts of interest
The authors report no conflict of interest related to this study.

Treatment of proximal hamstring tendinopathy-related sciatic nerve entrapment: presentation of an ultrasound-guided "Intratissue Percutaneous Electrolysis" application

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Summary

Background: **Proximal Hamstring Tendinopathy-related Sciatic Nerve Entrapment (PHTrSNE) is a neuropathy caused by fibrosis interposed between the semimembranosus tendon and the sciatic nerve, at the level of the ischial tuberosity.**
Methods: **Ultrasound-guided Intratissue Percutaneous Electrolysis (US-guided EPI) involves galvanic current transfer within the treatment target tissue (fibrosis) via a needle 0.30 to 0.33 mm in diameter. The galvanic current in a saline solution instantly develops the chemical process of electrolysis, which in turn induces electrochemical ablation of fibrosis. In this article, the interventional procedure is presented in detail, and both the strengths and limits of the technique are discussed.**
Results: **US-guided EPI eliminates the fibrotic accumulation that causes PHTrSNE, without the semimembranosus tendon or the sciatic nerve being directly involved during the procedure. The technique is however of limited use in cases of compression neuropathy.**
Conclusion: **US-guided EPI is a technique that is quick to perform, minimally invasive and does not force the patient to suspend their activities (work or sports) to make the treatment effective. This, coupled to the fact that the technique is generally well-tolerated by patients, supports use of US-guided EPI in the treatment of PHTrSNE.**

KEY WORDS: ablation techniques, entrapment neuropathies, tendon injuries, ultrasonography.

Introduction

Proximal hamstring tendinopathy (PHT) is an overuse injury of current interest in orthopaedic and sports medicine. PHT is clinically characterised by pain in the subgluteal region, at the proximal insertion of the hamstring muscles onto the ischial tuberosity, with possible radiation to the posterior region of the thigh; sprinting and sitting for long periods are the activities in which the symptoms are typically exacerbated[1, 2]. The proximal insertion of the semimembranosus (SM) muscle onto the ischial tuberosity is superior-lateral, relative to the insertion of the conjoint tendon of the biceps femoris and semintendinosus.[1,3-5]. In patients with PHT, the proximal SM tendon is the one that is typically degenerated, appearing thickened at the lateral edge[1].
In addition to this, the SM tendon is located in the vicinity of the Sciatic Nerve (SN)[6, 7] which runs just lateral to the tendon (Fig. 1). In patients with PHT, fibrotic adhesions between the SM tendon and the SN occasionally form[1,3,6,8]; this anatomical alteration can cause entrapment syndrome of the SN, overlapping symptoms of tendinopathy, and those typical of an irritation of the nerve (sudden stabbing pain, sciatica, burning sensation or other paraesthesias). Proximal Hamstring Tendinopathy-related Sciatic Nerve Entrapment (PHTrSNE) therefore represents a possible complication of PHT. Rapid movements of hip flexion and extension or maximum hip flexion can worsen

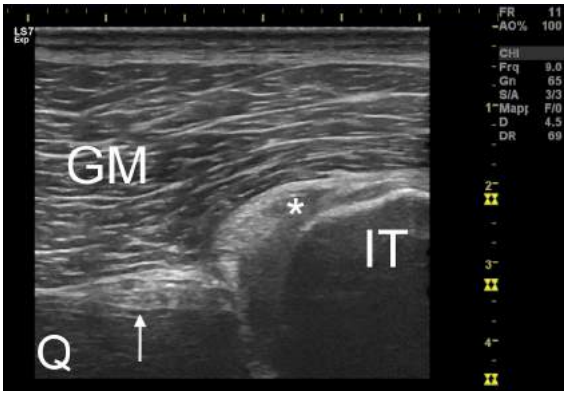

Figure 1. Transversal ultrasound section of the proximal semimembranosus tendon (*asterisked*) on the ischial tuberosity (IT). The sciatic nerve (indicated by the *arrow*) is easily recognizable lateral to the tendon. GM=gluteus maximus. Q=quadratus femoris.

the symptoms, being the SN bound to the hamstring tendon complex (anchoring fibrosis)[1,3,6,8]. However, distinguishing symptoms of tendinopathy from those of neuropathy is fairly complicated.

Conservative treatment and infiltrative therapies for the treatment of PHT are generally preferred to surgery, which is considered when these do not lead to satisfactory results. Potentially applicable treatments are numerous: shockwaves, injections of PRP or corticosteroids, eccentric exercises and others (review[2]). In addition to the dearth of scientific evidence about their effectiveness, the limitation of these therapies is that they are unspecific and most likely ineffective for the treatment of PHTrSNE, in case the latter has been detected and taken into consideration. One scenario that can occur is that symptoms related to tendinopathy recede, while those derived from irritation of the SN persist.

Surgical treatment for managing PHT involves tenotomy of the SM tendon, which is sutured to the tendon of the biceps femoris[1-2]. The positive outcome of SM tenotomy is that the SN is anatomically unbridled from the tendon; the intervention is therefore also valid for the treatment of PHTrSNE. The only significant disadvantage of the intervention is the long post-surgical recovery time (from 1 to 12 months)[2,9]; this point certainly has a significant impact, especially for professional athletes, who may decide to postpone excessively or not to undergo surgery at all.

Finding a technique that can eliminate fibrosis between the SM tendon and the SN without requiring long periods of post-interventional recovery is therefore challenging. Ultrasound-guided Intratissue Percutaneous Electrolysis fulfils these requirements. The aims of this article are: i) to present the rationale for using this technique in the treatment of PHTrSNE; ii) to present the method of application and iii) to discuss both the strengths and limitations of the technique. The hypothesis of the Authors is that Ultrasound-guided Intratissue Percutaneous Electrolysis may be a useful complement to non-surgical proposals in the treatment of PHT with concomitant PHTrSNE.

Materials and methods

This study was conducted in accordance with the Declaration of Helsinki and complied with the ethical standards of the Muscles, Ligaments and Tendons Journal[10].

Ultrasound-guided Intratissue Percutaneous Electrolysis

Intratissue Percutaneous Electrolysis (also known as Electrólisis Percutánea Intratisular or EPI) is a minimally invasive technique that involves galvanic current transfer within the treatment target tissue via a needle 0.30 to 0.33 mm in diameter. The galvanic current in a saline solution rapidly develops the chemical process of electrolysis, which in turn induces tissue ablation[11]. The EPI technique finds indications in the treatment of tendinopathies and fibrosis[12-16].

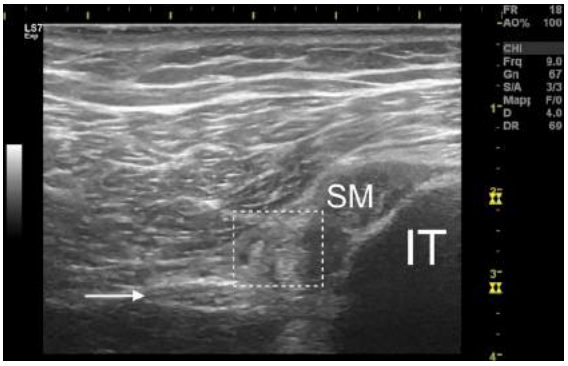

Figure 2. Proximal hamstring tendinopathy-related sciatic nerve entrapment. Between the sciatic nerve (indicated by *arrow*) and the tendon of the semimembranosus (*SM*) a fibrotic accumulation is interposed (hyper-echoic area visible within the *dashed box*) which makes it difficult to distinguish the anatomical limits of the structures. IT=ischial tuberosity.

The rationale for using EPI in the treatment of PHTrSNE is the ability of the technique to specifically degrade fibrotic adhesions that bind the SN and SM tendon. Use of the technique is indicated only when le evident ultrasound signs of fibrosis between the SN and SM tendon are identifiable (Fig. 2) concomitant to the presence of the clinical pattern of PHTrSNE. Clinical assessment is needed, but is not sufficient to diagnose PHTrSNE, as the SN can be trapped in many other areas in the sub-gluteal region[6].

We apply the EPI technique using a specifically developed and medically certified (Directive 93/42/EEC) device (EPI Advanced Medicine® Barcelona, Spain). The main feature of the device is that the cathodic flow is the only one usable. To ensure maximum precision, the technique must be performed in an ultrasound-guided manner (US-guided EPI). We use the GE Healthcare Logiq S7 Expert® ultrasound with a linear probe (6-15 MHz) to guide the insertion of the needle. The operator must be well-trained in the use of the technique, and must have experience in the ultrasound examination of the lower limb.

Procedure for the US-guided EPI intervention

The patient lies in a prone position. The gluteal, subgluteal and trochanteric regions are disinfected by applying an appropriate protocol. The proximal tendon insertions of the hamstring muscles on the ischial tuberosity are identified by the operator guiding the ultrasound probe using their non-dominant hand; a transversal section is required to be able to simultaneously view the tendon complex and the SN[7].

The needle is inserted by the operator with the dominant hand between the two structures through the gluteus maximus muscle, with an inclination of 0+30° around the vertical axis, in the medial-lateral direction

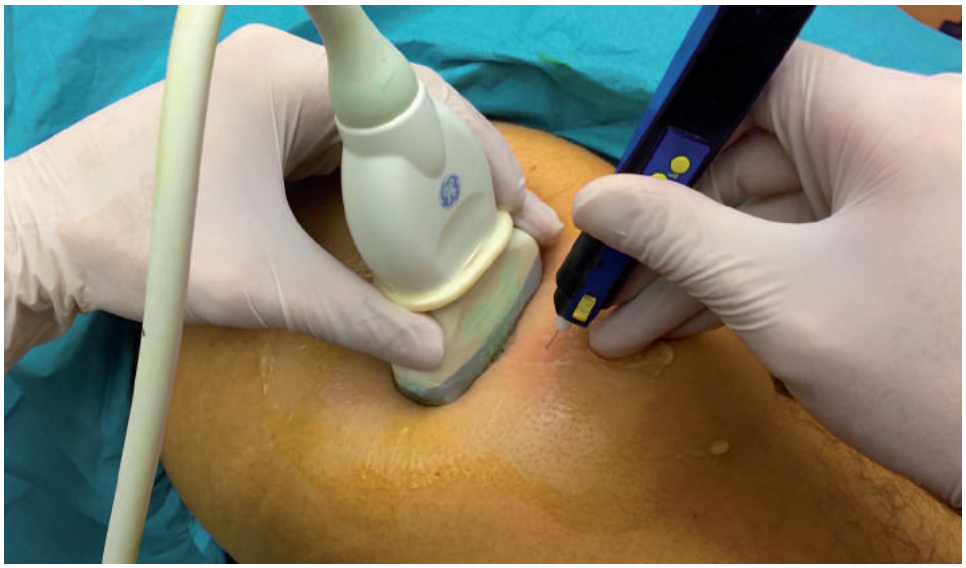

Figure 3. Ultrasound-guided insertion of the needle. Being the needle inserted perpendicular to the skin, it is displayed through movement of surrounding tissues.

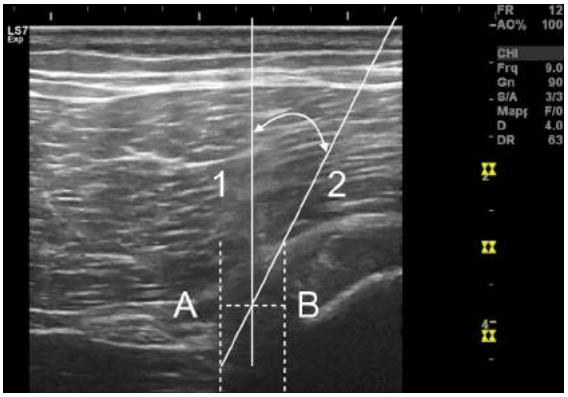

Figure 4. Schematic diagram of the Ultrasound-guided Intratissue Percutaneous Electrolysis intervention. The medial edge of the sciatic nerve and associated vessels is represented by *the vertical dashed line A*. The lateral limit of the semimembranosus tendon is represented by *the vertical dashed line B*. The needle is inserted into the area bounded by *line 1* (perpendicular to the axis joining lines A and B) and by *line 2* (tangent to the superior-lateral point of the semimembranosus tendon). In this way, the technique can be performed safely, without structures other than the fibrosis being involved in the intervention.

(Figs. 3, 4); the SN, the SM tendon, the inferior gluteal artery and the inferior gluteal vein must be avoided during insertion. Depending on the physical characteristics of the patient, the needle can have a variable length, starting at 50 millimetres.

When the needle tip is positioned inside the fibrosis, the galvanic current can be transferred; the intensity of the current is pre-set to 4 mA. The single application can have a variable duration between 2-10 seconds, depending on the tolerability of the technique to the patient (later) and the mechanical resistance offered by the tissue: where it is possible to penetrate the fibrosis with the needle by applying minimum pressure, the single application can be interrupted. At this point the needle is partially withdrawn (without exiting from the skin) and inserted again with a slight deviation to treat a different portion of the fibrotic accumulation.

One session can consist of 2-15 individual applications depending on the extent and hardness of the fibrosis. Consequently, administration of the galvanic current does not exceed 150 seconds in any one session; this should be taken into consideration as local anaesthetic drugs are not used. The session, including disinfection and dressing processes, lasts a maximum of 20 minutes in total.

Tolerability of pain

US-guided EPI is generally well-tolerated by patients. Some may have minor discomfort during the insertion of the needle. Application of the technique can cause mild to moderately strong pain. In addition to this, it is possible that the posterior femoris cutaneous nerve will be indirectly stimulated, causing tingling in the back of the thigh. Vagal reactions (nausea, headache, fainting) are rare but possible[17]; in this sense it is advisable to remind the patient before each session that he or she can ask for the session to be interrupted or stopped at any time. Bleeding in the area of needle insertion may occasionally occur. Patients sometimes report mild tenderness in the treated area, which generally does not last longer than 12-48 hours. The Authors do not advise conducting more than one session per week.

Discussion

The aims of this article are: i) to present the rationale for using US-guided EPI in the treatment of PHTrSNE; ii) to present the method of application and iii) to discuss both the strengths and limitations of the technique. The hypothesis of the Authors is that Ultrasound-guided EPI may be an useful complement to conservative proposals when treating PHT with concomitant PHTrSNE. By using the US-guided EPI technique it is possible to eliminate the fibrosis interposed between the SN and SM tendon, degrading it by electrolytic ablation, without expecting the patient to suspend sporting or work activities for more than 48 hours after the intervention.

Strengths and limitations of the technique

US-guided EPI is a technique that allows specific treatment of the fibrotic adhesions that cause PHTrSNE. The minimal invasivity and lack of necessity of suspending activities (work or sports) after treatment are the main strengths of this technique. The main limitation of the technique is the impossibility of completely resolving the symptoms if nerve irritation is caused by SN compression and not by its entrapment by the SM tendon.
EPI is an ultrasound-guided minimally invasive technique in which the needle is inserted with maximum precision into the structure to be treated, with minimal structural damage to any of the other tissues. In this way, one can eliminate a biomechanical cause of neuropathic symptoms, or the fibrosis that binds the SN to the SM tendon, without the nerve and the tendon being directly involved in the intervention. A further advantage of the mini-invasivity is the low chance of experiencing adverse events (in particular damage of the peri-nervous blood vessels).
One point that is certainly an advantage is that the patient does not need to undergo a specific rehabilitative intervention post US-guided EPI to render the treatment effective; this is particularly important for athletes suffering from PHTrSNE who will be required to suspend activities for 24-48 hours at most. US-guided EPI intervention does not therefore have a significant impact on the scheduling of sporting activities for an athlete.
The main limitation of the technique depends upon the type of anatomical alteration that has caused the neuropathy. In this article, SN entrapment neuropathy has been presented. It is however possible that the neuropathy is not derived from SN entrapment, but from compression of the nerve due to SM tendon hypertrophy[1,3]. The two conditions can be concomitant. Using the US-guided EPI intervention, it is not possible to reduce SM tendon hypertrophy in a consistent way; furthermore, on debriding the SN, it is possible that symptoms will persist because of compressive trauma suffered by the nerve. In such case, surgery remains the only therapeutic solution that can be considered.
Another possible scenario is the one in which the symptomatology persists due to irritation of the nerve at another location despite resolution of the PHTrSNE. The anatomy of the sub-gluteal region is in fact highly complex and many different conditions (e.g. piriformis syndrome, gemelli-obturator internus syndrome, quadratus femoris pathology and gluteal disorders) provoking sciatica fall within differential diagnosis[1,6]. As a consequence of this, identification of the primary etiological cause determining the symptoms can be challenging. Instrumental investigations have an important role in detecting anatomical alterations[1]; to date, Magnetic Resonance Imaging (MRI) is typically the procedure of choice[1-3,6,9,18], especially when lower back pain is concomitant (the exam is useful to exclude other pathologies). However, MRI findings can be not associated with symptoms. Medical history and clinical examination[1, 2] can be helpful but, considering that different conditions present similar symptoms, only few tests have shown to have good sensibility and specificity in the diagnosis of SN entrapment[6,19]. For all these reasons, PHTrSNE remains fundamentally a diagnosis of exclusion.
Consequently, in order to evaluate the benefit of the US-guided EPI technique in the treatment of PHTrSNE, the operator shall continuously monitor the evolution of the symptoms related to the disease. The Visual Analogic Scale (VAS)[9,18] and the Victorian Institute of Sport Assessment-Proximal Hamstring Tendons (VISA-H) questionnaire[20] are useful for this purpose. In particular, VISA-H has proven to have high degree of internal consistency and high test-retest reliability[20].

Ultrasound-guided EPI in the treatment of tendinopathies

US-guided EPI finds indications in the treatment of tendinopathies and fibrosis. To date however, few studies have tested the effectiveness of the technique. The therapeutic utility of EPI (by some Authors replaced with the acronym PNE, Percutaneous Needle Electrolysis) was tested for the treatment of patellar tendinopathy[12,13], sub-acromial syndrome[14], chronic lateral epicondylitis[15] and rectus abdominis-related groin pain[16]. The clinical results presented in this work are somewhat in conflict, especially given the different methodological choices of the Authors, in particular relative to the intensity and duration of administration of the galvanic current (which varied from 0.3 mA for 1.2 minutes to 3 mA for a few seconds) and suggested physiotherapy administered in combination with the technique.
The desired effects with the US-guided EPI are, on the one hand, elimination of the degenerated portion of the tendon and, on the other, development of an extremely localized and controlled inflammatory process, that may promote the tendon healing process. The histological effects of administering galvanic current within the tendon tissue are, however, only partially understood[11,21-24]. The method of applying the US-guided EPI technique presented in this article however differs to the one described in the arti-

cles listed above. In those articles, the technique is performed by inserting the needle within the degenerated portion of the tendon; the tendon is therefore the target of the therapy. In this work, the purpose was the electrolytic elimination of peri-tendinous fibrotic tissue, without treating the tendon. The ablative action is therefore the only one that has been fundamentally investigated. This also means there is no need to propose a specific rehabilitation protocol after the intervention.

Conclusions

US-guided EPI is a technique that allows specific treatment of the anatomical alterations that cause PHTrSNE, eliminating the fibrosis that binds the SN to the SM tendon. US-guided EPI is a technique that is quick to carry out, minimally invasive and does not force the patient to suspend their activities (work or sporting) to make the treatment effective. This, coupled to the fact that the technique is generally well-tolerated by patients, supports use of US-guided EPI in the treatment of PHTrSNE. Future studies with high quality designs are needed to test the efficacy of US-guided EPI in the treatment of PHTrSNE.

Conflicts of interest

The Authors declare no conflicts of interest concerning this article.

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TITLE PAGE

Therapeutic results after ultrasound-guided Intratissue Percutaneous Electrolysis (EPI®) in the treatment of Rectus Abdominis-related Groin Pain in Professional Footballers: a pilot study.

Abstract

Background. Rectus Abdominis-related Groin Pain (RAGP) is one of the possible clinical patterns that determine pubalgia. RAGP is one of the typical clinical patterns in footballers and is due to the degeneration/tendinopathy of the distal tendon at the level of the two pubic tubercles. Intratissue Percutaneous Electrolysis (EPI) is a recent technique used in the treatment of tendinopathies.

Aim. The aim was to examine the therapeutic benefits of EPI by contrasting the two basic components that characterize RAGP: painful symptoms and resultant functional deficits.

Design. Consecutive Case Series

Setting. The therapeutic interventions were performed within the facilities of the "Friuli" Stadium, in Udine (Italy), the sporting venue of the Udinese Calcio Spa Football Club.

Population. Eight professional footballers at Udinese Calcio Spa Football Club.

Methods. The footballers underwent ultrasound-guided EPI treatment. No other type of treatment was combined with EPI. Pain was monitored with the Verbal Rating Scale, while functional deficit was monitored using the Patient Specific Functional Scale. The scales implementation took place before treatment, then 24 hours, 1 week, 1 month and 6 months after the end of treatment.

Results. Treatment with EPI produced a complete reduction of pain symptoms in one month and enabled excellent functional recovery for walking and jogging in one week; getting out of bed, running, jumping and kicking within one month from the end of the treatment.

Conclusions. Treatment with ultrasound-guided EPI has shown encouraging clinical results for RAGP. Data are preliminary: considering the limitations of this study more complex study designs are necessary to test the efficacy of the technique.

Clinical Rehabilitation Impact. This study introduces the EPI technique for the first time in the treatment of professional footballers suffering from RAGP. Its future use is proposed as a treatment solution, including complementary to conservative treatment.

Key words: Soccer, Groin Pain, Rectus Abdominis, Tendinopathy, Electrolysis, Ultrasonography

Introduction

Groin Pain (GP), also known as Athletic Pubalgia or Sportsman's Groin is an injury common in the world of football [1-3] but it represents a problem that is, still today, far from being solved. GP is generically defined as a painful syndrome in the pubic/inguinal area [4], which potentially limits sporting performance and in the worst-case scenario forces the footballer to withdraw from playing. This anatomical region is very complex [5-8]. As a consequence of this, identification of the primary etiological cause determining the symptoms is a task that can be complex because many clinical conditions fall within differential diagnosis [4,9-10]. For this reason it is often necessary to use instrumental surveys to detect possible anatomic abnormalities, particularly magnetic resonance imaging [11-14] and ultrasonography [15-16]. In fact there is no agreement in the literature on the definition or diagnostic criteria and a Gold Standard has not been identified. The diagnostic task can be so complex that often the term "Groin Pain" and its synonyms are used inappropriately as a final diagnosis, when they should instead at best describe its symptoms.

Contrary to this tendency, Hölmich [17] defined Rectus Abdominis-related Groin Pain (RAGP) as one of the possible clinical patterns that determine pubalgia. RAGP is one of the typical clinical patterns in footballers and is due to the degeneration/tendinopathy of the distal tendon/enthesis, at the level of the two pubic tubercles. The footballer experiences pain immediately above the pubic symphysis. The painful symptoms negatively affect certain daily activities and especially sporting activities. In this case clinical evaluation is often sufficient to arrive at a diagnosis: RAGP is in fact clinically characterized by pain on palpation of the distal tendon or enthesis at the level of the pubic symphysis and pain on abdominal contraction against resistance [4,17-19]. However, if determining an

RAGP diagnosis tends to be simple, the main problem of how to treat it remains. In the literature there is a dearth of studies that evaluate the effectiveness of specific conservative treatment for RAGP (see reviews [20,21]); basically because it has never been considered as a separate clinical pattern in its own right. RAGP is in fact relatively rare compared with other clinical patterns [17], therefore the lack of specific treatment protocols is not surprising. Discussion concerning the effectiveness of conservative treatment in Groin Pain in general however is open. Conservative treatments generally involve: rest or limitation of activity; manual therapy for restoring the range of motion of the hip and normalisation of muscle stiffness and tone; all active exercises aimed at improving the stabilising capacity of the pelvic muscles (core stability) and recovery of muscular strength [20-26]. Nevertheless, the limits of treatment protocols are, on the one hand, their length and, secondly, the high possibility of recurrence. The duration of treatment may in fact even fluctuate between 13-20 weeks. These time-frames are inconceivable, since a professional footballer's absence from his activities has a significant economic and strategic impact. In addition to this, the recurrence rates are far from negligible. The tendency for the condition to become chronic along with the long recovery times are provoking renewed interest in the search for quicker, more effective therapeutic solutions that also substantially limit the possibility of recurrence.

Intratissue Percutaneous Electrolysis (EPI) is a recent technique used in the treatment of tendinopathies [27-29]. The EPI technique consists of the production of a galvanic current inside the tendon, using an acupuncture applicator. Galvanic current is produced in a solution of salt water through a chemical reaction. Salt (NaCl) and water (H_2O) are decomposed in their chemical constituent elements. They then form new substances such as NaOH. The NaOH is extremely important as it is highly caustic and destroys collagen and mixed substances in the area of the damaged tendon. EPI is a basic technique using a chemical process of non-thermal electrolytic ablation that induces a highly-controlled inflammatory response. When only treating the degenerated tendon tissue, EPI should be combined with the use of ultrasound to identify the structural alteration with absolute precision (ultrasound-guided EPI). Until now, no study has

reported on the effects of treating RAGP with ultrasound-guided EPI. Consequently, the aim of the present study was to examine the therapeutic benefits of ultrasound-guided EPI by contrasting the two basic components that characterize RAGP: painful symptoms and resultant functional deficits. The primary hypotheses of the authors were that treatment with EPI can lead to rapid reduction of the symptoms and recovery of optimal sports performance in a timescale that is acceptable to a professional footballer (no greater than one month from the end of treatment). According to the authors these possible clinical and functional outcomes would be the result of local tissue release induced by the EPI intervention, via the removal of anomalous deposits of collagen (fibrosis) around the tendinous insertion.

Materials and Methods

Subjects

Eight elite professional soccer players (mean ± SD; age 26.8 ± 4.4 years; height 184 ± 8.9 cm; weight 81.6 ± 9.6 kg) from the first team of Udinese Football Club during the seasons 2011-2014 participated in the current study (design: consecutive case series). The footballers were included in the study when a diagnosis of RAGP was confirmed and when the symptoms should have been present for at least 48 hours, where conservative therapy had not led to a substantial improvement. The footballers were excluded from the study when: the diagnosis of RAGP was being strongly debated (difficulty in interpretation of clinical signs); it involved pain on palpation of other structures in the vicinity of the pubic symphysis (inclusion of the adductor longus, the pubic ligament, fibrocartilage disc); there were no signs of degeneration of the tendon/enthesis upon ultrasound examination; other concomitant pathologies were detected (using MRI); the presence of a general or local contraindication to EPI was found [27,29]. The recruitment process initially envisaged clinical evaluation (identification of the primary clinical pattern) followed immediately

by ultrasound evaluation (identification of the degenerated tendinous portion of the Rectus Abdominis on the pubic tubercles). The final part of the assessment involved the registration of VRS and PSFS values. This would be followed by MRI. If the exam confirmed RAGP as the primary disease the footballer was included in the study. All participants were informed of the experimental risk and gave written informed consent. The University Human Research Ethics Committee granted the ethics approval for all of the experimental procedures.

Instrumentation

The ultrasound examination was carried out using a ultrasound GE Logiq S7 expert (GE Healthcare, Milwaukee, WI) with a 50 mm linear footprint matrix probe (5-15 MHz). The EPI technique was applied using a specifically developed medically certified (Directive 93/42/EEC) device (EPI® Advanced Medicine Barcelona, Spain).

Evaluation Protocols

All the soccer players were evaluate before treatment ('pre'); at 24 hours ('post24h'), 1 week ('post1w'), 1 month ('post1m') and 6 months ('post6m') after the end of treatment. An ultrasound examination was carried out to pinpoint the area of degeneration of the distal tendon or of the enthesis of the Rectus Abdominis. In order to document the clinical evolution of RAGP, The Verbal Rating Scale (VRS) was chosen for pain assessment, while the Patient Specific Functional Scale (PSFS) was used for functional evaluation. VRS is a commonly used scale for the assessment of pain in adults. It is an eleven-point numeric pain scale with 0 representing one extreme: "no pain", and 10 representing the other pain extreme: "the worst pain imaginable" [30]. This scale was chosen due to the fact that it is particularly valuable in the follow-up to the pain intensity measurements [31]. VRS values were recorded for: Palpation of the distal tendon/enthesis at the level of the two pubic tubercles (VRSpal); Abdominal contraction against resistance (VRScont). PSFS is an individualized functional outcome scale used to evaluate changes in disability over time [19,32]. PSFS requires

athletes to identify at least three activities that they are having difficulty with or are unable to perform. The athlete rates each activity on a 0 ("unable to perform activity") to 10 ("able to perform activity at same level as before injury or problem") scale. PSFS have been modified by the authors, who selected the activities to be measured, or rather those generally impaired by RAGP. PSFS values were recorded for the following activities: getting out of bed (PSFSbed), walking (PSFSwalk), jogging (PSFSjog), running (PSFSrun), jumping (PSFSjump), kicking (PSFSkick). VRS [31] and PSFS [33] show high test–retest reliability for evaluation of the pain and functional level for chronic diseases/syndromes such as rheumatoid arthritis, low back pain and lateral epicondylitis.

Treatment

The patient was made to lie down in the supine position. Subsequently, the pubic and suprapubic areas were thoroughly disinfected using isopropyl alcohol. For the treatment an EPI® device capable of generating galvanic current was used. The device parameters (intensity and duration of the current) were set at 3 mA for 4 seconds [27,29]. The device was connected to an acupuncture needle (0.25x30mm). At each session, the same operator, who is an expert in the use of ultrasound guided EPI, carried out 3 applications at the level of the tendinous degeneration. The anatomical area to be treated with EPI was precisely identified through the concurrent use of ultrasound (see Figure 1). No other type of treatment was combined with EPI. The number of sessions of EPI for each athlete was ~4 ranged from 2 to 6 sessions. The mean duration (±SD) of the treatment was 18.62±14.72 ranged from 4 to 45 days (median: 13 days). Treatment is considered completed when the player is subjectively satisfied with the therapeutic results and is able to practice his sport activity without symptoms that condition his performance.

Statistical Analysis

Variables are presented as the mean (± SD), and the estimated precision is indicated with 90% confidence limits (CL). In addition to the analyses for statistical significance (i.e., paired t-tests), possible differences between scores or interval times for the same player were analysed (pairwise

comparisons) for practical significance using magnitude-based inferences.[34] The data were log-transformed prior to the analysis to reduce non-uniformity of error. The standardised differences or effect sizes (90% confidence interval) between the scores and interval times were calculated. The threshold values for the Cohen effect size (ES) statistics were: trivial (0.0 – 0.19), small (0.2 – 0.59), moderate (0.6 – 1.1), large (1.2 – 1.9) and very large (> 2.0).[35-36] Probabilities were also calculated to establish whether the true (unknown) differences were lower, similar or higher than the smallest worthwhile difference (0.2 multiplied by the between-subject standard deviation, based on Cohen's effect size principle). The quantitative chances of higher or lower differences were evaluated qualitatively as follows: <1%, almost certainly not; <5%, very unlikely; <25%, unlikely/probably not; 25–75%, possibly/possibly not; >75%, likely/probably; >95%, very likely; >99%, almost certainly.[35-36] A substantial effect was established as >75%. If the likelihood of higher or lower differences was >75%, the true difference was assessed as clear (substantial).[37-38]

Results

Table I summarizes the mean values of VRS and PSFS. By comparing the average values for VRSpalp and VRScont recorded pre-treatment with those recorded at 'post24h', a substantial decrease was observed in the values by 52.51% and 56.88% respectively. It is *almost certain* that the differences between the average values are substantial (see Table II). The percentage differences were calculated as the difference between average values over a given time interval, divided by the average value recorded before treatment. An additional improvement of symptoms was observed at 'post1w' for both tests, with a total reduction of the VRSpalp and VRScont values by 87.17% and 95.78%. The differences between the 'pre' and the 'post1w' values are substantial (*very likely* and *likely* respectively): 96% and 94% that the differences are effectively substantial (see Table II). The average VRS values at 'post1w' were very low but only at 'post1m' all footballers were completely asymptomatic. No substantial differences were recorded between 'post1w', 'post1m' and 'post6m' values for the VRS variables.

As regards the level of functionality, the lowest PSFS values were recorded for PSFSbed, PSFSjump and PSFSkick (see Table I). At 'post24h' the values improved by 116.67%, 141.67% and 200% respectively, with an *almost certain* substantiality of the differences between the values. An additional functional improvement was obtained at 'post1w' for the three tests (moderate ES for PSFSbed and PSFSkick, small for PSFSjump). In this case the substantiality of the differences between 'post24h' and 'post1w' values is *almost certain* for PSFSbed and PSFSkick, *very likely* for PSFSjump (100%, 99% and 97% that the differences are effectively substantial). The maximum level of functional performance was achieved at 'post1m'. PSFSrun, PSFSjog and PSFSwalk were the least compromised activities at the pre stage. At 'post24h', functional recovery of 72.22%, 29.63% and 23.28% respectively was observed: the substantiality of the differences was *very likely* for PSFSrun, *likely* for the other two activities (98%, 93% and 94% that the differences were effectively substantial); an additional functional improvement was obtained between 'post24h' and 'post1w' (small ES for PSFSrun and PSFSjog, moderate ES for PSFSwalk): the footballers had recovered maximum functionality of jogging and walking at 'post1w', PSFSrun in the three subsequent weeks. All footballers had recovered the maximum level of sports performance at 'post1month'. No substantial differences were recorded between 'post1w', 'post1m' and 'post6m' values for the PSFS variables.

Discussion

The aim of the present study was to examine the therapeutic benefits of ultrasound-guided EPI by contrasting the two basic components that characterize RAGP: painful symptoms and resultant functional deficits. The primary hypotheses of the authors were that treatment with EPI can lead to rapid reduction of the symptoms and recovery of optimal sports performance in a timescale that is acceptable to a professional footballer (no greater than one month from the end of treatment). The main findings of this study were that treatment with EPI ensured substantial reduction of the

symptoms, eliminating the symptoms completely in 1 month. It also provided complete functional recovery for walking and jogging in 1 week, for get out of bed, running, jumping and kicking between 1 week and 1 month from the end of treatment.

For both clinical tests, VRSpalp and VRScontr, a substantial improvement of the symptoms (very large effect size) was observed between the pre-treatment and follow-up measurements recorded. Considering that no other type of treatment was combined with EPI (such as rest, NSAID or traditional physical therapy), it is legitimate to believe that the therapeutic effect can possibly be attributed to the EPI intervention. It can definitively be stated that all footballers were almost pain free 1 week after the end of treatment (mean (±SD) values: 1.25±2.12 and 0.38±0.74, respectively) and the proposed clinical tests were completely negative for the subsequent measurements. These data seem to confirm the initial hypothesis according to which EPI intervention can promote a rapid reduction of the symptoms of RAGP. The study design does not however allow for a definitive conclusion to be reached on this. These results, in the hypothetical situation where EPI is confirmed as effectively being the primary therapeutic factor, could be attributed to the direct ablation by EPI [28]. The intervention in fact induces focal tissue release via the removal of fibroses and degenerated components, consequently optimising the biomechanics of tendons, as described in the studies on the therapeutic benefit of EPI in the treatment of patellar tendinopathy [27,29].

PSFSkick, PSFSbed, PSFSjump were found to be the activities most compromised by RAGP. With these activities the footballers reported a substantial functional improvement at the end of treatment (large effect size), more or less sufficient for the footballer to consider the treatment satisfactory. Intuitively, the functional improvements were the consequence of the reduction of the pain symptoms described above and, hypothetically, by the indirect reparative action of EPI. EPI in fact made it possible to optimise the local healing process, especially if there was adequate subsequent mechanical stimulation of the tendon treated [27,29]. Therefore, with the requirement to complete the process, with timescales that tend to be long for tendon tissue, it is possible that substantial

functional recovery would not be achieved immediately. In possible agreement with the above, an increase of performance was also observed between 'post24h' and 'post1w' (small/moderate effect size) while complete recovery of performance was achieved in the three subsequent weeks, confirming the initial hypothesis that elevated levels of sports recovery is possible in short timescales via EPI intervention (treatment lasted 18.62±14.72 days; median: 13 days) and the excellent levels of less than one month from the end of treatment. As regards the other three activities evaluated (PSFSwalk, PSFSjog and PSFSrun) the improvements were quantitatively less consistent, most likely because the functional deficits were not so marked at the beginning of treatment. As regards functional recovery, without a control group, it is not possible to draw definitive conclusions.

In addition to what has been presented, it should be emphasised that none of the players have never suspended their sporting activities (training or match) during the treatment: the latter aspect is certainly important, as it shows how EPI, in addition to being a helpful technique for RAGP, does not impact on the strategic choices of the club.

Treatment with EPI has led to a rapid reduction in symptoms and shorter functional recovery times than those expected by the various Groin Pain conservative treatment protocols: the duration fluctuates between 4-20 weeks [21,35-36]. Considering the review by Jansen et al. [21] regarding treatment of longstanding GP in athletes, abdominis tendinopathy (possibly synonymous with RAGP) was taken into consideration in a single article on the 45 analysed. In this work carried out by Martens et al. [39] (1987) recovery times were 3 months in the first group (treatment: conservative managment; 36% excellent or good results) and 10-14 weeks in the second group 2 (treatment: surgery; 53%-72% excellent results). There is evidence that the methodological differences make for a speculative comparison between the results of this study (which does not consider RAGP as an isolated disease but associated with adductor tendinopathy) and with the others presented in the review (primarily because the diagnoses were different).

In general, the success of EPI treatment for tendinopathies is due to the fact that this technique has been shown to induce significant recovery of the degenerated tissue from a structural point of view, thus optimizing the physiological healing process [27-29].

RAGP is an overuse injury, so the prolonged stress on the structure over time determines the degeneration. In addition to this, the tendinous tissue, compared with muscle tissue, has a low metabolic rate, which corresponds to slow healing [40]. The loss of the tendons' adaptive capacity with respect to external stimuli is therefore an altogether predictable characteristic. Complete healing is, for these reasons, often very difficult to achieve in the short term and consequently creates the preconditions for chronic tendinopathy. It is no coincidence then that almost all symptomatic athletes suffering from GP present with chronic degenerative changes [41].

It is assumed, therefore, that conservative treatment demonstrates such high recurrence rates because it only produces a functional recovery of the degenerated tendon through the reduction of symptoms, but lacks the ability to induce a structural recovery thereof. The lessening of symptoms does not correspond to healing of the degenerated tendon tissue and relapse remains a distinct possibility. This is the typical condition of injuries resulting from overuse, in which the symptoms vary in an unpredictable manner, in relation to time, discounting that conservative treatment may have a significant impact in the long term [42].

EPI however offers the possibility of removing the degenerated parts of the tendon and optimising the healing process in terms of time and recovery quality. This study introduces the EPI technique for the first time in the treatment of professional footballers suffering from RAGP. Its future use is proposed as a treatment solution, including complementary to conservative treatment. It is hoped, therefore, that in the future the therapeutic efficacy of this technique in the treatment of tendinopathy will be confirmed by other studies.

The main limitations of the present study are: simple study design (case series – pilot study); low patient number (only with "isolated RAGP": the inclusion/exclusion criteria were expressly strict); no control group: As the participants were members of the same football club no control group was included. The primary risk was the discovery of the existence of the two groups and the two interventions by the participants. This would have given rise to negative conduct such as leaving or requesting a change of treatment or heavily distorting the results of the proposed treatment (especially in terms of patient reported outcome); no treatment protocol validation (EPI was established recently). In the context of Groin Pain a possible development would be to evaluate the clinical results obtainable with the ultrasound-guided EPI in the treatment of Adductor Longus-related Groin Pain, which is the most frequent clinical pattern in soccer players.

Conclusion

Conclusions. Treatment with ultrasound-guided EPI has shown encouraging clinical results for RAGP. Data are preliminary: considering the limitations of this study (case series with no control group), more complex study designs are necessary to test the efficacy of the technique.

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Titles of tables and figures

Table I. The VRS and PSFS values (mean ± SD)

Table II. Summary statistics for different times evaluation

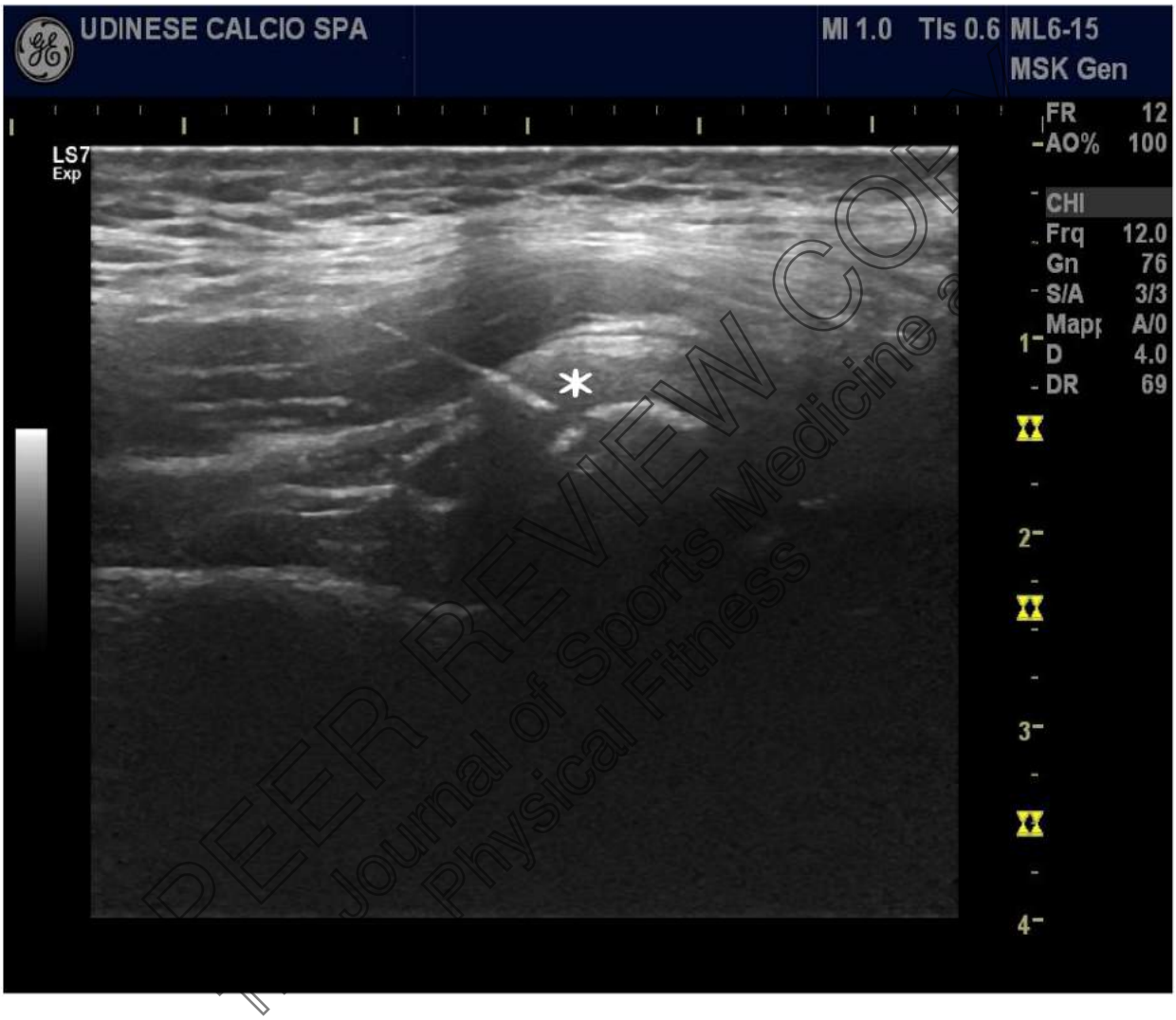
Fig.1 An author inserts the acupuncture applicator (asterisks) at the distal insertion of the Rectus Abdominis (longitudinal section). Using ultrasound, the needle can be seen and guided so as to reach the precise area to be treated.

Table I. The VRS and PSFS values (mean ± SD)

Variables	*pre*	*post24h*	*post1w*	*post1m*	*post6m*
VRSpal	9.75±0.71	4.63±2	1.25±2.12	0.00±0.00	0.00±0.00
VRScon	9±1.07	3.88±2.53	0.38±0.74	0.00±0.00	0.00±0.00
PSFSbed	3±1.85	6.50±1.41	9.75±0.71	10±0.00	10±0.00
PSFSwalk	7±2.33	8.63±1.60	10±0.00	10±0.00	10±0.00
PSFSjog	6.75±2.12	8.75±1.16	10±0.00	10±0.00	10±0.00
PSFSrun	4.50±2.45	7.75±1.16	9.75±0.71	10±0.00	10±0.00
PSFSjump	3±2.45	7.25±1.58	9.75±0.71	10±0.00	10±0.00
PSFSkick	2.25±1.91	6.75±1.16	9.50±0.93	10±0.00	10±0.00

Table II. Summary statistics for different times evaluation

Variables	pre vs. post24h ES (Magnitude of difference)	*Qualitative assessment*	pre vs. post1w ES (Magnitude of difference)	*Qualitative assessment*	post24h vs. post1w ES (Magnitude of difference)	*Qualitative assessment*
VRSpal	9.36 ± 3.69 (0/0/100)	*Almost Certainly*	14.01 ± 12.05 (4/0/96)	*Very Likely*	3.68 ± 6.61 (11/2/87)	*Likely*
VRScon	7.82±3.36 (0/0/100)	*Almost Certainly*	15.48±16.31 (6/0/94)	*Likely*	7.75±16.31 (10/0/90)	*Likely*
PSFSbed	1.41±0.51 (100/0/0)	*Almost Certainly*	2.14±0.60 (100/0/0)	*Almost Certainly*	0.80±0.25 (100/0/0)	*Almost Certainly*
PSFSwalk	0.57±0.4 (94/5/1)	*Likely*	0.95±0.60 (98/2/0)	*Very Likely*	0.38±0.30 (85/15/0)	*Likely*
PSFSjog	0.73±0.59 (93/6/1)	*Likely*	1.07±0.60 (99/1/0)	*Almost Certainly*	0.34±0.22 (87/13/0)	*Likely*
PSFSrun	0.94±0.53 (98/2/0)	*Very Likely*	1.43±0.66 (100/0/0)	*Almost Certainly*	0.48±0.21 (98/2/0)	*Very Likely*
PSFSjump	1.34±0.67 (99/1/0)	*Almost Certainly*	1.85±0.65 (100/0/0)	*Almost Certainly*	0.49±0.24 (97/3/0)	*Very Likely*
PSFSkick	1.61±0.84 (99/1/0)	*Almost Certainly*	2.45±0.65 (100/0/0)	*Almost Certainly*	0.69±0.31 (99/1/0)	*Almost Certainly*



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Clinical Image OMICS International

Intratissue Percutaneous Electrolysis (EPI®) in the Treatment of Achilles Tendinopathy

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Intratissue Percutaneous Electrolysis

Intratissue percutaneous electrolysis (EPI®) ultrasound-guided treatment [1-5] is the application of a direct current (DC) whose catodic flow is transferred to the area of the degenerative tendon [6-8] using an acupuncture needle. This accumulated electrical charge (AEC) in the degenerative tissue will produce the activation of the molecular, cellular and biological processes necessary to restore the regeneration mechanisms of the tendon (Figures 1 and 2). In recent studies it has been demonstrated that EPI® technique is effective in tendinopathy and sport muscular injuries (Figures 3 and 4).

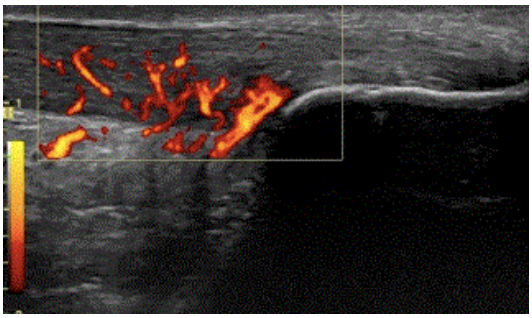

Figure 1: Ultrasound image with power Doppler. Longitudinal view of an Achilles neovascular tendinopathy with thickening of the tendon and hipoecoic image.

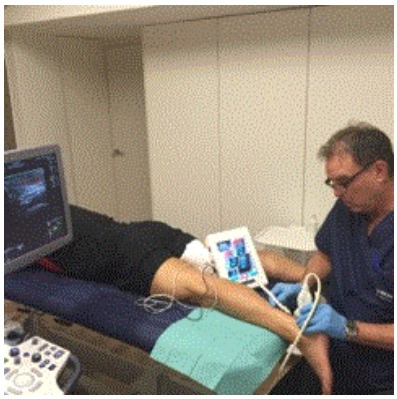

Figure 2: Achilles tendinopathy treatment using Intratissue Percutaneous Electrolysis (EPI®) technique.

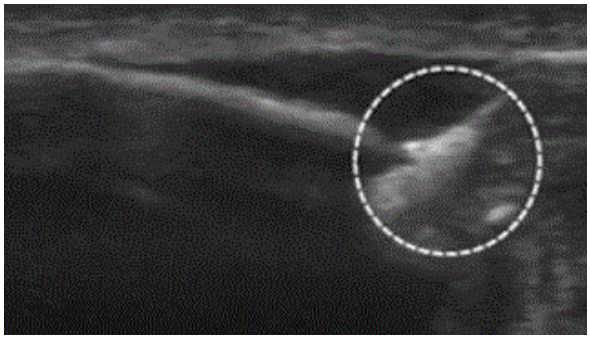

Figure 3: Hiperecoic image produced by the EPI® needle of 0.30 mm in the degenerative area of the tendon. This hiperecoic image correspondence to a gas density produced by the electrochemical response of the catodic flow (CF) in the degenerative extracellular matrix.

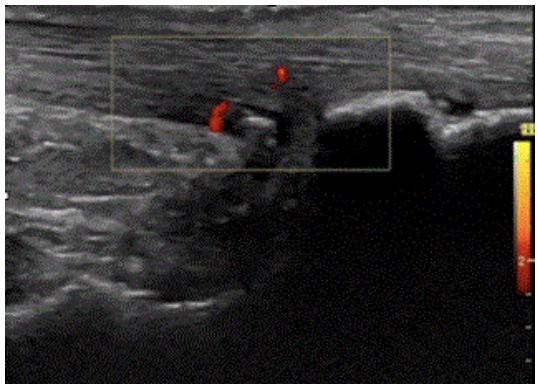

Figure 4: Ultrasound image in longitudinal view and color Doppler two months after the EPI® technique treatment ultrasound-guided. It is observed the degenerated area of the tendon that is substituted by a new connective tissue and decrease the neovascular effect.

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BMC Sports Science, Medicine & Rehabilitation

RESEARCH ARTICLE Open Access

An experimental study of muscular injury repair in a mouse model of notexin-induced lesion with EPI® technique

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Abstract

Background: The mechanisms of muscle injury repair after EPI® technique, a treatment based on electrical stimulation, have not been described. This study determines whether EPI® therapy could improve muscle damage.

Methods: Twenty-four rats were divided into a control group, Notexin group (7 and 14 days) and a Notexin + EPI group. To induce muscle injury, Notexin was injected in the quadriceps of the left extremity of rats. Pro-inflammatory interleukin 1-beta (IL-1beta) and tumoral necrosis factor-alpha (TNF-alpha) were determined by ELISA. The expression of receptor peroxisome gamma proliferator activator (PPAR-gamma), vascular endothelial growth factor (VEGF) and vascular endothelial growth factor receptor-1 (VEGF-R1) were determined by western-blot.

Results: The plasma levels of TNF-alpha and IL-1beta in Notexin-injured rats showed a significant increase compared with the control group. EPI® produced a return of TNF-alpha and IL-1beta values to control levels. PPAR-gamma expression diminished injured quadriceps muscle in rats. EPI® increased PPAR-gamma, VEGF and VEGF-R1 expressions. EPI® decreased plasma levels of pro-inflammatory TNF-alpha and IL-1beta and increased anti-inflammatory PPAR-gamma and proangiogenic factors as well as VEGF and VEGF-R1 expressions.

Conclusion: The EPI® technique may affect inflammatory mediators in damaged muscle tissue and influences the new vascularization of the injured area. These results suggest that EPI® might represent a useful new therapy for the treatment of muscle injuries. Although our study in rats may represent a valid approach to evaluate EPI® treatment, studies designed to determine how the EPI® treatment may affect recovery of injury in humans are needed.

Keywords: EPI, Technique, Notexin-induced, Muscle, Injury

Background

Soft tissue injuries are recurrent in sports and have an incidence rate of some 30% [1]. An overly conservative therapeutic approach conflicts with patients' economics interests and the ability to practice their chosen sport. Some authors have proposed qualitative and histopathological classifications of muscle injuries directly related to the appearance of the lesion and its evolution [2].

The inflammatory process is one of the most important parts of the immune system's response to injury. It is due to the fact that the biochemical mechanism and the signal cascade are consistent and durable, independent of the underlying cause of the wound [3]. Non-muscle cells such as leukocytes, phagocytes, macrophages, cytokines or growth factors play an important role in the inflammatory process in terms of recovery and regeneration following injury to the muscle as well as in the secondary damage that occurs during the inflammatory process. Certain substances, such as interleukin 1-β (IL-1β), released from the muscle injury act as intercellular messengers, start the process of inflammation and repair [4]. Moreover, tumor necrosis factor-alpha (TNF-α) is an important mediator of the inflammatory response after injury [5] whereas activation of PPAR, an anti-inflammatory protein, suppresses pro-inflammatory processes [6,7]. As a result of muscle injury, localized

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vasodilatation induced by two mechanisms comes about through the release of histamines from the cells present within the damaged area and by activating the route of the vascular endothelial growth factor and nitric oxide (VEGF-NO) [8]. VEGF is the most important capillary growth factor in skeletal muscle [7] and is essential to basal capillarization in the tissue and increased capillary growth in response to different mechanical stimuli [9].

Electrical stimulations are likely to serve as an integrator to organize cells into structured tissues in wound healing, development and tissues regeneration. Because cells possess signaling systems that make for electric stimulation, the exogenous application of therapeutic currents for wound healing is considered to have effects as well. The difficulties lie in the technical details such as types of electrodes, stimulation parameters, stimulation position, and the variability of intrinsic resistance [10].

The EPI® technique is an ultrasound guided physiotherapeutic and medical technique that consists in causing, by means of a galvanic current transmitted through an acupuncture needle, localized lysis in the damaged and/or degenerated tissue [11-13]. The application of a galvanic current brings about a chemical reaction, which causes the dissociation of molecules of sodium chloride and water. This process results in the formation of molecules of sodium hydroxide, which cause the destruction of the damaged tissue and activate the inflammatory repair response. The application of EPI® can stimulate the inflammatory response and promote wound healing in degenerated patellar tendon in rats [11] and has proven effective in the treatment of chronic patellar tendinopathy [12,13].

Currently there is no published basic research relative to the effect on muscle tissue injury upon applying this treatment. Accordingly, the objective of this study was to determine whether the application of EPI® therapy could have a beneficial effect on damaged muscle. An experimental design was carried out with the EPI® treatment after 7 days of Notexin-induced injury. Notexin has been described as inducing necrosis of skeletal muscle fibers in experimental inflammation models. Notexin, a presynaptic phospholipase A_2 neurotoxin isolated from snake venom, produced inflammatory events associated with enzymatic activity and the release of arachidonic acid metabolites or mechanism related to phospholipid hydrolysis [14].

The experimental hypothesis is that the application of intratissue percutaneous electrolysis therapy after Notexina induced muscle damage causes muscular effects that may be conducive to the recovery of injured muscle tissue.

Methods

Twenty-four Sprague-Dawley rats weighing 250-300g were divided into four groups. To induce muscle injury, 200 μl of Notexin was injected intramuscularly at a concentration of 10 μg/ml in the quadriceps of the left extremity, causing total degeneration of the muscle. As control, a group of rats (n = 6) were injected with 200 μl of saline solution. At seven days, rats were sacrificed and samples were obtained to determine the effects of Notexin-induced muscle injury. To study the effects of EPI® treatment on tissue injury, a specific approved EPI® device (EPI Advanced Medicine, Barcelona, Spain) was used. The following protocol was performed: on day seven of Notexin-induced muscle injury, one group of rats (n = 6) were treated with EPI®. This treatment consists in the application of a continuous current of 4 pulses at an intensity of 3 mA for 5 seconds conveyed to the muscle. As an electrode, an acupuncture needle with a diameter of 0.32 mm was used. To study how the injury evolves without receiving EPI® treatment, another group of rats (n = 6) was maintained dover 14 days after Notexin-induced injury. Previous to each treatment, rats were anesthetized intraperitoneally with sodium pentobarbital (90 mg/kg). The evolution of the muscle tissue injury was assessed by means of ultrasound images. The same evaluations were carried out after seven days of EPI® treatment. After the protocol, rats were sacrificed and muscle tissue was removed from the treatment area and samples were analyzed by using Western blot. Additionally blood samples were collected to detect TNF-α and IL-1β cytokines plasma levels with ELISA. The Ethical Committee of the University of Medicine of Valencia, Spain (A1301314899794) approved the study. All animal procedures were carried out in accordance with the European legislation on the use and care of laboratory animals (CEE 86/609).

Ultrasonography was performed before and after EPI® treatment to follow up on the muscle tissue injury induced by Notexin (Figure 1). This examination was performed according to the protocol previously described [15].

Plasma levels of cytokines IL-1β and tumor necrosis factor-α (TNF-α) were determined with ELISA kits (Thermo Scientific Laboratories, Rockford, USA) following manufactorer's recommendations.

Muscle tissues were homogenized in a lysis buffer of (in mM) 50 Tris-HCl, 125 NaCl, 1 EDTA, 1 EGTA and 1% Nonidet (NP-40 containing 5% Complete Mini-tab cocktail proteinase inhibitor (Roche Biochemicals). It was then centrifuged at 10000 rpm for 15 min at 4°C. The protein concentration was determined using a modified Lowry method. Protein was resolved in 12% SDS-PAGE and electrophoretically transferred onto a PVDF-membrane using a Mini Trans-Blot cell (BioRad laboratories, California). Membranes were put in blocks in 5% skim milk for 1 hour at room temperature and then incubated with the corresponding antibodies following the

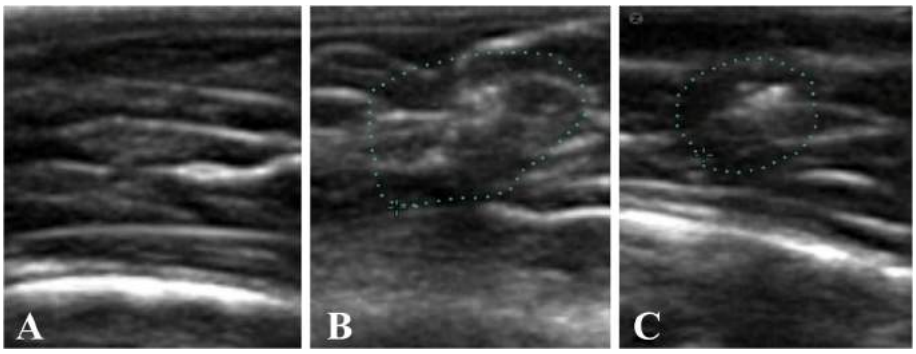

Figure 1 Comparison control tissue **(A)**, muscle tissue 21 days after injury induction with Notexina **(B)** and the effect of the application of EPI® from7 days of the induced lesion **(C)** in ultrasound imaging (US). It is possible to observe the area of disruption in the middle portion of the quadriceps muscle of rats from 21 days of the induced lesion (surrounded area), compared to normal tissue from the same area **(B)**. Image **(C)** shows an area of less disruption in the same muscle portion treated with EPI® from 21 days after induction of injury (surrounded area).

manufacturer's recommendations. After washing, the membranes were incubated with horseradish peroxidase-conjugated secondary antibody (Sigma Aldrich). The blots were then visualized using a InmunostarTM HRP Substrate Kit (BioRad), again, in accordance with manufacturer's instructions. The relative densities of the bands were analyzed using Image Gauge v4.0, Fujifilm. The proteins were normalized with tubulin. Monoclonal anti-vascular endothelial growth factor (VEGF) (1:500), anti-vascular endothelial growth factor receptor 1 (VEGF-R1) (1:500), anti-PPAR-γ (1:500) and anti-tubulin (1:1000) were used.

For statistical analysis, data are expressed as mean ± standard deviation (SD). An analysis of variance (ANOVA factor) was performed to analyze the relationships within and between variables. Post-Hoc and Dunnet tests were also done to compare the different groups with the control group and the Scheffe test was used to compare all groups. A probability value of less than 0.05 was considered significant.

Results

Notexin produced tissue injury characterized as an anechoic ultrasound image with fluid collection corresponding to a muscle lesion (Figure 2A). Treatment with EPI® produced resorption of the fluid and repair without scar tissue thickening (Figure 2B).

The levels of TNF-α and IL-1β pro-inflammatory factors in Notexin injured rats showed a significant increase ($p < 0.05$) in plasma concentration relative to the control. In addition, a significant decrease in the concentration of TNF-α and IL-1β was observed when the Notexin + EPI group and the Notexin group ($p < 0.05$) were compared. So, the application of the EPI® treatment after Notexin provoked the decrease of both TNF-α and IL-1β to control levels (Figure 3A and B). After 14 days of Notexin treatment without EPI® application, the values of cytokines continued increased (Figure 3A and B). These results rule out spontaneous recovery of the muscle damage.

Similarly, Notexin-induced injury decreases PPAR-γ expression values ($p < 0.05$) in rat quadriceps muscle. The application of EPI® increased PPAR-γ expression and were returned to the values of the control, showing that EPI® treatment produces an improvement in anti-inflammatory PPAR-γ protein (Figure 4). Furthermore, at 14 days of Notexin treatment without EPI® application, PPAR-γ protein expression remains decreased, thus indicating that an increase in PPAR-γ protein expression is not spontaneous but due to the EPI® treatment.

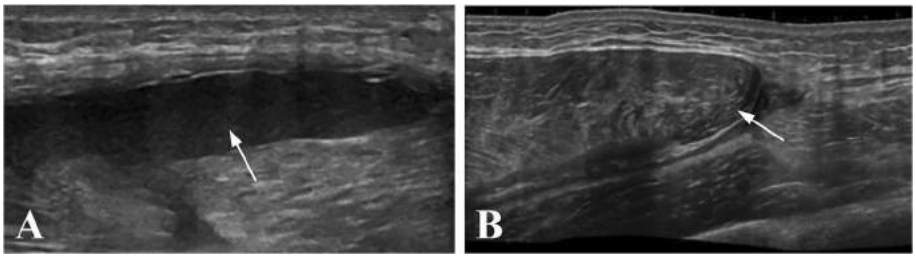

Figure 2 Longitudinal ultrasound images of left rat quadriceps. After 7 days treated with Notexin **(A)**, an anechoic image with fluid collection (arrow) indicating muscle lesion was observed. After EPI® treatment **(B)** a complete resorption of the haematoma with muscle repair (arrow) can be seen.

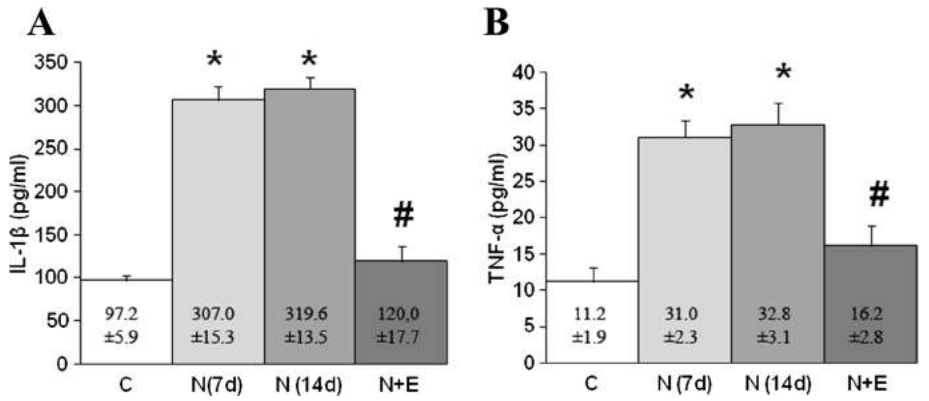

Figure 3 Plasma levels of IL-1β **(A)** and TNF-α **(B)** in control (C), Notexin (N7d, N14 d) and Notexin + EPI (N + E) groups. Values were measured by ELISA assay as indicated in methods. Data are mean ± SD of six independent experiments. *$p < 0.05$ *vs* control group; # $p < 0.05$ vs both Notexin groups.

Notexin (7 and 14 days) treatment produced an increase in both VEGF and VEGF-R1 protein expression compared with the control ($p < 0.05$). Furthermore, EPI® treatment significantly potentiated the increase in VEGF and VEGF-R1 protein expression induced by Notexin (Figure 5).

No adverse events were presented during the study.

Discussion

The main findings of this study is that EPI® applied after Notexin-induced muscle injury in rats decreases the production of the inflammatory mediators TNF-α and IL-1β, increases the protein expression of anti-inflammatory factor PPAR-γ and the angiogenic involved proteins VEGF and VEGF-R1.

An increase in the TNF-α plasma levels was described in the first days of tissular injury [16,17] and remained elevated due to its action on cellular necrosis [18]. TNF-α disrupts the differentiation process and can promote cell catabolism thereby accelerating protein degradation [5]. Furthermore, TNF-α inhibits myogenesis through redox-dependent and independent pathways [19]. One potential mechanism by which TNF-α might directly stimulate catabolism is by inhibiting myoblast differentiation, an action that might limit the regenerative response of satellite cells to muscle injury [5]. A second mechanism, apoptosis, appears less important. The third mechanism consists in a direct catabolic effect on muscle tissue. In a muscular cell culture, TNF-α directly decreases total muscle protein and the loss of muscle-specific proteins, including adult fast-type myosin heavy chain [5,19].

Our data shows an increase in the plasma level of TNF-α due to Notexin-induced injury. EPI® treatment normalized the levels of TNF-α to reach control group values. By contrast, in the group of rats without EPI® treatment, the TNF-α levels remained elevated with respect to the control group at 14 days after application.

TNF-α action is also sensitive to other ligand/receptor interactions (e.g. interleukin-1 and interleukin-6). Notexin caused a significant increase of IL-1β compared to the control group. The maintenance of IL-1β over time has been associated with its condition as a pro-inflammatory cytokine more than for its action on tissue necrosis [16].

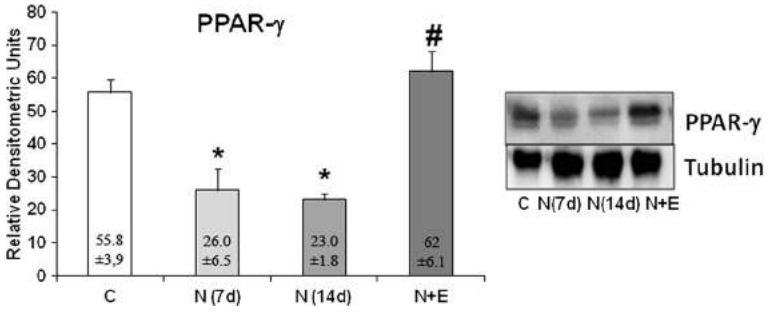

Figure 4 PPAR-γ protein expression (relative densitometric units) in control (C), Notexin (N7d, N14 d) and Notexin + EPI (N + E) groups. Values were determined in left rat quadriceps muscles by Western blot. A representative inmunoblot is shown and tubulin was used as control amount of protein. Data are mean ± SD of six independent experiments. *$p < 0.05$ *vs* control group; # $p < 0.05$ vs both Notexin groups.

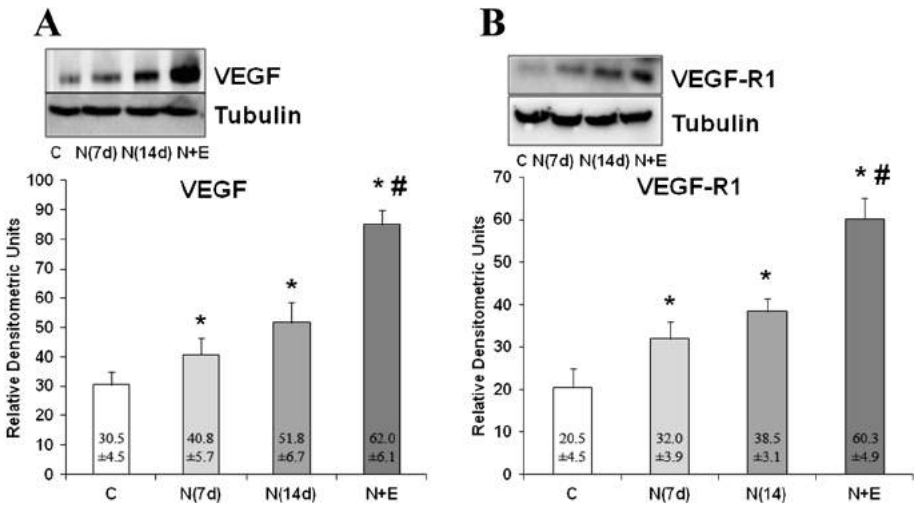

Figure 5 Analysis of VEGF and VEGF-R1 proteins. VEGF **(A)** and VEGF-R1 **(B)** protein expression in control (C), Notexin (N7d, N14 d) and Notexin + EPI (N + E) groups were determined by Western blot. Values were determined in left rat quadriceps muscles. In each panel, a representative inmunoblot is shown and tubulin was used as control amount of protein. Data are mean ± SD of six independent experiments. *$p < 0.05$ *vs* control group; # $p < 0.05$ vs both Notexin groups.

Furthermore, IL-1β induces inhibition of protein synthesis in skeletal muscle [20]. EPI® treatment returns IL-1β plasma levels to normal values. On the contrary, after 14 days of application without EPI®, the levels of IL-1β remain significantly high compared to control values. Taken together, the results indicate that EPI® treatment is effective in diminishing pro-inflammatory mediators. Further studies are needs to determine the mechanisms involved in the inflammatory effects of EPI® treatment. Besides that, EPI® decreases pro-inflammatory mediators and anti-inflammatory proteins may also be activated. PPAR-γ has been recognized as playing a fundamental role in the immune response through its ability to decrease the expression of pro-inflammatory genes [21]. It also increases the expression levels of genes that are involved in anti-inflammatory effects and tissue repair [22,23]. Furthermore, PPAR-γ induces the expression of VEGF and its receptors in cultured cardiac myofibroblasts [24]. Our data indicated that Notexin produced a significant decrease in PPAR-γ protein expression, similar at 7 and 14 days, compared with control. EPI® treatment significantly increases PPAR-γ protein expression reduced by Notexin and returns levels to control values. In addition, PPAR-γ promotes the myocellular storage of energy by increasing fatty acid uptake and esterification while simultaneously enhancing insulin signaling and glycogen formation, which have beneficial effects on metabolic health and therefore on tissue repair [25].

Electrical stimulation has multiple effects in directing cell division, vascular endothelial cells, angiogenesis and endothelial migration, all of which are important elements in wound healing [10]. Vascular endothelial growth factor (VEGF) is a paracrine factor. Its main function is to promote angiogenesis by improving cellular survival, inducing proliferation and enhancing the migration and invasion of endothelial cells. Skeletal muscle fibers can control capillary growth by releasing VEGF from intracellular vesicles during contraction [26]. Recent evidence suggests that VEGF has effects on skeletal muscle regeneration by stimulating the myogenic differentiation of muscle-derived stem cells [27,28].

Our results indicate a clear induction of VEGF protein expression after Notexin-induced damage. These results are in accordance with a greater production of VEGF in damaged tissue than in normal tissue [29]. Furthermore, VEGF-R1, the more actively induced receptor by tissue injury, is also increased as has been described in trauma patients [30]. EPI® treatment further significantly increases both VEGF and VEGF-R1 thus suggesting an active role in maintaining blood flow in the microcirculation and also may increase the systemic level of soluble anti-inflammatory and cytoprotective mediator events that can improve the recovery from injury [30].

Despite the many treatments proposed to treat muscle injuries, the rate of re-injury is still very high. This is probably due to the fact that a greater understanding and analysis of the type, size and location of the lesion in each case [31] is required.

Some authors argue that the size of the lesion correlates with the time the patient will need to return to competition [32]. By contrast, other study groups suggest that neither the presence of ultrasound findings nor the size of them correlate with the time needed to return

to competition. Thus, the prognosis for muscular injuries should not be guided by these results alone [33,34].

Although the number of cases may be considered low, the difference between the variables studied was very high. Therefore, sufficient power was obtained so as to detect differences with a significance ranging from 55 to 58% for VEGF and VEGF-R1 variables as well as from 88% to 100% in TNF and IL-1B variables.

The work has some limitations such as the use of rats. As such, it might not be possible to extrapolate the result to humans. In spite of that possibility, rats have been used in many valid experimental studies [14-17,20,27]. Another limitation is the lack of a histological or functional evaluation, which could give physiological relevance to the interpretation of the data presented [35]. The electrolysis and/or sodium hydroxide produced by the EPI® technique may interfere with IL-1beta and TNF-alpha values, affecting the existing cytokines. Therefore, we wait 7 days after the EPI® technique application to see its beneficial effects. Cytokines from the cells at the local position will be produced chronically and maintained over time when inflammation and damage is present. We detect a reduction of pro-inflammatory cytokines after EPI® induction. Thus, cells are probably in a state of less inflammation with less cytokine production in comparison to cells without the EPI® technique.

Despite the limitations exposed, the present work is the first investigation on the effect of EPI® on muscle tissue that shows the biomolecular mechanisms triggered by the application of the same. This experimental work is the basis upon which clinical trials to confirm the effectiveness of the EPI® in humans should be developed.

Conclusion

The application of EPI® on rat muscle previously injured with Notexin causes a significant decrease in pro-inflammatory mediators like TNF-α as well as IL-1β levels. On the other hand, the application of EPI® produced an increase in the expression of anti-inflammatory proteins (PPAR-γ) and also increases VEGF and VEGF-R1 expression. Therefore, the use of EPI® may affect inflammatory mediators in damaged muscle tissue and influence the new vascularization of the injured area. These results suggest that EPI® might represent a useful new therapy for the treatment of muscle injuries.

Although our study in rats may represent a valid approach to evaluate EPI® treatment, studies designed to determine how EPI® treatment may affect recovery of injury in humans are needed.

Competing interests

The authors declare that one of the author (SIJM) have the patent for the EPI® devices. This author has participated in the intervention process, but not in data acquisition and/or the analysis of this study. All authors have made substantial contributions to the conception and design of the study, acquisition of data, the analysis and interpretation of data, drafting the article, revising it critically for important intellectual content and final approval of the version submitted. No fundings was obtained for this study.

Authors' contributions

AF, SLV, SIJM, PEG and MJC conceived of the study, and participated in its design and coordination and drafted the manuscript. AF, SLV, SIJM and GHS carried out the immunoassays and helped to draft the manuscript. PF, JA, SLV and GHS carried out the molecular studies helped to draft the manuscript. All authors read and approved the final manuscript.

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Original article

Effectiveness of the Intratissue Percutaneous Electrolysis (EPI®) technique and isoinertial eccentric exercise in the treatment of patellar tendinopathy at two years follow-up

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Summary

Objectives: **to show the effect of Intratissue Percutaneous Electrolysis (EPI®) combined with eccentric programme in the treatment of patellar tendinopathy.**
Methods: **prospective study of 33 athlete-patients consecutively treated for insertional tendinopathy with Intratissue Percutaneous Electrolysis (EPI®) and followed for 2 years. Functional assessment was performed at the first visit, at three months and two years with the Tegner scale and VISA-P.**
Results: **an average improvement in the VISA-P of 35 points was obtained. The mean duration of treatment was 4.5 weeks. Some 78.8% of the patients returned to the same level of physical activity as before the injury by the end of treatment, reaching 100% at two years.**
Conclusion: **intratissue percutaneous electrolysis (EPI®) combined with an eccentric-based rehab program offers excellent results in terms of the clinical and functional improvement of the patellar tendon with low morbidity in a short-term period.**
Level of Evidence: **Therapy, level 4.**

KEY WORDS: EPI, intratissue percutaneous electrolysis, patellar, tendinopathy, tenopathy, eccentric.

Introduction

The treatment of tendinopathy is a clinical challenge that some authors describe as one of the biggest problems in sports medicine[1,2]. Some studies suggest the use of the term tendinosis as it has proven to be more a degenerative condition rather than inflammatory[3]. Furthermore, authors like Maffulli[4,5] recommend using the term tendinopathy or tenopathy because it is a broader term that describes changes in and around the tendon. Recent studies emphasize the complex three-dimensional structure of the tendon[6].
Patellar tendon injuries are generally found on the insertional level at the attachment of the tendon at the inferior pole of the patella. It usually presents with pain in the tendon, tenderness to palpation and anterior knee pain[1]. Patellar tenopathy has a variable rate of prevalence and can reach 40 to 50% in sports like volleyball or those that involve jumping or braking[1,2]. The important degenerative changes in the development of tendinopathy are significant. They may even arrive at producing changes in the muscle ultrastructure after tendon rupture[7,8].
Intratissue Percutaneous Electrolysis (EPI®) is an ultrasound-guided physiotherapeutic and medical technique that produces a non-thermal electrochemical ablation using a cathode flow directly oriented toward the tendon degeneration. The EPI® treatment causes an organic reaction that produces localized inflammation, exclusively in the treatment zone, that leads to rapid regeneration of injured tendon[9,10].
Different techniques are currently used to treat patellar tenopathy[11-13]. The purpose of this paper is to show the effect of Intratissue percutaneous electrolysis (EPI®) guided by ultrasound together with an eccentric programme in the treatment of patellar tendinopathy. The working hypothesis is that EPI® combined with eccentric exercises improves the clinical aspect and functionality in patellar tendinopathy over a short period of time.

Method

It was a prospective study of 33 patients diagnosed with insertional patellar tendinopathy treated by the same therapist. The diagnosis of all patients was

based on clinical examination and a color Doppler ultrasound study with a linear probe (6-15MHz).
The patients' demographic variables and pre-injury and post-treatment functional statuses were studied. The clinical research ethics committee of our institution (08/062/0048) approved the study. To be included in the study, patients had to sign informed consent agreeing to treatment as well as the prospect of having pain in the lower insertional pole of the patella, living with the presence of pain for a minimum of 4 weeks, accepting the inability to continue participating in their sport and confirming an age of under 60 years old. Patients who presented with chronic arthropathy or another associated knee injury (such as a cruciate ligament injury or meniscopathy) were excluded. The use of anti-inflammatory drugs or corticosteroids was restricted throughout the first three months of the study. Patients received the Intratissue percutaneous electrolysis (EPI®) technique treatment until there was clinical improvement or no improvement in the symptomology was seen after 10 sessions.

Follow-up evaluation

Functional assessment was performed using the validated scale of the *Victorian Institute of Sport Assessment for the patellar tendon* (VISA-P)[14] and the Tegner scale. The VISA-P score ranges from 0 to a theoretical 100 when the patient is asymptomatic. The Tegner scale classifies patients according to their level of activity where zero is no activity or walking on a flat smooth floor and 10 is competitive sport at the highest level. The values of the scales were compiled from the written questionnaires given during patients' visits to the clinic; at the initial consultation, at discharge, at 3 months and in the evolutional control at 2 years. Patients were divided into two groups according to their initial symptomatology based on the VISA-P score. Group 1 was made up of patients whose VISA-P value was less than 50 and Group 2 was those whose VISA-P value was greater than 50. This division makes it possible to display the results depending on the degree of injury (more affected VISA-P<50 or less affected VISA-P >50).
At the same times as the functional assessment, patient satisfaction the EPI® treatment was evaluated with the Roles and Maudsley scale[15]. It classifies the degree of satisfaction as excellent (no pain and full activity), good (occasional discomfort with full activity), reasonable (occasional discomfort after prolonged activity) or poor (pain that limits activity).

Treatment Protocol

The EPI® technique described here should be performed with a specifically developed medically (EPI Advanced Medicine. Barcelona. Spain) certified device[9,10] (Directive 93/42/EEC) (Fig. 1A). It produces an adjustable galvanic current through a negative flow cathode electrode. For transmission of the flow to the treatment area, needles of from 0.30 to 0.32 mm in diameter and a modified electric scalpel are used (Fig. 1B). The intensity can be adjusted by changing both the duration and the milliamperes that are administered. Placement of the patient supine to minimize potential vagal reactions following the puncture is recommended. A thorough ultrasound inspection with a 6-15 MHz linear probe and color Doppler, following the European Society of Musculoskeletal Radiology guidelines[16], was performed to permit the identification of any existent neovascularization (Figs. 2 A,B) and changes in terms of structural improvement and decreased neovascularization obtained with the EPI® treatment (Figs. 2 C,D). Preparation of the skin with isopropyl alcohol before puncture is required despite the bacteriostatic action the device has. Subsequently, 3 milliamps echo-guided punc-

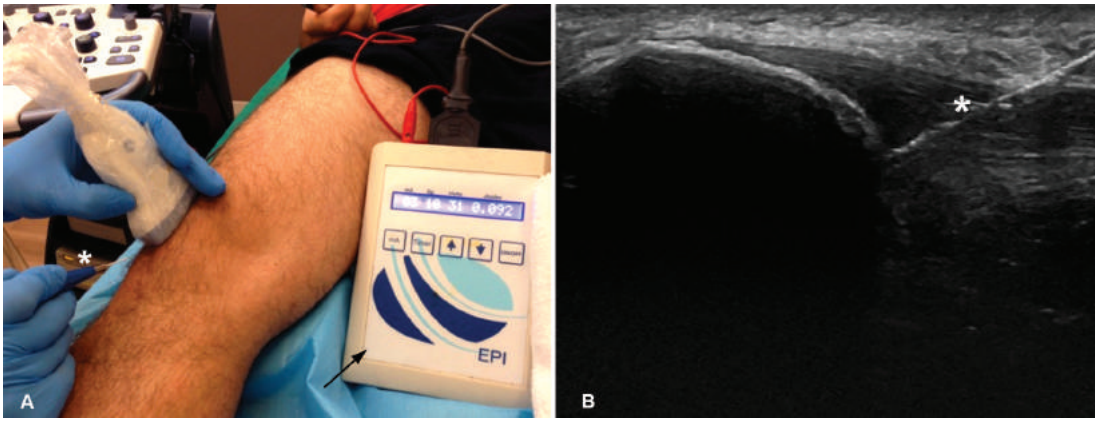

Figure 1. **A**. Device designed specifically to administer Intratissue percutaneous electrolysis (arrow). Echo-guided punctures (*) for the administration to specific areas of treatment with a 0.3mm needle located with ultrasound targeting the treatment area. **B**. The image belongs to higher hyperechogenicity of the needle, increasing when the cathode flow passes form EPI® through it (*).

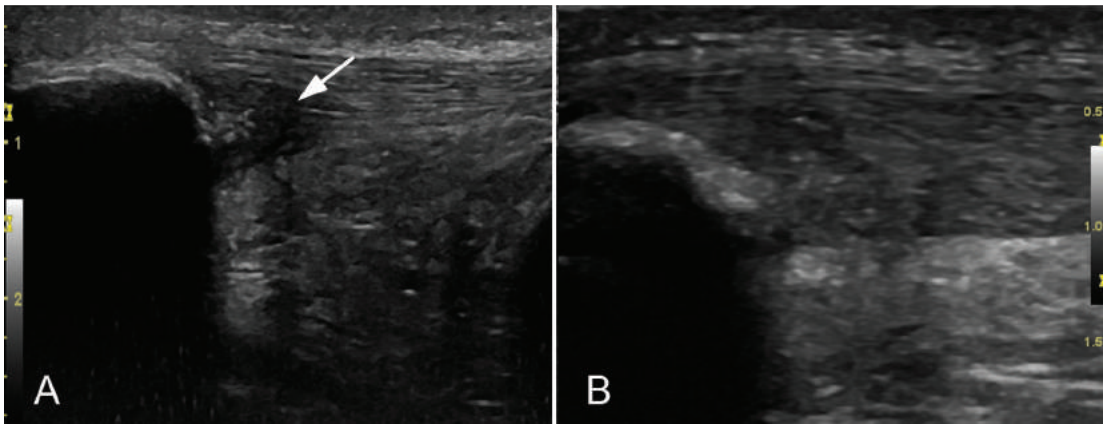

Figure 2. Ultrasound high-resolution Gray-scale longitudinal view with 6-15 MHz lineal probe image of the proximal patellar tendon pre-treatment with EPI® (**A**) and 3 months of treatment (**B**) in the same patient. In the pre-treatment image (**A**) intensive hypoechoic zones (arrow) and thickened tendon is shown. At the lower pole of the patella, cortical irregularities were detected. In post EPI® treatment image (**B**) a significant decrease of the hypoechoic zones and echotexture improvement was detected (arrow).

tures are made with the device to obtain controlled debridement of the injured tendon. The debridement was assessed with the sonographic images.

All patients received a weekly session of EPI® and two weekly sessions of eccentric exercise using isoinertial resistance machines (YoYo^{TM} Technology AB, Stockholm, Sweden) consisting of 3 sets of 10 repetitions. Each repetition was performed with the concentric phase with both extremities whereas the eccentric phase was only performed with the affected limb at a maximum 60º of knee flexion as recommended by Romero-Rodriguez[17].

Statistical Analysis

Initially, the comparison of the basal situation of the study patients was taken up. Quantitative variables were described based on their mean value and standard deviation (SD). The comparison was terminated with a t-test of independent data, without assuming the existence of homoscedasticity. For ordinal variables, the median of each group as well as the minimum and maximum values were provided. For categorical variables, the percentage and the number of cases and inference using Fisher's exact test or Chi-square was calculated. An ANOVA study was used to analyze the different variables and the sphericity correction was carried out with the Greenhouse-Geisser test. Statistical analysis was performed with SPSS v.18 (SPSS Inc., Chicago, Illinois) with statistical significance set at 0.05.

Results

Thirty-three patients were available for the final assessment at two years. Both groups were comparable in terms of in age (p=0.536), gender (p=0.335), dominant limb (p=0.398) or affected side (p=0.093). The mean age was 25.3 years (range 16-53). The patellar tendon affectation was located in the dominant limb in 48.5% (n=16) of the patients. The patients consisted of some 12.1% (n=4) women and 87.9% (n=29) men. Some 57.6% (n=19) of the patients were football players, 3% (n=1) basketball players, 3% (n=1) played volleyball and the remaining 36.4% (n=12) engaged in other sports often involving vertical jumping. A sportsperson from first division or a similar classification by type of sport was considered professional. Second division sportspeople who were always paid for to practice it were considered semi-professional and amateurs were those who practiced sport with no economic incentive. Some 12.1% (n=4) were practicing their sport at the professional level, another 66.7% (n=22) at the semi-professional level and 21.2% (n=7) at the amateur level.

The mean duration of the symptoms of pain in the patellar tendon before coming to our center was 19 months (range 1-72 months). Patients had to have left their sport because of that pain for a mean period of 11.6 months (range 0-48). Treatment with EPI® lasted an average of 4.5 weeks (range 1-10) with a need for an average 4.4 sessions (range 1-10). According to the Roles and Maudsley scale, patient satisfaction at end of treatment at 3 months was excellent in 26 cases (78.8%), good in 6 cases (18.2%) and fair in 1 case (3%). At two years follow up, 87.9% of the patients (n=29) scored their satisfaction as excellent and the remaining 12.1% (n=4) as good. No adverse effects occurred during treatment or follow-up.

Functional Results

The overall pretreatment value of the VISA-P (Fig. 3) was 50.7 ± 21.6 points (range 10-90). This value in-

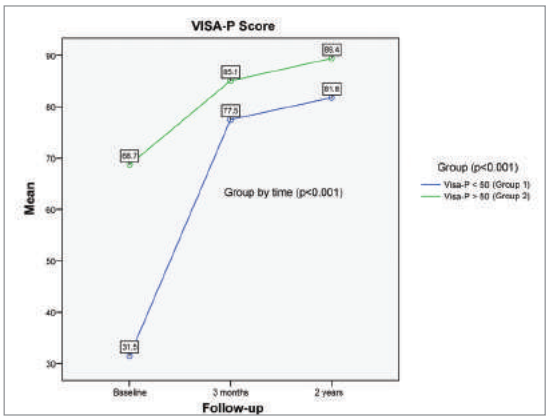

Figure 3. Column chart of the VISA-P values throughout follow up.

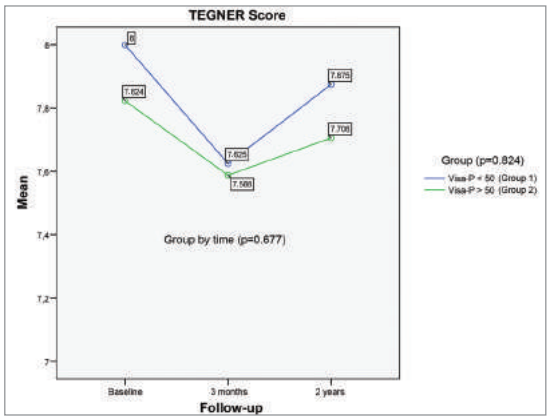

Figure 4. Lineal representation of the mean Tegner values during the follow-up.

creased significantly to 81.4 ± 12.8 points (range 55-100) at 3 months (p<0.001) and maintained a slight improvement with 85.7 ± 11.9 points (range 60-100) at 2 years (p<0.001). Upon studying the value of the VISA-P groups, the fact that group 1 had a pretreatment value of 31.5 ± 10.9 points (range 10-48), improving to 77.5 ± 15.3 points (range 55-99) at 3 months (p<0.001) and to 81.8 ± 14.5 points (range 60-99) at 2 years (p<0.001) was observed. Similar behavior was seen in group 2 where the initial value of the VISA-P was 68.7 ± 10.3 points (range 52-90), improving to 85.1 ± 9 points (range 60-100) at 3 months (p <0.001) and to 89.4 ± 7.6 points (range 70-100) at 2 years (p<0.001). In the comparison between the two groups, it can be seen that at both 3 months (p=0.091) and two years (p=0.065), there are no differences in values on the VISA-P scale. The Greenhouse-Geisser test showed a statistical significance of p <0.001 for the different VISA-P values throughout the time intervals for the two groups. In turn, there were no statistically significant differences when comparing those patients who performed professional sports versus those who performed at the semi-professional or amateur level.

The average pre-injury Tegner value was 7.9 points (range 4-10), showing a value of 7.6 points (range 3-10) after three months of treatment, showing no statistically significant differences (p=0.677) compared to the assessment at two years of 7.8 points (range 4-10). Group 1 (Fig. 4) started from a Tegner of 8 points (range 6-10) before treatment and reached 7.6 points (range 4-10) at 3 months and 7.9 points (range 5-10) at 2 years (p=0.824). Group 2 showed a similar trend, starting from a pretreatment value of 7.8 (range 4-9), standing at 7.6 points (range 3-9) at 3 months and 7.7 points (range 4.9) (p=0.824) at two years. Of those patients who were considered professional athletes (pre-injury Tegner 10 points) at three months, 100% (n=4) returned to the same level of sport activity and stayed at the same level in the control at two years. Of the semi-professional group, with a pre-injury Tegner average of 8.1 (range 7-9), 81.8% (n=18) were able to practice their sport at the same level as before the injury at 3 months and 18.2% (n=4) were practicing at the control of two years. In the amateur group, which started from a pre-injury Tegner of 6 points (range 4-8), 57.1% (n=4) were able to return to their sport at the same level, while 42.9% (n=3) did it at the control at 2 years. Some 78.8% of the patients returned to the same level of physical activity as before the injury by the end of treatment, reaching 100% at two years. The relationship between treatment duration and Tegner values obtained are not significant (p=0.677). The difference between the groups is not significant (p=0.824).

Discussion

The principal finding of this study was the fact that when Intratissue percutaneous electrolysis (EPI®) was combined with eccentric exercise, superior results were found compared to studies using eccentrics only[18-20]. Equally good outcomes were achieved in a short period of time without comorbidities are shown in the presented treatment of insertional patellar tendinopathy.

The main limitation of this study is focused on combining intratissue percutaneous electrolysis (EPI®) with eccentric exercise. However, this combination is frequent in studies of tendinopathy. Thereupon, future studies should compare Eccentrics only versus Eccentrics plus EPI®. The lack of control group (difficult in private practice) and external validation must also be highlighted. Finally, a study with a mean follow-up time (two years) is presented. Thus, an RCT with a longer follow up would be necessary to demonstrate that this benefit lasts over time. Despite these limitations, this study provides the first analysis for up to two years of the treatment of patellar tendinopathy with intratissue percutaneous electrolysis (EPI®) in combination with eccentrics.

Percutaneous electro-stimulation with an electrolytic effect, denominated intratissue percutaneous electrol-

ysis (EPI®), is a minimally invasive technique that involves the application of a galvanic current of high intensity through an acupuncture needle that stimulates a local inflammatory process in soft tissue. It makes phagocytosis and the repair of the affected tissue possible[9,10]. As shown in this work, electrolysis combined with eccentrics has brought about a notable improvement (average 35 point increase in the VISA-P) that allows for the resumption of sports activity to pre-injury levels in few sessions (mean 4.4), a short recovery period (average of 4.5 weeks) and low morbidity.

Multiple therapies for the treatment of patellar tendinopathy have been put forward but not one of them has been set as the standard treatment[18-30]. The role of physiotherapy in the treatment of tenopathies remains unclear and it is not possible to draw any conclusions about its effectiveness based on scientific evidence[19,20]. Eccentric exercises are included within the few measures that have demonstrated efficacy in the treatment of these conditions. The problem is that the results are expressed in the medium and long term, between 3 to 6 months, with a mean cure of 40% to 60%[20]. Diathermy raises the temperature of the deep tissue from 41 to 45°C by means of electromagnetic energy. Recent research in long head biceps tendinopathy showed that hyperthermia is effective in the short-term, but it requires long-term monitoring to confirm its therapeutic efficacy[28]. Extracorporeal shock wave is also used for sports physiotherapy and for the treatment of tenopathies. However, a meta-analysis performed by Maffulli et al.[19] concluded that, on the basis of present knowledge, it is not recommended as a suitable protocol for the specific treatment of tenopathies.

In the case of the patellar tendon tenopathy, most patients opt for surgical treatment when conservative treatment fails. This achieves good or excellent results in 45% of the cases. These results are not higher than those obtained with eccentric exercise[18]. Recently, some novel methods have been proposed for the treatment of tenopathy. They include the likes of injections with platelet rich plasma (PRP)[27], injections with polidocanol[26] and injections of aprotinin[29]. Then again, these techniques require further study to demonstrate their effectiveness and consistency in the medium or long term.

Conclusion

The combination of Intratissue percutaneous electrolysis (EPI®) and eccentric exercise offers excellent results in terms of clinical and functional improvement in patellar tendinopathy with low morbidity in a half study period.

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Research Article Open Access

Large Tear of the Pectoralis Major Muscle in an Athlete. Results after Treatment with Intratissue Percutaneous Electrolysis (EPI®)

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Abstract

Background: Injuries to the pectoral is major muscle can result in functional limitation. Previous reports on conservative treatment on large tears of the pectoral is major muscle showed inconsistent results with several treatment modalities. The best option to treat this pathology is still under discussion.

Methods: A 30 year-old male patient with a large pectoral is major muscle tear was treated with ultrasound-guided EPI® technique once a week and eccentric exercise. Echography study was performed during the follow-up. Functional evaluation was assessed with Tegner scale, the criteria described by Bak et al. and the subjective outcomes described by Anthony et al.

Results: Ultrasound scan showed a correct arrangement of muscle fibers. Functional evaluation showed excellent results and at four weeks of treatment, the patient had returned to their level of activity prior to the injury.

Conclusion: Treatment with the US-guided EPI® technique on pectoral is major muscle tear resulted in a high improvement in function and a rapid return to the previous level of activity after few sessions. The procedure has proven to be safe with no recurrences at one-year follow-up.

Keywords: Pectoralis major; Muscle; Tear; Athlete; Treatment; Intratissue percutaneous electrolysis; EPI

Introduction

Injuries to the pectoral is major muscle are important because as they can result in functional and aesthetic deficiencies of the upper extremity. They typically arise through indirect means, with the muscle being in a state of maximum elongation and contraction at a point of sudden overload [1-3]. This type of injury has been observed in activities like weight lifting, wrestling, American football and water skiing [4,5].

A purely clinical assessment of the pectoralis major injury may be deficient, so additional tests with imaging are needed to refine the diagnosis. Magnetic resonance imaging has been successfully used to assess the characteristics of injuries to the pectoral is major [6]. Similarly, ultrasound has been used to determine the extent and location of the lesion [7,8]. However, diagnosing with imaging is not without problems due to the anatomical complexity of the distal tendon of the pectoral is major as this has a 180° twist that comprises the sternal and clavicular portions [7,8]. The anatomical location of the muscle tear is very important because an avulsion of the tendon at its insertion into the humerus requires surgical repair, while myotendinous junction lesions are usually treated with conservative treatment [2,5,9].

Among the conservative treatment options, Intratissue percutaneous electrolysis (EPI®) stands out. This is a minimally invasive medical and physiotherapeutic technique that involves the application of a high-intensity galvanic current through a conductive stylus that provokes a rapid and localized regenerative process in the target tissue [10,11]. This allows for phagocytosis and the subsequent repair of affected tissue while making it possible to aspirate the hematic content of the injury and reducing the production of a secondary fibrotic lesion [12]. This is vitally important because it decreases the fibrous scar that occurs in muscle injuries and therefore the risk of re-rupture.

With this paper, the aim is to present the clinical and functional results in the treatment of an athlete affected by a large partial tear of the pectoralis major muscle treated with the EPI® technique.

Materials and Methods

A 30 year-old male patient who came to our clinic with pain and a functional limitation in the upper left extremity. The pain appeared suddenly during his usual gymnastic practice when performing a pull-up on the horizontal bar. The patient had no relevant medical history

or concomitant therapies and had never received injections to the affected area.

Clinical examination showed a clear indentation in the musculature of the left pectoralis major that became more pronounced when the patient pressed their palms together to contract the large pectoral muscles bilaterally. An obvious indentation was seen on the left upon comparing it to the right pectoral, which indicated a major tear of the muscle.

Ultrasound evaluation of the pectoral is major was performed longitudinally and transversally to the muscle fibers and the tendons were evaluated from origin to insertion. The distal pectoral tendon was identified and evaluated on the transverse plane at the level of the bicipital groove of the humerus, where the pectoral tendon and the tendon of the long head of biceps brachii cross. Equally, an evaluation of the flow was performed with high-resolution color Doppler. The images were compared to the contralateral side, placing the patient's shoulder in abduction and external rotation for the examination.

The ultrasound study was performed by two specialists in musculoskeletal ultrasound using a color Doppler device and lineal probe of 5-16 Mhz and longitudinal and transverse views. At the same time, a radiographic study of the shoulder was performed with AP projection, an axillary "Y" view as well as in internal and external rotation.

The functional assessment was performed according to the criteria described by Bak et al. [13] in which results for patients without symptoms with normal range mobility without cosmetic changes, without adduction weakness and able to return to their sport activity were considered as excellent. Those results with almost normal range of mobility without cosmetic changes and less than a 20% deficit in peak torque in the isokinetic test were considered good. The poor results are those in which there is limited range of mobility, poor cosmetic results and the patient is unable to return to their sport activity. Finally, those results where the pain persists and revision surgery is needed were considered bad.

As a second item in the functional assessment, the test for assessing subjective outcomes described by Schepsis et al. [14] was used for the evaluation of lesions of the pectoral is major. Patient follow-up was conducted over a year while getting clinical and functional results before treatment, at one month as well as 2, 6 and 12 months. The Tegner scale was used to rate the level of activity of patients before and after the injury.

Treatment was consisted of the application of the ultrasound-guided EPI® technique once a week and eccentric exercise twice a week. The EPI® technique was performed with the patient supine using the device designed specifically to carry out this technique, the EPI Medical Tissue Remover® (EPI Advanced Medicine, Barcelona. Spain).

A 40mm-long sterile 20G needles were used. The application was performed by means of stratified ultrasound-guided puncturing. In the first treatment session, a puncture was performed in the center of the hematic injury to do the first EPI® pulse of 5 seconds duration (Figure 1a), activating then the vacuum system (Figure 1b) of the device itself so as to get quick closure of the muscle injury.

Once the closure of the lesion was successful (Figure 1c), EPI® was continued at the edges of the lesion without removing the needle and applying 4 pulses of 10 seconds each in the geographical margins of the lesion. In 3 subsequent weekly sessions, 0.3x30 mm needles were used to apply the EPI® technique to minimize the pain of the puncture, using 4 pulses of 10 seconds in the length of remnant muscle scar.

Results

According to the classification of Tietjen [15], it was a pectoral is major muscle injury type II at the mid-portion of the muscle. Ultrasound examination detected a marked accumulation of fluid (hypoechoic) in the pectoral is major muscle (Figure 1). The diameter of the lesion was 30x7 millimeters with plenty of hematic content. The radiographic studies showed no abnormalities or bony avulsions.

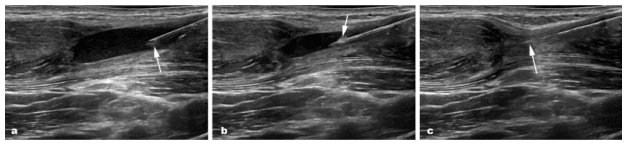

Figure 1: Sequence of images with high definition ultrasound with a 5-16Mhz lineal probe in a longitudinal view where the application of the ultrasound-guided EPI® technique in the focus of the hematoma (a) is observed. Upon activating the EPI® the hematoma begins to dissolve with the smoke effect appearing (arrow). After the first 5 seconds of treatment, the MTR® suction system (b) is activated to obtain a complete evacuation of the hematoma, leaving the injury virtually sealed (c).

In the functional evaluation, according to the criteria of Bak et al. [13], the good results that were seen at one month passed to excellent at 2 months and remained at the same level at 12 months.

The results obtained according to the criteria of Schepsis et al. [14] are shown in Table 1. Four weeks after the treatment starts, the patient had returned to their level of activity prior to the injury that was 8 points on the Tegner scale. These results were maintained in controls at 2, 6 and 12 months.

Question	1 month FU	2 months FU	6 months FU	1 year FU
Pain Relief	98	98	98	98
Range of Motion	95	100	100	100
Return to strength	96	97	100	100
Cosmetic satisfaction	86	86	95	95
Treatment Satisfaction	98	100	100	100
Average answers from the subjective questionnaire described forSchepsis et al. Values presented as percentages based on 100%.				

Table 1: Results obtained according to the criteria of Schepsiset al. [14] during the follow-up

The ultrasound scan performed during follow-up showed a correct arrangement of muscle fibers without evidence of fibrous scarring or accumulations of hematic residuals (Figure 2). During the procedure, no medical complications related to treatment presented.

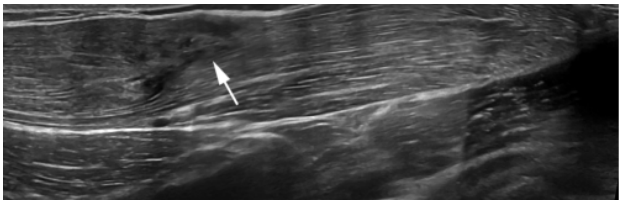

Figure 2: Ultrasound control with a 5-16Mhz lineal probe in a longitudinal panoramic view at 1 month after treatment in which a correct disposition of the pectoralis major muscle fibers without evidence of fibrotic scarring or complications.

Discussion

This paper shows that the treatment of injury in the pectoral is major of a gymnast treated with the Intratissue percutaneous electrolysis (EPI®) technique obtained excellent results and allowed for an early return to sports activity.

The pectoral is major muscle is a powerful internal rotator, flexor, and adductor of the arm and has its origin in the collarbone, sternum and the cartilages of the first six ribs. The pectoral is major muscle fibers converge in three bundles that rotate 180° that join to form a tendon which inserts into the lateral aspect of the humeral bicipital groove [8]. Patients with lesions of the pectoral is major muscle are clinically characterized by pain, bruising, swelling, and decreased range of motion. Clinically speaking, it is difficult to assess the extent and location of this type of injury except through ultrasound or magnetic resonance imaging evaluation. It is possible that a small initial injury of the pectoral is major muscle associated with lifting weights is not identified by ultrasound, but the patient may have pain in the anterior region of the chest [7,8,16,17]. In these cases, the immediate suspension of strength training is important so as to avoid further muscle ruptures of a serious nature within the first 6 weeks [1,4].

Tears of this muscle occur more frequently in the myotendinous junction or the insertion of the humerus and partial tears are more frequent than complete tears. The most commonly used clinical classification of this lesion is described by Tietjen [15]. It focuses on both the type of injury and the location of the lesion in relation to the origin or insertion. A type I injury refers to a concussion; a partial tear refers to type II, and type III to a complete rupture. On the other hand, it also stands out if the location of the lesion is in the sternal origin in the muscle, at the myotendinous junction or the humeral insertion.

The injuries of the pectoral is major muscle usually occurs during a high intensity eccentric action when the muscle is exposed to high tensile forces [4,5,7]. The main sports injury associated with the pectoral is major muscle are weightlifting, wrestling, gymnastics or wind-surfing.

Although MRI has been used to evaluate injuries of the pectoral is major muscle [6,7], ultrasound may also be useful in the assessment of this type of injury. Ahypoechoic image corresponding to hematic collection inside the rupture of the pectoral is major muscle can be seen [18].

Treatment options for an injury of the pectoral is major muscle are based on an accurate assessment of the extent and location of the lesion. Treatment is usually conservative in partial tears and sometimes in total ruptures in non-athletes. Surgical repair is used for complete tears and ruptures of the distal tendon in athlete patients [1-4]. The chosen method of treatment varies greatly depending on the literature consulted.

The Intratissue percutaneous electrolysis (EPI®) technique has proven effective in the treatment of soft tissue injuries [10,11] and experimental studies [12] have demonstrated that the early use of this technique reduces the fibrotic reactions secondary to these lesions. By using a high-intensity galvanic current, directed through a needle, rapid regeneration of damaged tissue is achieved. At the same time, the suction capacity provided by the EPI Medical Tissue Remover® device during the application of the technique makes it possible to evacuate the hematic content of the lesion, thereby facilitating healing and preventing potential later complications.

In the case presented, the ultrasound findings showed a large partial tear of the pectoral is major muscle with a large collection of blood. After treatment with the eco-guided Intratissue percutaneous electrolysis (EPI®) technique, the hematic fluid significantly decreased and proper remodeling of injured tissue was obtained, allowing the athlete to return to sports competition at 4 weeks after injury. The study with ultrasonographic images showed a repair of the myotendinous junction of the pectoral is major muscle with no signs of the formation of fibrotic scar tissue and no signs of hypoechoic thickening of the tendon.

Conclusion

Treatment with the US-guided EPI® technique on pectoral is major muscle tear resulted in a high improvement in function and a rapid return to the previous level of activity after few sessions. The procedure has proven to be safe with no recurrences at one-year follow-up.

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Orthopedic & Muscular System: Current Research

Research Article Open Access

Ultrasound-Guided EPI® Technique and Eccentric Exercise, New Treatment for Achilles and Patellar Tendinopathy Focused on the Region-Specific of the Tendon

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Abstract

Treatment of tendon injuries is a subject of frequent debate in sports medicine and physiotherapy. Achilles and patellar tendinopathy is a common, painful, overuse disorder, and is associated with a failure of the tendon repair process they have a low potential for healing with the usual techniques.

Therefore, new treatments for tendinopaties drawn from the existing literature as well as from their own experience dealing with this condition to deal with this delicate pathology have been developed over recent past decades.

This brief review aims to update recent information on the treatment with the ultrasound-guided EPI® technique and eccentric exercise in Achilles and patellar tendinopathy resulted in a great improvement in function and a rapid return to the previous level of activity.

Keywords: Tendinopathy; EPI® technique; Eccentric exercise therapy

Introduction

The Achilles tendon and patellar tendon are most affected, in both elite and recreational athletes, in sports that heavily load the lower extremities [1]. It is tendons play an essential role in the musculoskeletal system by transferring the tensile loads from muscle to bone so as to enable joint motion and stabilization [2]. Despite this ability to adapt to physiological loads tendinopathies it represents a clinical problem which affects both professional and recreational athletes as well as people involved in repetitive work [3,4]. Tendinopathies overuse represents 30 to 50 % of all sports injuries and result in a significant amount of morbidity and spending health care [5], it is estimated that they could cost the United States health system some 30 billion dollars, annually [6].

The etiology de la Achilles and patellar tendinopathy includes lifestyle, loading pattern, biological variables (genetics, age, sex) as well as different pharmacological agents [7].

Achilles tendinopathy is more prevalent in the lower extremity, with a frequency of 5.9% in sedentary and about 50 % for endurance athletes [8,9]. Patellar tendinopathy is most common involvement in the knee and its prevalence has been reported to be 44.6% in elite volleyball players [10] and 31.9 % in elite basketball players [11] and also represents two thirds of all pathologies of the knee between these two sports [8].

The traditional model of "tendonitis" as an inflammatory process is now obsolete since the appearance of several publications, which have described the pathological process of the tendon as mainly degenerative (tendinosis) [12,13]. This is justified due to the absence of inflammatory cells, the presence of areas of collagen degeneration, myxoid degeneration and an increase in fundamental substance and is associated with a failure of the tendon repair process [12,13].

Achilles and patellar tendinopathy is a clinical diagnosis and typically is based on medical history and clinical findings. Imaging techniques: such as Color Doppler Sonography (CDS) and Magnetic Resonance Imaging (MRI) are valuable tools to confirm the diagnosis and provide guidance for treatment [14].

The tendon injury can occur in the tenotendinous region, as in the Achilles tendon. However, most of the tendon pathology and pain is located in the osteotendinous, such as elbow lateral epicondyle, patellar tendon and the medial epicondyle tendons and tendons in the groin [15]. While osteotendinous and tenotendinous and are morphologically different region in normal state, the occurrence of extracellular matrix pathology induced cellular changes are indistinguishable [16].

Achilles and patellar tendinopathy this is accompanied by an excessive nociceptive signalling from the tendon, causing pain and restricted mobility [17] he mechanisms behind these structural and neurological changes are not fully understood. A more recent theory ascribes part of the tendinosis changes to an increased production of biochemical agents, such as substance P (SP) [18] and NMDAR1 glutamate receptor [19,20].

Overall tendinopathies are characterized by prolonged, localized pain, associated with physical activity requiring cyclic mechanical stimuli. Patients respond poorly to most conservative treatments, however, a broad spectrum of disorders of the tendon within the concept of tendinopathy that share some common characteristics (paratendinitis, tendinitis, tendon overuse injuries, spontaneous tendon rupture, calcifying tendinitis) or gaps, often converge in the same tendon (Figure 1). In this sense, there is no single etiology and pathogenesis that can explain all these processes [15].

Treatment options have changed over the last decade in parallel to

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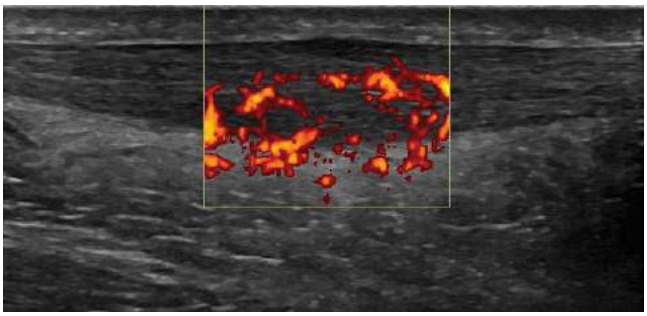

Figure 1: Longitudinal ultrasound view of Achilles tendinopathy. Gray-scale and power-doppler ultrasound showing the sonographic findings characteristic of Achilles tendinopathy. The sonogram reveals the hypoechoic, darken area of the Achilles tendon, tendon thickening and neovascularization.

the pathophysiological and histopathological findings in tendinopathy. Since the underlying pathology of chronic tendinopathy can be defined as a "defective healing response", treatment should aim to encourage regeneration of the tendon, pain modulation and the restoration of the biomechanical properties [21].

Current treatment options include eccentric training, open or arthroscopic surgery, extracorporeal shockwave therapy, non-steroidal anti-inflammatory drugs, platelet-rich plasma injection and aprotinin. These studies have also suggested that, in general, patients with a worse functional status before treatment obtain inferior final outcomes. However, due to the limited evidence-based therapies, there are still several controversies regarding the real efficacy of these treatment modalities [22].

In this paper the authors will update the knowledge about Achilles an patellar tendinopathy and current treatments with EPI® technique and eccentric exercise focused on the region-specific of the tendon drawn from the existing literature as well as from their own experience dealing with this condition.

Eccentric exercise therapy

Eccentric exercise therapy has shown to cause an upregulation of Insulin-like Growth Factor (IGF-I). This upregulation of IGF-I is associated with cellular proliferation and matrix remodelling within the tendon [23].

Programs of eccentric exercise have been proposed as a key element in strength training in rehabilitation because they can supposedly counteract the response of defective healing that apparently underlies tendinopathy by promoting the creation of collagen fibers within the tendon [24,25]. The literature places increasing emphasis on the importance of a proper choice of the load used [26].

The continuum model in tendinopathy (reactive tendinopathy, tendon dysrepair and degenerative tendinopathy) provides a reasoned basis for believing that the protocol to be performed depends on the current clinical presentation [15]. The protocol proposed by Alfredson et al. is generally used [24] it consists of three sets of 15 repetitions, performed twice a day, seven days a week for 12 weeks.

Ohberg et al. [27] examined tendon structure by grey-scale ultrasound in 26 tendons with Achilles tendinosis, which had been treated with eccentric exercise. Remarkably, after a mean follow up of 3.8 years, 19 of 26 tendons had a more normalised structure, as gauged by their thickness and by the reduction of hypoechoic áreas.

Visnes et al. [28] suggested that eccentric training had a positive effect on patellar tendinopathy and recommended that athletes suspend sports activity during rehabilitation.

The gradual progression from eccentric- concentric to eccentric followed by a faster loading can benefit patients with Achilles tendinopathy can not start with a program proposed by eccentric Alfredson et al [24] due to pain or weakness of the sural triceps muscle [29].

Isoinertial eccentric training (YoYoTechnology AB, Stockholm, Sweden) resulted in an improvement of muscle function and reduced pain in patients with patellar tendinopathy [30]. The combination of EPI® technique and isoinertial eccentric exercise offers good results in the treatment patellar tendinopathy [31].

Ultrasound-guided EPI® technique

In recent years, the intratissue percutaneous electrolysis (EPI®) technique has become more relevant in the scientific literature [31-33] given the good results yielded in the treatment of degenerative tendinopathy in comparison to other previous conservative treatments.

This technique, created by Sánchez-Ibáñez JM [34,35] and who have over 15 years experience in its use, uses a flow of cathodic current directed exclusively to the area of degenerated tendon through an ultrasound guided needle that brings about an organic reaction that leads to rapid regeneration of the degenerated tendon.

The application of EPI® technique produces a non-thermal electrochemical reaction centered on degenerated tissue (tendinosis). This leads to a controlled local inflammatory reaction that leads to the regeneration of damaged tissue [33,36].

The EPI® technique (Figure 2) achieves a very localized organic reaction in the clinical focus by using a specially designed EPI® device for this purpose (EPI Advanced Medicine®, Barcelona, Spain. EPI® technique videos online: www.epiadvanced.com), which leads to the rapid regeneration of degenerated tissue. This leads to the production of new immature collagen fibers that become mature by means of eccentric stimulus [32], thereby obtaining good results in the short and

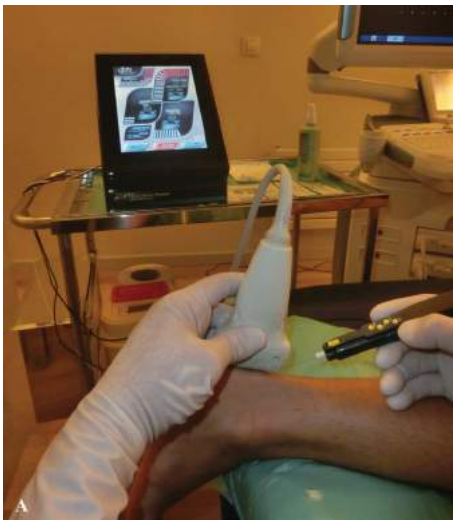

Figure 2A: Treatment of Achilles tendinopathy with ultrasound-guided EPI® technique (EPI Advanced Medicine®, Barcelona, Spain).

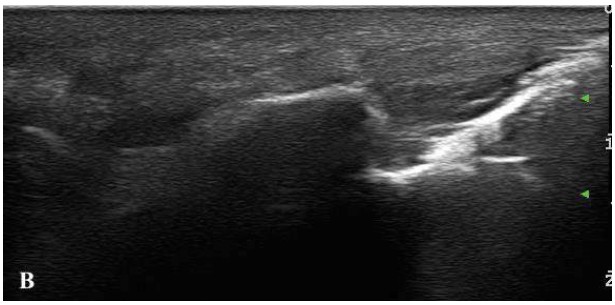

Figure 2B: Longitudinal ultrasound view of Achilles tendinopathy. Treatment is directed exclusively to the area of tendon injury. Note the non-thermal electrochemical reaction (white area) produced on the tip of the needle, just in the area of damaged tissue.

long-term in terms of pain and function.

In experimental studies with human tendon injury, there has been a disproportionate expression of certain cytokines and matrix metalloproteinase (MMPs), prostaglandin E2 (PGE2), interleukin -6 (IL-6) and interleukin -1b (IL-1b) [37,38]. IL- 1b in turn increases the production of matrix metalloproteinase -1 (MMP-1), matrix metalloproteinase -3 (MMP-3) and prostaglandin E2 (PGE-2) [39].

A recent experimental study [33] showed that with the use of ultrasound-guided EPI® technique in patellar tendinopathy increase of anti-inflammatory proteins, like peroxisome proliferator-activated receptor gamma (PPAR-γ). These proteins play a key role in the inhibition of expression of proinflammatory molecules secreted by macrophages, such as tumor necrosis factor alpha (TNF-α), IL-6 and IL-1β, thus producing in the treated tissue a highly beneficial molecular response during degenerative tendinopathy. This, in turn, results in an increase of the expression of vascular endothelial growth factor (VEGF) and vascular endothelial growth factor receptor 2 (VEGFR-2), mediators responsible for angiogenesis anti-inflammatory response. The EPI® technique makes for the activation of molecular and cellular mechanisms of the tendon responsible for phagocytosis and the regeneration of degenerated tissue [33,36].

In recent research [31] to evaluate the therapeutic effects EPI® technique and eccentric exercise on the patellar tendinopathy. The primary outcome measure was knee function using the Victorian Institute of Sport Assessment–Patella (VISA-P) score, a specific validated questionnaire to quantify pain and knee function and ability to play sport in patients with patellar tendinopathy [40,41]. The VISA-P score ranged from a maximum of 100 in asymptomatic patients to the theoretical minimum of 0. The authors of the score suggested that a score between 80 and 100 points might be considered as the optimal outcome category. Functional evaluation was further assessed with Blazina's classification [42]. This classification categorizes the symptomatic patients as in phase I (pain only after activity), phase II (discomfort during activity), phase III (pain during activity that interferes with participation) and phase IV (complete tendon disruption). The Tegner score was also used to assess the influence of the treatment in terms of restoring the previous sports activity level. All the written questionnaires were personally filled out by all patient before treatment, at the end of the treatment (at 3-month) and at the 2-year follow-up. The questionnaires corresponding to the 5 and 10 year follow-up evaluations were all filled out through a telephone interview. Patient satisfaction was measured according to the Roles and Maudsley score [43]. In this score, patients are classified as Excellent (no pain, full movement and full activity), Good (occasional discomfort, full movement and full activity), Fair (some discomfort after prolonged activity) or Poor (pain limiting activities). The results documented were good and stable with the VISA-P score, Tegner scores and Roles and Maudsley score, and terms of clinical and functional improvement in patellar tendinopathy and providing a follow-up of 10 year.

In recent research [44] to evaluate the therapeutic effects EPI® technique and eccentric exercises on the Achilles tendinopathy. A prospective study of 39 patients with Achilles tendinopathy was carried out. The patients were evaluated using the Victoria Institute of Sports Assessment - Achilles (VISA-A) score and the Foot and Ankle Disability Index for Sport scale (FADI); at the beginning of the study and after being monitored for 3 months. At the beginning of the study, the VISA-A score was an average of 47 ± 19.8 (mean ± SD ;) and after being monitored for 3 months the score was an average of 90.8 ± 5.5 (mean ± SD), showing statistically significant differences ($p<0.001$). The results of the FADI showed that the average score at the beginning was 64.5 ± 26.9 (mean ± SD) and after 3 months it was 123 ± 1.5 (mean ± SD). Statistically significant differences were identified ($p<0.001$). The use of the EPI® technique in combination with eccentric exercise in Achilles tendinopathy has shown evidence of a significant improvement in terms of pain and function. Not many sessions are required and the treatment time is short. The procedure has proven to be safe.

Discussion

Treatment of Achilles and patellar tendinopathy is a subject of frequent debate in sports medicine and physiotherapy. Multiple techniques have been described for their treatment and although some of them [31,45-48].

To date, there is no consensus on the optimal treatment of Achilles and patellar tendinopathy. It has been suggested that the incomplete understanding of the underlying mechanisms (etiology of the condition) limits the ability to develop effective treatment strategies [49].

Doubts have mainly centered on the fact that there are few controlled prospective studies that analyze all aspects of tendinosis, and few studies that investigate the early stages of these processes and their healing mechanisms. The exact mechanism by which tendinopathy develops in humans remains the target of numerous investigations. A variety of degenerative characteristics associated tendinopathies, including accumulation glycosaminoglycan (GAG), calcification and lipid accumulation nerve damage and hyperinnervation, is one of the theories whose publications are scarce, despite its special interest in explaining the possible pathophysiological mechanisms of pain in tendinopathy [50].

In several studies it has been shown that there is a correlation between tendinopathy and hyperinnervation, citing that the production of Nerve Growth Factor (NGF) and the corresponding hyperinnervation could be induced by repetitive ischemic crisis in osteotendinous union [51,52]. This growth of nerve fibers, which causes chronic pain, could be part of a process of abnormal tissue repair, preceded by repetitive microtrauma [53].

Despite its prevalence, the precise pathogenic mechanisms of tendinopathy are not clear and, as a result, current treatments of tendinopathies are largely empirical and not always efficient [15,54]. The continuum model of tendon pathology was proposed to provide a model for the staging of tendon pathology and to assist clinicians in managing this often complex condition. The model presents clinical, histological and imaging evidence for the progression of tendon

pathology as a three-stage continuum: reactive tendinopathy, tendon disrepair and degenerative tendinopathy [15].

One of the clinical effects that eccentric exercises might have in tendinopathy is in pain modulation due to changes in glutamate content or in the central nervous system with increased activation of inhibitory neurons and cortical reorganization [48,55]. There is little evidence that isolated eccentric exercise reduces pain in tendinopathy compared with concentric exercise [56].

It is considered that hypoxia could be responsible for neovascularization in tendinopathies, capillary flow and post-capillary pressure decreased following 12 weeks of eccentric loading [57].

In the treatment of tendinopathy, there is conflicting evidence that eccentric exercises are superior to other load programs [56]. Eccentric work on an inclined plane did not improve functional outcomes when it was done during a competitive season in volleyball [58]. In another study, continuous sporting activity did not compromise clinical outcomes at 12 months, as long as the sport was introduced incrementally ensuring minimal pain during and after loading [59]. Eccentric decline squat training and heavy slow resistance training showed good long-term clinical results, and heavy slow resistance training also resulted in advantages in pathological improvement and increased collagen turnove [60].

Some authors have demonstrated better results with eccentric exercise on corporeal tendinopathies in comparison with enthesopathies [22].

On the other hand, maximal eccentric loading may be best for some groups of patients and permit adaptive changes in the tendon [30].

Despite the fact that the eccentric muscle workout has become the dominant conservative strategy in treating Achilles and patellar tendinopathy, up to 45% of patients do not respond to this treatment [61].

A recent study suggests that sedentary subjects with Achilles tendinopathy may show less promising results with eccentric exercise therapy compared to athletic subjects [62].

Despite some good results reported with eccentric programmes [61,63], it is still unclear as to the more effective exercise protocol, its frequency, load and dosage.

Despite over 15 years of experience in the use of the EPI® technique and its widespread deployment in sporting clubs around the world, this technique has grown in relative to scientific dissemination in recent years [31-33].

The EPI® technique is contraindicated mainly in patients with tumors, articular or systemic infection and bleeding disorders [34].

An experimental study showed that after application of the degenerated tendon EPI® technique, an increase in anti -inflammatory proteins, like PPAR-γ has been observed after treatment with the EPI® technique. These proteins play a key role in the inhibition of expression of proinflammatory molecules secreted by macrophages, such as TNF-α, IL-6 and IL-1β [64] thus producing in the treated tissue a highly beneficial molecular response during tendinopathy. This, in turn, results in an increase of the expression of VEGF and VEGFR-2, mediators responsible for angiogenesis anti-inflammatory response [65,66].

In another recent study by Sánchez-Ibàñez and co-workers [31] reported that treatment with the ultrasound-guided EPI® technique and eccentric exercises in patellar tendinopathy resulted in a great improvement in knee function and a rapid return to the previous level of activity after few sessions. The limitations of this study are the absence of a control group.

References to the use of the EPI® technique in combination with eccentric exercise can be found in the literature. In those cases the EPI® technique focuses on biological tissue recovery, leaving the functional recovery of tissue biomechanics to eccentric exercise [31].

Conclusions

Achilles and patellar tendinopathy is a condition that causes many patients significant pain and disability. Currently, the aetiology of tendinopathy is still unclear, it is multifactorial, and influenced by intrinsic and extrinsic factors. Tendinopathy often becomes chronic because the exact pathogenesis remains largely unknown. Physicians and physiotherapist have a variety of therapeutic options available to treat tendinopathies but, in each case, there is a lack of evidence supporting their use as the gold standard treatment.

The combination of EPI® technique and eccentric exercise offers good results in terms of clinical and functional improvement in Achilles and patellar tendinopathy with low morbidity in a half study period.

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Author Contributions

Wrote the first draft of the manuscript: JMS, MEF, CM, DM, PB. Contributed to the writing of the manuscript: JMS, MEF, CM, DM, PB. Agree with manuscript results and conclusions: JMS, MEF, CM, DM, PB. Jointly developed the structure and arguments for the paper: JMS, MEF, CM, DM, PB. Made critical revisions and approved final version: JMS, MEF, CM, DM, PB. All authors reviewed and approved the final manuscript.

Disclosures and Ethics

The authors declare that one author has the patent for the EPI devices® and one author are the creators of the EPI® Technique.

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The Ultrasound-Guided Intratissue Percutaneous Electrolysis (EPI®) For the Treatment of Refractory-Neovascular Patellar Tendinopathy

Clinical Images

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Introduction

Refractory patellar tendinopathy (RPT) is a chronic disease with progressive degeneration of extracellular matrix, microtearing, and loss of tendon micro architecture as a hallmark. The essential pathologic lesion of tendinopathy is often described as a failed healing response of the tendon, and persistence of the lesion is attributed to the tissue anchored in the proliferative or angiogenic phase, as shown in histopathology [1].

Structural findings of collagen degeneration and angiofibroblastic neoplasia have been well described and are now referred to as "neovascular tendinosis." The presence of neovascularization has been theorized to cause pain in patients with tendinopathy [2].

Recent studies have examined the role of neo-vessels and neo-innervations on chronic tendon pain and dysfunction, and interventions targeting this process have reported favorable outcomes in RPT [3].

Ultrasound-guided Intratissue percutaneous electrolysis (EPI®) treatment is the application of a direct current (DC) whose catodic flow is transferred to the area of the degenerative tendon using an acupuncture needle [4]. This accumulated electrical charge (AEC) in the degenerative tissue will produce the activation of the molecular, cellular and biological processes necessary to restore the regeneration mechanisms of the tendon. In recent studies it has been demonstrated that EPI® technique is effective in tendinopathy and sport muscular injuries [5-7].

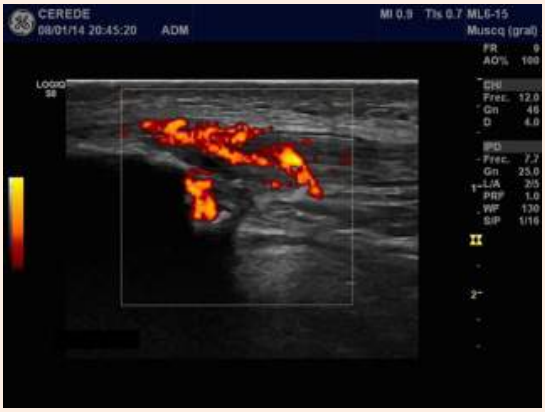

Figure 1: Ultrasound image with power Doppler. Longitudinal view of a Patellar neovascular tendinopathy, with thickening of the tendon and hipoecoic image.

Figure 2: Patellar tendinopathy treatment using EPI® device (EPI Advanced S.L. Barcelona, Spain)

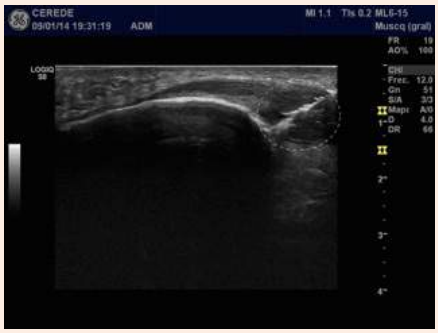

Figure 3: Hiperecoic image produced by the EPI® needle of 0,30mm in the degenerative area of the tendon. This hiperecoic image corresponded to a gas density produced by the electrochemical response of the catodic flow (CF) in the degenerative extracellular matrix.

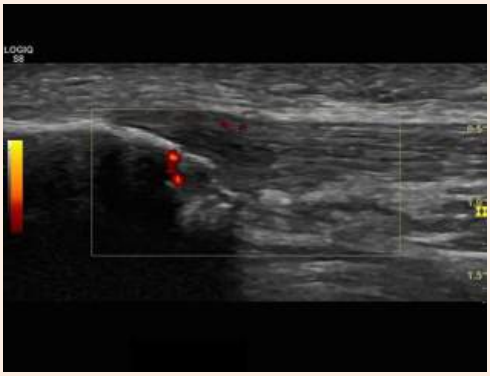

Figure 4: Ultrasound image in longitudinal view and colour Doppler two week after the EPI® technique treatment ultrasound-guided. It is observed the degenerated area of the tendon that is substituted by a new connective tissue and decrease the neovascular effect.

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TITLE PAGE

TITLE

Intratissue Percutaneous Electolysis (EPI®) combined with Active Physical Therapy for the treatment of Adductor Longus Enthesopathy-related Groin Pain: a randomised trial

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ABSTRACT

BACKGROUND: Adductor Longus Enthesopathy-related Groin Pain (ALErGP) is the most common cause of groin pain in soccer players. The aim of this study was to evaluate the therapeutic utility of Intratissue Percutaneous Electrolysis (EPI®) technique in combination with an Active Physical Therapy (APT) program to treat ALErGP.

METHODS: twenty-four non-professional male soccer players diagnosed with ALErGP were included in this study and randomly divided into two groups. Group A was treated with EPI® technique in combination with a standardized APT program. Group B only underwent the APT program. The Numeric Rating Scale (NRS) and the Patient Specific Functional Scale (PSFS) were used to assess the effectiveness of the two interventions. The follow-up covered a 6-month period.

RESULTS: both groups significantly improved pain and functional scores after treatment and maintained this therapeutic result throughout the follow-up. The combined intervention of APT program and EPI® ensured a greater and faster reduction of pain in Group A. In addition, functional recovery tended to be greater in Group A than B after the treatment and throughout the follow-up by 7.8±3.8% (p=0.093).

CONCLUSIONS: EPI® treatment in association with APT ensured a greater and more rapid reduction of pain and tended to promote greater functional recovery in soccer players with ALErGP compared to APT only. This positive therapeutic result lasted for at least 6 months after the end of the treatment. These findings support the combined use of EPI® and APT to treat ALErGP.

KEYWORDS (MeSH 2015): Groin Pain – Tendinosis – Soccer – Electrolysis – Ultrasonography

INTRODUCTION

Groin Pain (GP) can generally be defined as a syndrome characterized by pain in the pubic and inguinal regions [1], which results in a functional deficit that can lead to severe impairment of different motor tasks, such as kicking and twisting movements while running [2], and to the suspension of athletic activities [3]. In soccer, the incidence of this condition ranges between 10 and 18% of all time-loss injuries with relapse rates as high as 30% [3-4]. In fact, the term "longstanding" GP is often used to describe the impact of the syndrome in the long term [5]. The anatomy of the region is extremely complex and many different conditions provoking GP can be factors into a differential diagnosis [1,6-8]. Hence, the identification of the primary cause of GP can be challenging. Despite the difficulties in diagnosis, Adductor-related GP has been identified as the most common clinical pattern of GP in soccer players [9]. This is clinically characterized by pain that is exacerbated by the palpation of the insertion of the Adductor Longus (AL) on the pubic tubercle (unilaterally or bilaterally), as well as by the counter-resistance contraction of the muscle [1,9]. This clinical condition is often associated with AL enthesopathy, which involves also alterations of the tendon portion in close proximity to its insertion [10] (Figure 1), and is recognized as the most common disease in athletes with pain localized in the proximity of the pubic symphysis [6,11]. Therefore, Adductor Longus Enthesopathy-related GP (ALErGP) is identified as one of the main causes of GP in soccer players. Etiopathogenesis of AL enthesis degeneration is associated with repeated functional overloading, as the fibrocartilaginous enthesis is vulnerable to prolonged biomechanical stimuli over time [12-13]. Repeated functional overloading results in the progressive manifestation of histological and anatomical alterations, detectable with ultrasound and MRI [11,14-17]. The fibrosis and the formation of calcifications (Figure 2) are compatible with a chronic failure of the physiological processes of adaptation and healing, resulting in ineffective micro-cycles of injury-repair [12-13]. Also, histological alterations of the enthesis contribute to the progressive loss of the biomechanical

properties of the tissue and finally to the onset of symptoms and functional deficits typical of an overuse injury [1,11,15].

Physiotherapy is usually preferred over surgical intervention to treat GP. On the other hand, surgery is considered when the rehabilitative programs are unsuccessful [18]. The more conservative treatments usually involve: rest (or restriction of activities); passive physiotherapy (i.e. massage, laser and transcutaneous electrical nerve stimulation [19]) to recover the joint mobility of the hip, sacroiliac joints, and lumbar spine, as well as the restoration of the visco-elastic properties of the muscles (the adductors, in particular); active physiotherapy targeted at improving the stabilizing ability of the abdominal and pelvic muscles, especially the Transversus Abdominis [2,20-23]. It has been shown that a program of active physiotherapy is more effective than one of exclusively passive physiotherapy in the care of Adductor-related GP [19], and that a multimodal program promotes even faster results than active physical therapy per se [24]. The physical therapy interventions usually last for 6 to 8 weeks [25].

In addition to the abovementioned interventions, another therapeutic approach to consider is Intratissue Percutaneous Electolysis (EPI®), a novel technique that plays a role in the treatment of tendinopathy, enthesopathy, and fibrosis [26-28]. Furthermore, a recent study reported the use of this technique for the treatment of muscular lesions as well [29]. EPI® is an ultrasound-guided minimally invasive technique that makes it possible to degrade the diseased tissue through the electrolytic action of EPI® (electrochemical ablation), as well as to develop an extremely localized inflammatory process that can induce the healing process in the treated structure (indirect reparative action) [29]. Other works described the therapeutic benefits of EPI® technique in the treatment of patellar tendinopathy and how this technique, in conjunction with a program of active physical therapy -eccentric exercises in particular- can promote considerable structural and functional benefits that are maintained in the long term [26-27]. However, further studies are still needed to

evaluate the usefulness of this technique in the treatment of other tendinopathies and enthesopathies.

The aim of this study was to evaluate the therapeutic utility of the EPI® technique in combination with an APT program to treat ALErGP, while comparing the results achieved solely from the APT program in a group of non-professional soccer players. We hypothesized that *i)* the combination of EPI® and APT can promote greater and faster clinical and functional improvements than treatment relying solely on an APT program, and that *ii)* the functional improvements obtained in the study group will be more solidly maintained over time compared to the control group that underwent APT program alone.

MATERIALS AND METHODS

Participants and Sample Size

Between February and July 2014, 37 male soccer players affected by generic GP were clinically and instrumentally evaluated (see below). These athletes usually performed 2 to 4 training sessions per week, thus were considered non-professional players [24]. Twenty-four of these athletes (age: 26.0±4.7 year; stature: 178.7±8.0 cm; body mass: 73.9±6.9 Kg) were diagnosed with ALErGP, satisfied the inclusion and exclusion criteria (Table I) and thus were initially enrolled in the study (see Flow Diagram, Figure 3). Two subjects did not complete the study protocol; hence, data recorded from 22 players were taken into account for further analysis.

The study was ethically designed and conducted according to national and international standards. The research reported in the paper was undertaken in compliance with the Helsinki Declaration and the International Principles governing research on humans. All participants were informed of the experimental risk and gave written informed consent. In addition, the present study was designed

taking into consideration the guidelines on reporting standards for clinical research on groin pain in athletes indicated by Delahunt et al.[30]

Patients initially took part in a medical interview. Their anthropometric data were collected, as well as sport-specific (level of activity, position, dominant foot) and GP-specific (laterality and duration of the symptoms) information. The final part of the interview involved the registration of Patient-Specific Functional Scale (PSFS) values. This was followed by the clinical evaluation, including recordings of the Numeric Rating Scale (NRS) values. After this evaluation, an ultrasound examination was administered. If the inclusion criteria were met, the patient was asked to undergo an MRI scan. Based on an analysis of the final report, a decision was made whether to enroll the subject. MRI scans were performed by a private clinical facility, while all other assessments and therapeutic interventions were performed within the facilities of the "Friuli" Stadium, in Udine (Italy), the sporting venue of the Udinese Football Club.

Clinical evaluations

For the clinical evaluation, a standardized assessment protocol was used for athletes with GP [31]. This protocol was shown to be particularly valuable because it was subject to limited variation between operators. All the clinical assessments were performed by a well-trained physiotherapist who followed precisely the protocol details found in the appendix "Examination techniques for the evaluation of GP in athletes" used in the intra-observer and inter-observer reliability study [31]. The assessor was not aware of the treatment type received by every subject.

Pain assessment

The NRS scale [32-34], which showed high test–retest reliability [32], was selected among the available scales for pain assessment in adults. The patient was asked to verbally assign a value to his pain, ranging from 0 (total absence of pain) to 10 (the most intense pain imaginable). The NRS values were collected to assess the pain: upon palpation of the insertion of the AL into the pubic tubercle (NRSpalp) (if pain is present bilaterally, the highest value was always recorded); upon bilateral isometric contraction against resistance (NRScontr). The values were recorded at enrolment, at the end of treatment, and at 2, 4, and 6 months after treatment (follow-up).

Functional assessment

As suggested by Hedegus et al [33], the PSFS was chosen to assess the functional level of subjects with GP. The patient was asked to select the activities with a reduced level of performance and to assign them with increasing values from 0 to 10, representing a complete deficit in the performance of the activity and the ability to perform the activity at the highest level of performance, respectively. To ensure uniform assessment in the sample, the authors selected 10 activities to which the patient was asked to assign a performance level, 6 non-sport specific and 4 sport specific (SS): linear running; linear sprinting; rapid braking in a sprint; twisting movements; jumping, pulling with dominant foot; jumping, pulling with the non-dominant foot; passing with the dominant foot (SS); passing with the non-dominant foot (SS); kicking with the dominant foot (SS); and kicking with the non-dominant foot (SS). The sum of the values obtained could range from 0 to 100, where 100 is the maximum level of athletic performance. The values were recorded at enrolment, at the end of treatment, and at 2, 4, and 6 months after treatment (follow-up). PSFS showed also high test–retest reliability for evaluation of the functional level for chronic syndromes such as low back pain and chronic lateral epicondylitis [35].

Instrumental evaluations

Ultrasound assessment was performed by a well-trained operator (more than 10 years of experience in evaluating the lower limb muscle-skeletal system in professional and non-professional soccer players) using the GE Healthcare Logiq S7 Expert ultrasound (GE Healthcare®, Milwaukee, WI) with a linear probe (6-15 MHz). Ultrasound assessment was performed only before the intervention; it was aimed at evaluating any eventual anatomical alterations of the proximal tendon and enthesis of the Adductor Longus, which was painful during clinical examination, in order to define the inclusion / exclusion criteria (see Table I). The assessor was neither aware of the clinical evaluation results nor the type of treatment that the subject would have received.

Ultrasound evaluation was followed by an MRI of the pubic region which was necessary to confirm the diagnosis and to rule out any other condition: subjects with significant comorbidities (such as inguinal hernia, muscle injuries, femoroacetabular impingement, visceral diseases, etc.) were excluded from the study.

Treatment protocols

Two randomized groups were created: the study group, or group A, and the control group, or group B. In group A, the EPT® technique was used along with a standardized APT program, whereas group B only underwent the APT program. To randomize the groups, the following tool was used: "Create a blocked randomization list" (Sealed Envelope Ltd. 2014), available online from: https://www.sealedenvelope.com/simple-randomiser/v1/lists. The block size was set at 10 subjects (1:1 allocation). The tool also generated a unique randomization code. After the assessments, each subject included in the study was given their personal code assigning them to one of the two groups. The code was enclosed in sealed envelopes (numbered to identify the block).

Eco-Guided EPI® intervention.

The patient was placed in a supine position, with the limb in slight abduction and external rotation of the hip in order to better expose the enthesis of the AL to be treated. The entire pubic and inguinal region was previously disinfected with isopropyl alcohol. The treatment was performed by a well-trained operator (more than 10 years of experience in applying this technique for ALErGP in professional and non-professional soccer players) using a specifically developed medically certified (Directive 93/42/EEC) device (EPI Advanced Medicine® Barcelona, Spain). The chemical process of electrolysis is induced by the modulated galvanic current generated by the device. The current is transferred to the tissue to be treated using an appropriate needle (0.33 x 50mm); its insertion is ultrasound-guided in order to reach precisely the targeted area. In the present study, the GE Healthcare Logiq S7 Expert® ultrasound with a linear probe (6-15 MHz) was used to guide the insertion of the needle (Figure 4). Group A subjects received EPI® intervention during Phase 1 of the APT program. EPI® intervention protocol was similar to that reported by Abat et al. [26-27] for the treatment of patellar tendinopathy. In particular, two treatment sessions were held each week during Phase 1 of the APT program (EPI® intervention was completed 15 minutes prior to the start of the physical therapy session). The pre-set program "Adductors Tendinopathy" was used, with the device set at 3mA (current intensity). Each session consisted of 3 applications (3 right + 3 left if the ALErGP was present bilaterally), with a duration of 5 seconds each. Each session had a maximum duration of 10 minutes.

EPI® intervention was overall well tolerated by the subjects. Some of them experienced minor discomfort during needle insertion. In addition, the electrolytic treatment caused moderate to moderately strong pain in some of the participants; however, the short duration of every stimulus, 5 seconds, resulted in a tolerable pain. Indeed, none of the subjects asked to pause or stop the treatment, being these options available after every single 5-second stimulus. Furthermore, no

adverse events such as fainting or nausea occurred during the treatment. Some patients reported minor pain in the treated location up to 12 hours after the end of EPI® intervention.

The standardized Active Physical Therapy (APT) program.

For all participants, the program began within 10 days of enrolment and was performed under the constant supervision of a physical therapist, who did not know which subjects were also treated with Eco-Guided EPI® intervention. Table II specifically shows the therapeutic proposals of each of the 3 phases comprising the treatment. The APT protocol was defined taking into consideration: *i)* previous studies that investigated the effects of active physiotherapy (i.e. isometric and eccentric muscle contractions performed against manual resistance) on GP [19,24]; *ii)* previous studies aimed at examining the combined effects of EPI® technique and isoinertial eccentric exercises on the treatment of patellar tendinopathy[27]; *iii)* previous studies that examined the effects of isoinertial eccentric exercises on muscle function in healthy athletes [36-37] and *iv)* pilot studies carried out by our research group. The duration of each phase depended on the functional and symptomatic improvement shown by each individual. In particular, the achievement of specific NRSpalp, NRScontr and PSFS threshold values (see below) resulted in the phase completion. However, each subject was required to perform at least 1 week of training for each phase.

Phase 1. The aim of this phase was to reduce the ALErGP symptoms. Subjects were required to completely suspend all sport-related activities and perform three rehabilitative sessions per week, which included isometric lower limb adductions and AL eccentric contractions performed against manual resistance (Table II). The duration of each session was about 30 minutes. At the beginning of each session, NRSpalp and NRScontr tests were replicated. When the values of both tests were ≤3/10, subjects advanced to Phase 2.

Phase 2. The objective was non-sport specific functional recovery. As in the previous phase, 3 sessions per week (30 minutes/session) were performed by the subjects. Phase 2 involved the use of a machine (Element Sport™, Sevilla, Spain; Figure 5) for performing isoinertial eccentric exercises. This isoinertial machine was equipped with a 7 kg flywheel (moment inertia: 0.09 kg/m^2) and additional overloads (between 3 and 6 kg) that were appropriately set by the operator (Table II), and was very similar to those described in other studies that used isoinertial exercise as an intervention [27,36-37]. In particular, an important feature of this machine is that the concentric-eccentric phase transition is extremely fast (i.e. the isometric phase is negligible). During the concentric contraction phase, the kinetic energy is transmitted to the spinning cone (flywheel) through the extraction of the nylon cord wrapped around it. When the cord is completely extended, the stored energy causes the cone to continue its rotation through inertia, in turn rewinding of the cord. At this point the subject is required to perform an eccentric contraction (proportional to the effort exerted during the concentric phase) in order to break and stop the rotation of the cone, thereby completing the repetition. During APT Phase 2 (as well as Phase 3), the two initial exercises were proposed as controlled warm-up activity (see Table II). The initial 3 repetitions of each of the subsequent exercises were performed by the subjects at a lower intensity because they were aimed at familiarizing with the isoinertial equipment. It is worth noting that eccentric exercise was reported to be effective as an "active stretching" intervention for tendon tissue [38]. In addition, isoinertial eccentric exercise was shown to be effective for increasing muscle mass and improving muscle function [36-37]. At the beginning of each session, the PSFS was assessed for the non-sport specific activities. When the score of this test was ≥8, subjects advanced to Phase 3.

During phase 2, subjects were also allowed to perform up to two unsupervised training sessions per week, performing linear running, sprinting, twisting movements and jumping; during these sessions, the use of the ball was not allowed. The duration of the first unsupervised training sessions was 10 minutes; if no adverse events occurred, the subject was allowed to increase the duration of the

subsequent session by 10 minutes. Duration increments were allowed in order to reach a maximum session length of 40 minutes. In addition, subjects were required to limit the exercise intensity during the unsupervised training sessions. In particular, the perceived exertion should have been lesser than 3/10 (moderate exertion) referring to the Borg CR-10 Scale, which is commonly used for rating the perceived exertion in male soccer players [39].

Phase 3. The goal was to restore a level of physical performance sufficient for participating consistently in subsequent full training sessions as well as soccer matches. The endeavors started in Phase 2 were continued, while increasing the sessions load. Each session lasted up to 40 minutes, and was performed twice a week. In order to achieve the goal of this phase and complete the APT program, preliminary observations carried out by our team suggested that the player was required to obtain at least 80 points on the PSFS, assigning each of the sport specific and non-sport specific activities a score of ≥8. We did not set a "complete recovery" threshold (100/100) because this would have exponentially delayed the restart of individual soccer activities, conceivably impairing the compliance to the study protocol and increasing dropout.

During Phase 3, subjects were allowed to perform two unsupervised soccer-specific training sessions per week, the maximal duration of which was set as 60 minutes. Similar to Phase 2, the maximal duration of the first unsupervised training sessions was 20 minutes; if no adverse events occurred, subjects were allowed to increase the duration of the subsequent session by 20 minutes. Also, the perceived exertion of each session was required to be equal or lesser than 5/10 (hard exertion) referring to the Borg CR-10 Scale [39]. During these soccer-specific training sessions, subjects were allowed to perform passing and kicking as well as running, sprinting, twisting movements and jumping.

Follow-up. From the end of APT program to the end of the follow-up period (6 months), subjects were allowed to perform up to 3 soccer-specific training sessions (duration: 60 minutes) and one official game every week.

Statistical Analysis

Data are reported as means ± standard deviation (SD). The distribution of quantitative variables was tested for normality using the Kolmogorov–Smirnov test with the Lilliefors correction to apply a parametric or non-parametric test for group comparison. Since the assumption of normality distribution for the investigated variables was not met, the differences between independent samples were analyzed using the non-parametric Mann–Whitney *U* test, and the differences between related samples were analyzed using the non-parametric Friedman Test and Kendall Coefficient of concordance. Alpha level for all of these analyses was set at $p < .05$ (two-tail test). Data were analyzed using SPSS 13.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Characteristics of the participants

Group A and B presented similar characteristics at baseline. Age, stature and body mass were not significantly different between the two groups (Table III). Also, when the medical interview occurred, soccer-related activities were already restricted or suspended for 6 players (Group A) and 7 players (Group B). In addition, GP was recurrent in all Group A subjects and in 10 out of 13 players enrolled in Group B.

Pain and functional assessments

Both Groups significantly improved pain and functional scores after treatment ($p<0.001$, Table IV). Furthermore, NRSpalp, NRScontr, and PSFS values recorded after treatment were similar to those recorded throughout the follow-up in both groups ($p>0.05$).

When comparing the two groups, baseline values of NRSpalp and NRScontr were also similar between group A and B (p = 0.442 and p = 0.505, respectively; Table IV). However, at the end of the APT program, NRScontr was significantly lower in Group A (0.9 points, p = 0.047). Lower NRScontr values in group A were also recorded at the three follow-up time points (p<0.05). Furthermore, time x group interaction was also significant for this parameter (p = 0.013, Table IV). NRSpalp showed a trend similar to NRScontr, with values that tended to be lower in Group A than Group B at the end of treatment and follow-up (Table IV); however, statistical significance was achieved only at the 2- and 4-month follow-up (p = 0.003 and p = 0.005, respectively).

On the other hand, no significant difference for PSFS between the two groups was found (p = 0.093, Table IV). However, while the PSFS baseline value was very similar between group A and B (55.5±22.2 and 56.7±20.6, respectively), it tended to be greater in group A after treatment and throughout the follow-up by 7.8±3.8%.

It is also worth noting that the duration of Phase 1 was on average 8.8 days shorter in Group A (p = 0.048). The same trend, without statistical significance, was also shown by Phase 2, 3 and total duration (Table V).

DISCUSSION

This study investigated the therapeutic utility of the EPI® technique in combination with a standardized APT program to treat ALErGP in non-professional soccer players. The assessment of pain- and functional-related outcomes in the experimental group (A), who underwent the APT program in combination with EPI® treatment, and in the control group (B), who underwent the APT program only, revealed that: *i)* both groups significantly improved pain and functional scores after treatment and maintained this therapeutic result throughout the 6 months after treatment; *ii)* the combined intervention of APT program and EPI® ensured a greater and faster reduction of pain

compared to the APT programme alone; *iii)* functional recovery was not significantly different between the two groups, although it tended to be greater in Group A after the treatment and throughout the follow-up.

APT program with and without EPI® effectively reduced pain and improved functional recovery

High quality studies on non-surgical treatment of long-standing adductor-related GP are rather scanty [40]. For example, Hölmich et al [19] showed that 79% of the patients with adductor-related GP that were treated with exercise therapy (static and dynamic exercises aimed to improve strength and coordination of the pelvic muscles) resumed their usual physical activity without symptoms. On the other hand, in the study conducted by Weir et al [24], the success rate of an active physiotherapy programme aimed at the strengthening of adductor and core muscles, associated to a return-to-running programme, decreased to 50%. The present study supports the view that an active physiotherapy programme that promotes significant eccentric muscle contraction of the AL via isoinertial eccentric training is conceivably a valuable intervention for long-lasting pain reduction and functional improvement. Indeed, both Group A and B significantly improved pain and functional scores after the treatment. Generally, the time course of these improvements throughout the ATP program was related to the initial GP symptoms of each individual: the more severe the symptoms, the longer the duration phases. Also, pain and functional scores were similar at the end of the ATP program and throughout the subsequent 6-month follow up.

The positive effects of active physiotherapy on adductor-related GP can be related to the connective tissue remodeling that occurs physiologically as a result of the mechanical stimulation exerted by the exercise [38,41]. In particular, Apostolakos et al. [12] emphasized that biological factors are important for the proper modulation and regulation of collagen production, while mechanical stimuli are crucial for the proper collagen fibers orientation; thus, both factors are essential for the proper

healing of the degenerated enthesis. For this reason, eccentric exercise represents one of the most considered therapeutic solutions in the treatment of collagen-rich tissues pathologies [38,41-43], and isoinertial eccentric training one of the effective methods to perform eccentric exercise [27,36-37].

The integration of EPI® and APT interventions promoted greater and faster pain reduction compared to APT intervention alone.

The pain-related clinical testing proposed in the present study showed substantial differences between Group A and Group B after the treatment and during the 6-month follow up. In particular, the scores of the active test form proposed in the present study (NRScontr) were significantly lower in Group A than Group B at the end of the treatment and for the entire duration of the follow-up. The "time x group" interaction was also significant for this parameter. In addition, NRSpalp values tended also to be lower in Group A after the treatment, and significantly lower at the 2-month and 4-month follow up. Interestingly, Mosler et al. [44] supported the view that NRScontr is better than NRSpalp for evaluating and quantifying GP in athletes.

The relevant effect of EPI® treatment integration with the APT intervention on GP was also underlined by the fact that the duration of Phase I of the APT programme, which was focused on pain reduction, was significantly shorter (-8.8 days) in Group A than in Group B. These results support the view that the combination of EPI® and APT interventions was more effective than APT intervention alone for reducing AL enthesopathy-related symptoms. It is plausible that EPI® electrolytic action promoted the removal of excessive deposits of connective tissue (fibrosis), so decreasing the tendon tissue tension [28] and consequently reducing GP. It is worth noting that EPI® intervention initially induces a local and controlled inflammatory process that subsequently promotes the histological enthesis healing process [28], the duration of which is reported to be longer than 14 days. [12] Hence, a proper protocol of active exercises should be proposed as a parallel

intervention to the EPI® treatment in order to ensure that the new production of collagen (resulting from the inflammatory process) develops adequately from a biomechanical point of view [40]. With this respect, the association of EPI® intervention and isoinertial eccentric exercises has already produced encouraging results in the treatment of patellar tendinopathy, and in particular for the tendon tissue repair [26-27].

Effects of EPI® intervention on functional recovery

In the present study, functional recovery was evaluated by PSFS, which consisted of 10 motor tasks (see Methods) that did not require a selective, sustaind and maximal AL muscle contraction. For example, maximal effort soccer kick requires a substantial level of AL activation during a limited part of the kicking swing phase (30% to 45) [45]; furthermore, AL activation is primarily aimed at controlling the hip extension rather than contributing substantially to hip flexion and to completing this complex motor task [45]. In addition, Delmore et al. [46] underlined that AL activation intensity recorded by EMG during twisting movements was about half of that observed during Adductor Squeeze Test. In the present study, the experimental group that underwent EPI® intervention and APT programme tended to achieve greater functional recovery after treatment and throughout the follow up (+7.8% ± 3.8 %) compared to the control group that underwent APT programme only. However, this difference was not statistically significant. The fact that PSFS lacks in motor tasks that specifically and substantially involve AL activation is conceivably one of the main causes of this finding. The total duration of the treatment was also not significantly different between the two groups, although it tended to be shorter (-10.9 days) in Group A. These data suggest that further studies are required to better assess the effectiveness of EPI® treatment on functional recovery in soccer players suffering from ALErGP. It is also worth noting that an intrinsic limit of the non-surgical treatments is that they reduce only to some extent the anatomical alterations of the enthesis. Therefore, while the functional recovery and symptoms reduction can be achieved by these non-

surgical treatments, the connective tissue alteration often persists [15], even in asymptomatic patients [17]. As a consequence, these residual anatomical alterations of the enthesis might result more likely in a premorbid condition. From this perspective, further studies should investigate whether the substantial reduction of the enthesis anatomical alteration brought about by EPI® intervention may eliminate or reduce such premorbid condition.

Limits of the study

One of the limitations of this study is the lack of a graduation in the severity of the ultrasound imaging of the proximal tendon of the AL: we differentiated between "tendons with anatomical changes" and "healthy tendons". However, we hypothesize that a worse ultrasound image could potentially be associated with a lower expectation of therapeutic success, regardless of the intervention. In addition: II) the EPI® intervention protocol lacks validation (the technique has recently been developed); III) research participants were not blinded with respect to the treatment received; thus, placebo effect could have played a role in the subjective scoring, especially in the earlier stage of the study protocol. On the other hand, it is less likely that any eventual EPI®-related placebo effect could have lasted throughout the follow-up; IV) the copresence of GP secondary clinical patterns (i.e. Ilepsoas-related GP, Rectus Abdominis-related GP) or comorbility (snapping Ileopsoas, hip arthrosis, ilioinguinal nerve entrapment) could have potentially played the role of confounding variables. Finally, V) the subjects of this study resumed independent soccer-related activities without supervision after the end of the treatment. So, different factors such as amount and characteristics of the physical activity performed by each individual could also have influenced the follow-up results.

CONCLUSIONS

EPI® treatment in association with active physiotherapy ensured a greater and more rapid reduction of pain and tended to promote greater functional recovery in soccer players with ALErGP compared to active physiotherapy only. This positive therapeutic result lasted for at least 6 months after the end of the treatment. This finding, together with the fact that EPI® treatment is minimally invasive and was overall well tolerated by the patients, support the combined use of EPI® and active physiotherapy in soccer players with GP syndrome. Further studies on the effects of EPI® treatment on functional recovery in ALErGP and on clinical conditions similar to ALErGP (i.e. Rectus Abdominis enthesopathy and tendinopathy, Gracilis enthesopathy, degenerative pubic symphysis, Ileopsoas Syndrome, Rectus Femoris aphophysitis) are needed to gain more insight into the effectiveness of EPI® treatment on GP syndromes.

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TITLES OF TABLES AND FIGURES

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Table II. The standardized Active Physical Therapy program: description of the exercises and method of administration.

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Figure 1. Longitudinal ultrasound section of the Adductor Longus (AL). The tendon insertion on the pubic tubercle (PT) is recognized as a hypoechoic area (*arrow*). Additionally, the intramuscular tendon, or central aponeurosis, of the Adductor Longus (the hyper-echoic horizontal structure indicated by an *asterisk*), and the Adductor Brevis (AB) can also be seen.

Figure 2. Anatomic changes of the proximal tendon/enthesis of the Adductor Longus (AL) in the ultrasound examination. In the vicinity of the pubic tubercle (PT) the presence of significant calcification of the tendon can be seen (*dotted box*), as well as many fibrotic areas at the level of the enthesis (*small arrows*), which appears to be clearly deconstructed. Furthermore, it is possible to

identify significant fibrotic thickening near the myotendinous unit of the muscle (*thick arrow*). AB=Adductor Brevis.

Figure 3. Study profile.

Figure 4. Ultrasound-guided Intratissue Percutaneous Electrolysis. The operator inserts the needle (*asterisk*) into the treatment area.

Figure 5. Isoinertial machine. The nylon cord (NC) is wrapped around the flywheel (FW) and secured at the athlete's ankle. A concentric contraction (CON) of the adductor muscles results in the initiation of FW rotation while unwinding the NC. Once the pushing CON phase has been completed, the NC rewinds because of the kinetic energy of the FW and pulls the lower limb toward the machine. Hence, the athlete is required to perform an eccentric contraction (proportional to the effort exerted during the concentric phase) in order to break and stop the rotation of the FW, thereby completing the repetition. After bringing the FW to a stop, a subsequent CON muscle contraction is instantly initiated.

Table I. Enrolment phase: inclusion and exclusion criteria.

	Inclusion Criteria	*Exclusion Criteria*
General Criteria	Non-professional soccer players Age 18-35 years	Previous Groin/Hip surgery
Clinical Criteria	Presence of pain upon palpation of the enthesis of the Adductor Longus (unilaterally or bilaterally) Presence of pain upon contraction against resistance (Adductor Squeeze Test) of the enthesis of the Adductor Longus (unilaterally or bilaterally)	Adductor-related Groin Pain is not the primary clinical entity
Imaging Criteria	The ultrasound testing revealed anatomical alterations of the proximal tendon/enthesis of the Adductor Longus, which was painful during clinical examination	The ultrasound and MRI showed and absence of anatomical alterations of the enthesis of the Adductor Longus, which was painful during clinical examination Presence of major pathologies revealed by the MRI
After randomisation		Consumption of NSAIDs or local infiltration during treatment Absence from more than 20% of scheduled physiotherapy sessions or absence from more than one scheduled EPI® session.

Table II. The standardized Active Physical Therapy program: description of the exercises and method of administration.

Phase 1	1) **Bilateral isometric contraction of the AL**: patient in supine position. Isometric adduction against a fit ball (Ø=30cm) positioned between the knees.	10sec of holding (+20sec pause) for 8 repetitions
	2) **Bilateral isometric contraction of the AL:** patient in supine position, hips flexed at 45°. Isometric adduction against a fit ball (Ø=30cm) positioned between the knees.	10sec of holding (+20sec pause) for 8 repetitions
	3) **Unilateral eccentric contraction of the AL**: patient in supine position, hip in neutral position. The physiotherapist slowly abducts the hip up to 45° and the patient is asked to slow down the muscle elongation.	5sec of contraction (+5sec pause) for 8 repetitions for 4 sets (2 for each leg)
	4) **Bilateral eccentric contraction of the AL**: patient in supine position, hips flexed at 45° and fully adducted. The physiotherapist slowly abducts both hips up to 30°, while the patient is asked to slow down the muscle elongation.	5sec of contraction (+10sec pause) for 8 repetitions for 2 sets
Phase 2	1) **Spinning Bike (** warm up).	10min
	2) **Bilateral eccentric contraction of the AL**: patient in supine position, hips flexed at 45° and fully adducted. The physiotherapist slowly abducts both hips up to 30°, while the patient is asked to slow down the muscle elongation (warm up).	5sec of contraction (+10sec pause) for 8 repetitions for 4 sets
	3) **Isoinertial Eccentric Training for AL:** patient in supine position. Overload: 2 Kg (Concentric + Eccentric phases duration: ~ 3sec).	6 repetitions for 4 sets (2 for each leg).
	4) **Isoinertial Eccentric Training for AL:** patient in upright position. Overload: 4 Kg (Concentric + Eccentric phases duration: ~ 3 sec).	6 repetitions for 4 sets (2 for each leg).
Phase 3	1) **Spinning Bike** (warm up)	10min
	2) **Bilateral eccentric contraction of the AL**: patient in supine position, hips flexed at 45° and fully adducted. The physiotherapist slowly abducts both hips up to 30°, while the patient is asked to slow down the muscle elongation (warm up).	5sec of contraction (+10sec pause) for 8 repetitions for 4 sets
	3) **Isoinertial Eccentric Training for AL:** patient in supine position. Overload: 3 Kg (Concentric + Eccentric phases duration: ~ 3 sec).	6 repetitions for 4 sets (2 for each leg).
	4) **Isoinertial Eccentric Training for AL:** patient in supine position. Overload: 4 Kg (Concentric + Eccentric phases duration: ~ 6 sec).	4 repetitions for 4 sets (2 for each leg).
	5) **Isoinertial Eccentric Training for AL:** patient in upright position. Overload: 4 Kg (Concentric + Eccentric phases duration: ~ 3 sec).	6 repetitions for 4 sets (2 for each leg).
	6) **Isoinertial Eccentric Training for AL:** patient in upright position. Overload: 6 Kg (Concentric + Eccentric phases duration: ~ 6 sec).	4 repetitions for 4 sets (2 for each leg).

AL: Adductor Longus

Table III. Baseline characteristics of the participants.

	Group A	*Group B*	*p value*
Age (years) (mean±SD)	26.9±4.5	25.2±4.9	0.384
Stature (cm) (mean±SD)	176.3±7.9	180.7±7.8	0.164
Body mass (kg) (mean±SD)	74.5±8.3	73.4±5.7	0.816
Position			
Goalkeeper	1	1	
Defender	2	5	
Midfielder	3	4	
Striker	5	3	
Dominant foot			
Right	7	11	
Left	4	2	
Athletic activity/week			
<6 hours	1	2	
>6, <10 hours	7	7	
>10 hours	3	4	
Activity status			
Normal	5	6	
Restricted	3	3	
Suspended	3	4	
Duration of the symptoms			
0-4 weeks	5	6	
4-10 weeks	4	3	
10-26 weeks	2	3	
>26 weeks	0	1	
Groin Pain			
First Case	0	3	
Recurrent	11	10	
ALErGP laterality			
Right	7	7	
Left	1	2	
Bilateral	3	4	

ALErGP: Adductor Longu Enthesopathy-related Groin Pain

Table IV. Numeric Rating Scale (NRS) and Patient Specific Functional Scale (PSFS) values registered at the end of treatment and during the follow-up (2, 4, and 6 months).

		Pre	End	2 months	4 months	6 months	Time	Group	Time x Group
NRSpalp	Group A	7.5±1.9 #	1.6±1.1	0.7±0.8 **	1.0±0.9 **	1.1±0.9	< 0.001	0.010	0.457
	Group B	8.1±1.9 #	2.5±1.5	2.4±1.3	2.3±0.9	2.0±1.5			
NRScontr	Group A	8.5±1.4 #	1.3±0.9 *	1.3±1.1 *	0.7±0.7 *	0.5±0.7 *	< 0.001	0.011	0.013
	Group B	8.0±1.6 #	2.2±1.7	2.8±1.6	2.2±1.4	1.6±1.3			
PSFS	Group A	55.5±22.2 #	91.6±3.8	93.7±3.6	93.8±4.2	95.4±4.1	< 0.001	0.093	0.200
	Group B	56.7±20.6 #	87.5±5.6	81.5±10.8	86.3±7.5	89.9±6.8			

NRSpalp: Numeric Rating Scale: pain upon palpation of the insertion of the Adductor Longus. Scale: 0-10; lower score indicates better outcome.

NRScontr: Numeric Rating Scale: pain upon bilateral isometric Adductor Longus contraction against resistance. Scale: 0-10; lower score indicates better outcome.

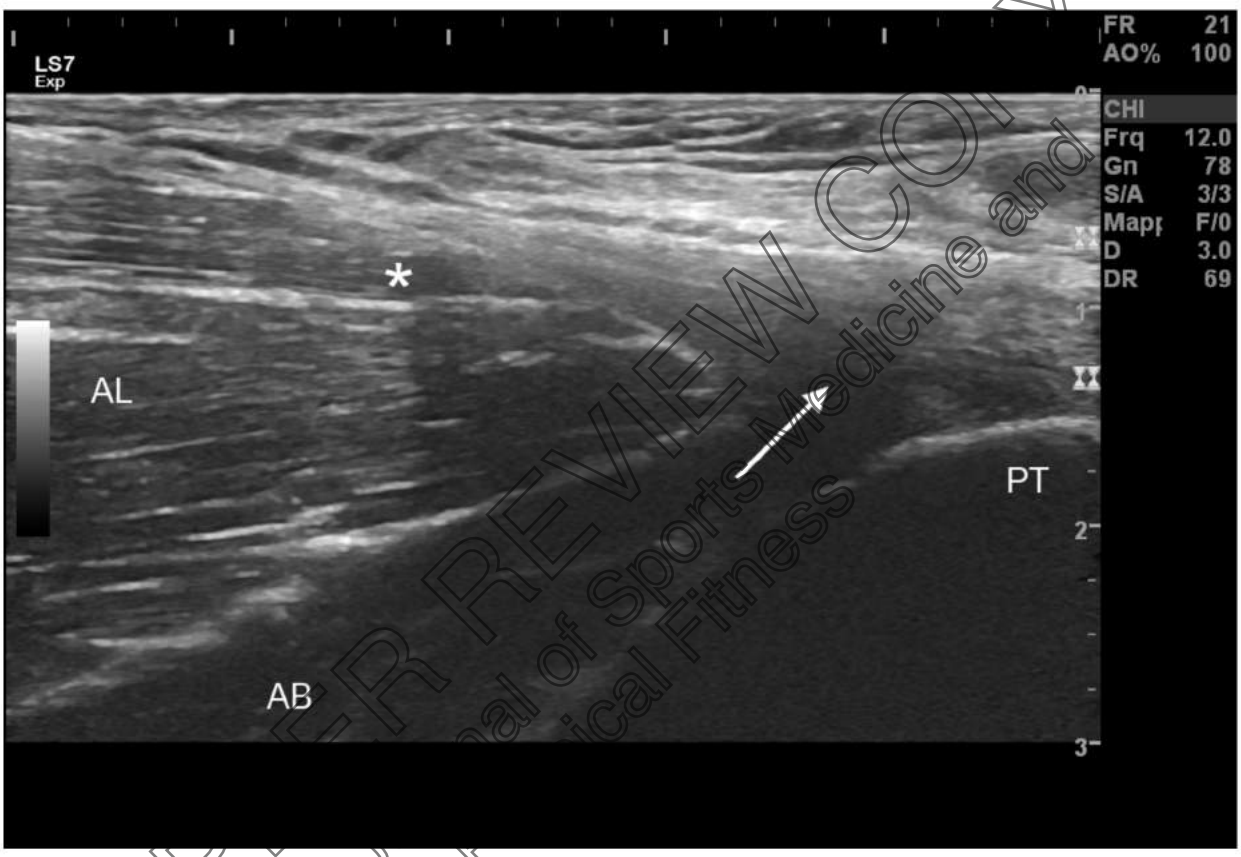
PSFS: Patient Specific Functional Scale: 0-100; higher score indicates better outcome.

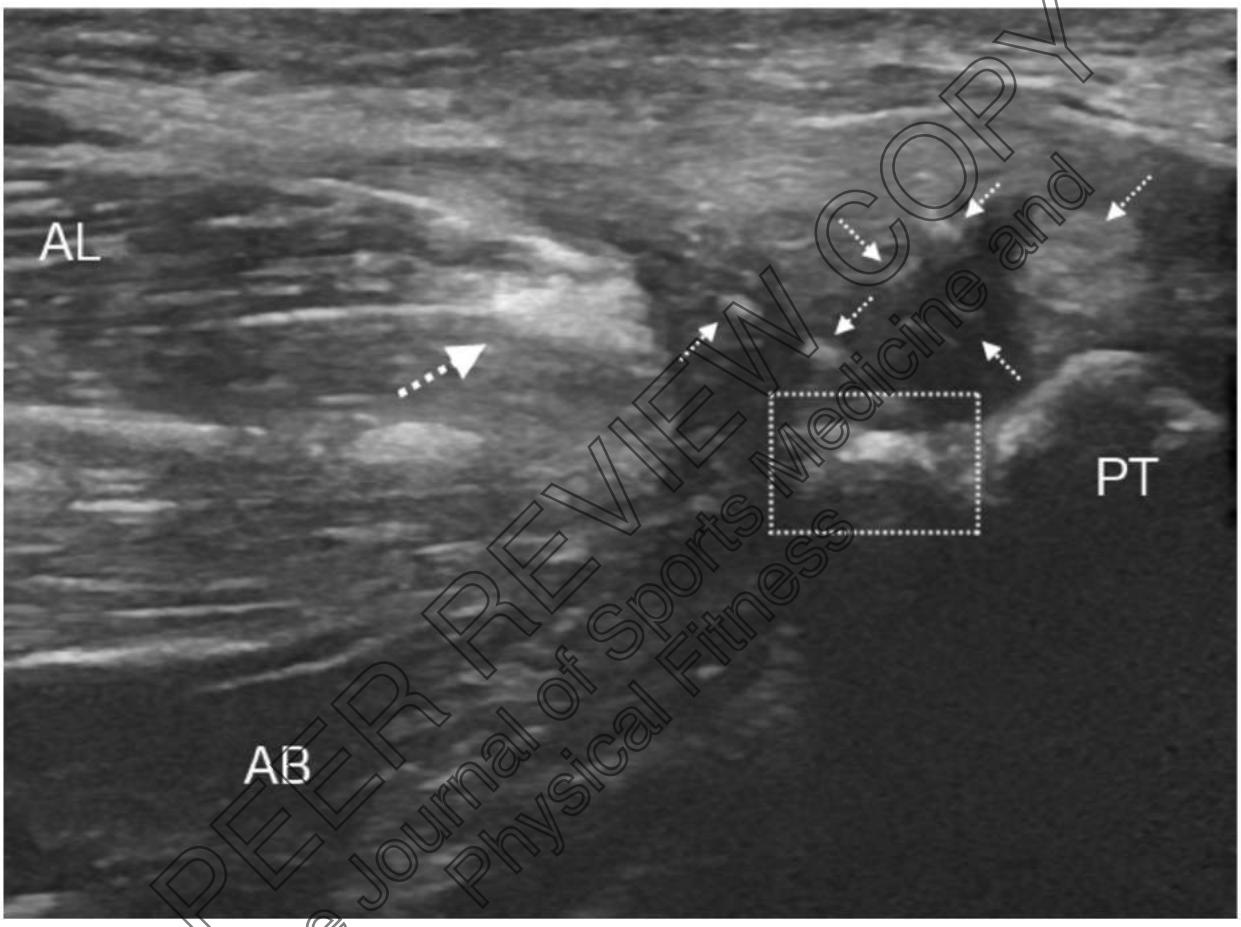
#: Time effects. Values recorded at Pre were significantly different ($p<0.01$) than those recorded at the other time points.

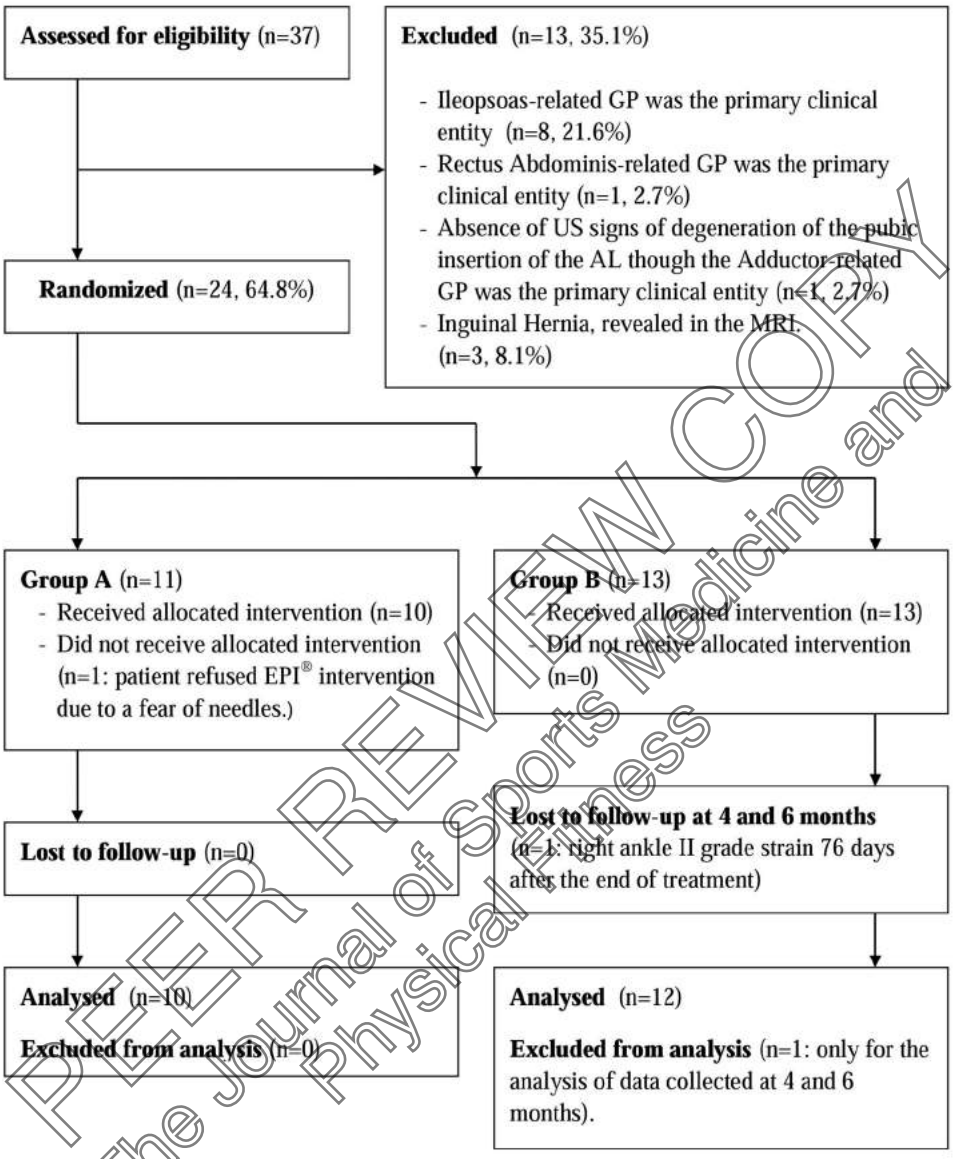
*: Significant differences between the two groups: * $p<0.05$; ** $p<0.01$.

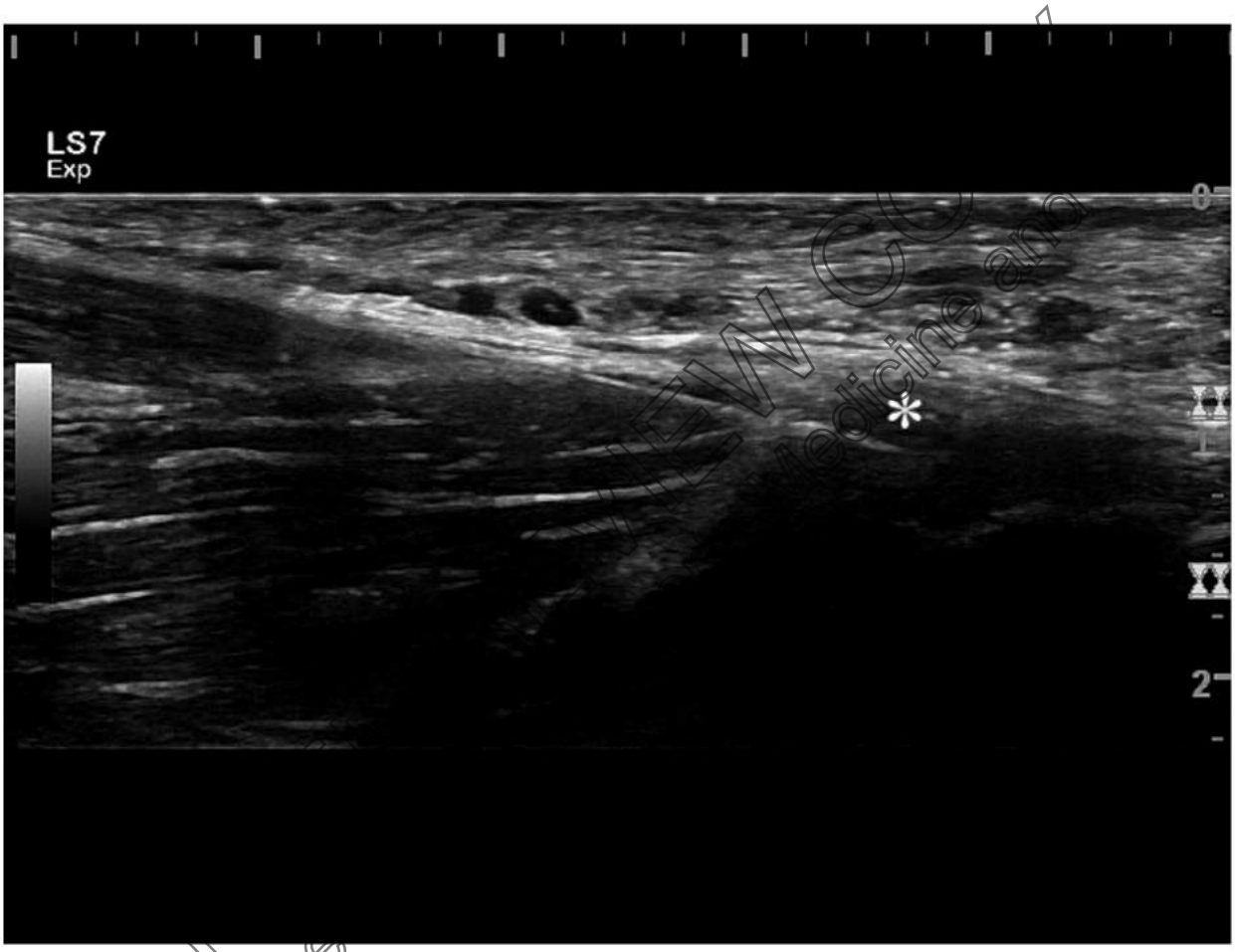
Table V. Active Physical Therapy program duration.

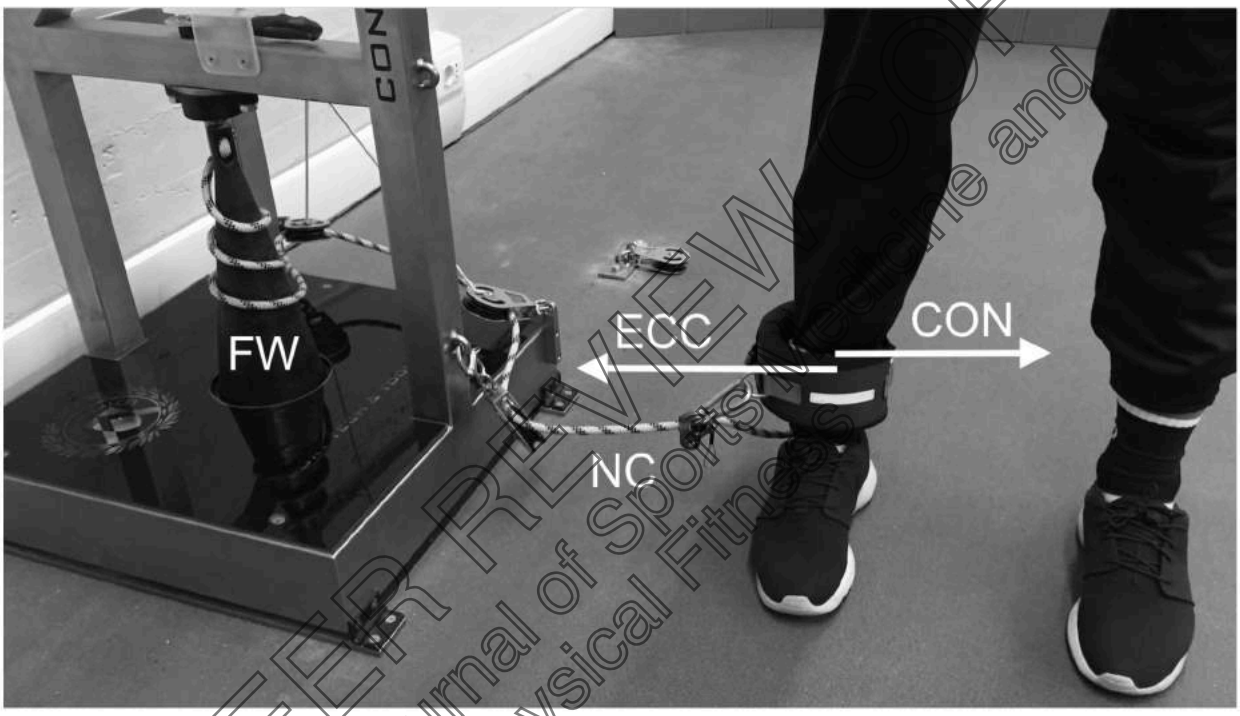
	Group A	Group B	p value
Phase 1 (days)	11.9±4.7	20.7±9.3	0.048
Phase 2 (days)	14.8±4.8	16.0±4.2	0.948
Phase 3 (days)	11.0±3.8	12.7±3.3	0.512
Total duration (days)	37.9±8.5	48.8±9.4	0.098











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INVESTIGACIÓN

Mecanismos moleculares de reparación mediante la técnica Electrólisis Percutánea Intratisular en la tendinosis rotuliana

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PALABRAS CLAVE
Tendinopatía;
Electrólisis Percutánea Intratisular;
Mecanismos moleculares;
Regeneración;
Tendón

Resumen
Objetivo: Investigar los mecanismos moleculares de respuesta tisular tras el tratamiento con la técnica Electrólisis Percutánea Intratisular (EPI®) en la tendinosis inducida por colagenasa tipo I en ratas Sprague Dawley.
Métodos: En una muestra de 24 ratas Sprague Dawley de 7 meses de edad y 300 g se indujo tendinosis mediante la inyección en el tendón rotuliano de 50 μg de colagenasa tipo I. Se procedió a dividir la muestra en 4 grupos: un grupo control, un grupo colagenasa y 2 grupos de tratamiento con técnica EPI® a 3 y 6 mA, respectivamente. Se aplicó una sesión de tratamiento EPI® y tras 3 días se procedió al análisis de los tendones mediante técnicas de inmunodetección y electroforesis. Se analizaron las proteínas citocromo C, Smac/Diablo, factor de crecimiento endotelial vascular y su receptor 2. También se analizó el factor de transcripción nuclear peroxisoma proliferador activado del receptor gamma.
Resultados: Se observó un aumento estadísticamente significativo en la expresión del citocromo C, Smac/Diablo, factor de crecimiento endotelial vascular, su receptor 2 y peroxisoma proliferador activado del receptor gamma en los grupos a los que se les aplicó la técnica EPI® respecto al grupo control.
Conclusiones: La técnica EPI® produce, en la lesión tendinosa inducida con colagenasa tipo I en ratas, un aumento de los mecanismos moleculares antiinflamatorios y angiogénicos.

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KEYWORDS
Tendinopathy;
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Molecular mechanisms;
Regeneration;
Tendon

Molecular repair mechanisms using the Intratissue Percutaneous Electrolysis technique in patellar tendonitis

Abstract
Objective: To investigate the molecular mechanisms of tissue response after treatment with the Intratissue Percutaneous Electrolysis (EPI®) technique in collagenase-induced tendinopathy in Sprague-Dawley rats.
Methods: Tendinopathy was induced by injecting 50 μg of type I collagenase into the patellar tendon of 24 Sprague Dawley rats of 7 months of age and weighting 300 g. The sample was divided into 4 groups: the control group, collagenase group, and two EPI® technique treatment groups of 3 and 6 mA, respectively. An EPI® treatment session was applied, and after 3 days, the tendons were analysed using immunoblotting and electrophoresis techniques. An analysis was also made of cytochrome C protein, Smac/Diablo, vascular endothelial growth factor and its receptor 2, as well as the nuclear transcription factor peroxisome proliferator-activated receptor gamma.
Results: A statistically significant increase, compared to the control group, was observed in the expression of cytochrome C, Smac/Diablo, vascular endothelial growth factor, its receptor 2 and peroxisome proliferator-activated receptor gamma in the groups in which the EPI® technique was applied.
Conclusions: EPI® technique produces an increase in anti-inflammatory and angiogenic molecular mechanisms in collagenase-induced tendon injury in rats.

Introducción

La tendinosis rotuliana afecta a un número importante de atletas cuyo denominador común es realizar saltos o movimientos balísticos[1]. Actualmente se considera la tendinosis un proceso degenerativo más que un proceso inflamatorio, y a pesar de que se han descrito múltiples opciones terapéuticas, ninguna se ha establecido como método estándar[2,3].

El uso de modelos experimentales basados en la inducción de tendinosis mediante colagenasa (metaloproteinasa capaz de romper los enlaces peptídicos del colágeno) ha sido aplicado previamente[4]. Para el estudio experimental de las tendinosis se ha utilizado previamente la valoración de proteínas como el citocromo C, Smac/Diablo, factor de crecimiento endotelial vascular (VEGF), su receptor 2 (VEGFR-2) y el factor de transcripción nuclear peroxisoma proliferador activado del receptor gamma (PPAR-γ). El citocromo C es una proteína monomérica capaz de activar las caspasas desencadenantes de las últimas fases de la apoptosis en las tendinopatías[5]. La Smac/Diablo es una proteína mitocondrial, cuya liberación al citosol celular induce la apoptosis, presumiblemente siguiendo las mismas rutas de salida que el citocromo C[6]. El VEGF es una proteína señalizadora implicada en la angiogénesis y vasculogénesis que ha demostrado, in vitro, estimular la división y la migración de células endoteliales[7]. El VEGFR-2 es un receptor tirosina-quinasa que actúa como el mediador más importante de la respuesta angiogénica del VEGF[8]. Por último PPAR-γ, de la familia de los factores de transcripción nucleares (superfamilia de receptores esteroideos), ha demostrado producir una disminución de la respuesta inflamatoria[9].

La técnica Electrólisis Percutánea Intratisular (EPI®) produce una ablación electrolítica no termal que induce una respuesta inflamatoria controlada, permitiendo activar los mecanismos celulares implicados en la fagocitosis y en la regeneración del tejido blando dañado[10].

Dado que trabajos recientes han demostrado buenos resultados clínicos con la técnica a estudio[11], el objetivo del presente análisis fue investigar mediante técnicas de inmunodetección y electroforesis los mecanismos moleculares de respuesta tisular implicados en el tratamiento con técnica EPI®, tras la inducción de tendinosis con colagenasa en ratas Sprague Dawley.

Material y método

Para llevar a cabo el estudio se utilizaron 24 hembras de rata Sprague Dawley de 7 meses de edad y aproximadamente 300 g de peso. El estudio cumplió con los requisitos éticos y fue aprobado por el Comité de Bioética de la Universidad de Medicina (A-1301314899794). Se siguieron las normas del Real Decreto 1201/2005, de 10 de octubre, relativo a la protección de los animales utilizados para experimentación (BOE n.º 252. p. 34367-34391).

Los animales se distribuyeron en 4 grupos: 6 ratas de control que no recibieron ninguna intervención (grupo control), 6 ratas inyectadas con colagenasa que no recibieron tratamiento con técnica EPI® (grupo colagenasa), 6 ratas inyectadas con colagenasa y tratadas con técnica EPI® a 3 mA de intensidad (grupo EPI®-3 mA), y 6 ratas inyectadas con colagenasa y tratadas con técnica EPI® a 6 mA de intensidad (grupo EPI®-6 mA).

La técnica EPI® consistió en la aplicación ecoguiada a través de una aguja de 0,32 mm de una corriente continua mediante un dispositivo especialmente diseñado y certificado para tal fin (Directiva CE 93/42/EEC. EPI Advanced Medicine®, Barcelona, España).

Modelo experimental

Se inyectó en la zona proximal del tendón rotuliano de las ratas 50 μg de colagenasa de tipo I (Laboratorios Sigma-Aldrich, St. Louis, MO, EE. UU.), produciendo una tendinosis comprobada por ecografía siguiendo el protocolo definido por la European Society of Musculoskeletal Radiology para el estudio de tendinopatías[12].

Para la realización de la técnica EPI® se realizaron 3 punciones ecoguiadas de 4 s de duración cada una, en la zona proximal del tendón rotuliano de las ratas, con una intensidad de 3 o 6 mA, dependiendo del grupo a estudio. Tras 7 días las ratas fueron sacrificadas y se extrajo quirúrgicamente una muestra del tendón siguiendo el procedimiento estándar.

Se utilizó el método Lowry[13] para determinar la concentración de proteína en la muestra de tejido en rangos de 0,01-1 mg/ml, y se analizaron las muestras por inmunodetección y espectrofotometría (λ = 660 nm). Se analizaron las proteínas citocromo C, Smac/Diablo, VEGF y VEGFR-2. A su vez, se estudió el factor de transcripción nuclear PPAR-γ. Se validaron los resultados por estudio *western blot* contra tubulina, expresando los resultados en unidades de densitometría relativas.

Análisis estadístico

Los resultados se expresan como media ± desviación estándar. El análisis estadístico se realizó mediante la prueba t-test. Se realizó análisis ANOVA para valorar las relaciones entre las variables, así como pruebas post-hoc y de Dunnett para comparar los diferentes grupos con el grupo control y la prueba de Scheffé para comparar todos los grupos entre sí. El nivel de significación se fijó en el 5% ($p < 0,05$). El análisis estadístico se realizó con el programa SPSS® versión 17 (SPSS Inc., Chicago, Illinois, EE. UU.).

Resultados

El estudio del citocromo C (fig. 1) mostró niveles elevados de esta proteína en todos los grupos en comparación con el grupo control ($p < 0,001$). Se encontraron diferencias estadísticamente significativas al comparar el grupo EPI®-3 mA y el grupo EPI®-6 mA ($p < 0,013$), al igual que al compara el grupo EPI®-6 mA y el grupo colagenasa ($p = 0,002$).

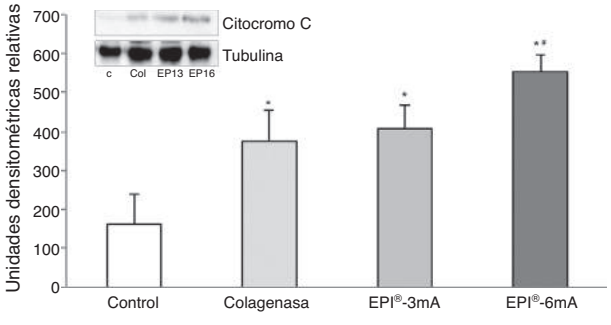

Figura 1 Histograma del análisis de la proteína citocromo C. Media ± desviación estándar expresadas en unidades de densitometría relativas. El asterisco determina significación al comparar con el grupo control, y la almohadilla, al comparar con el grupo colagenasa.

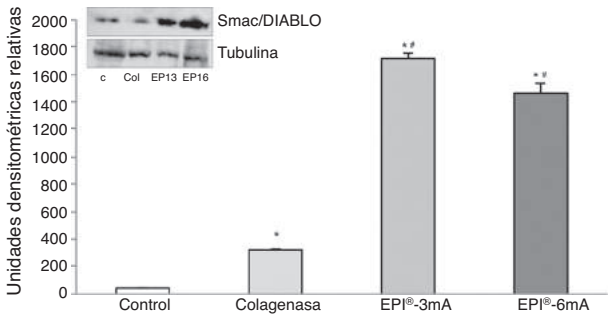

Figura 2 Histograma del análisis de la proteína Smac/Diablo. Media ± desviación estándar expresadas en unidades de densitometría relativas. El asterisco determina significación al comparar con el grupo control, y la almohadilla, al comparar con el grupo colagenasa.

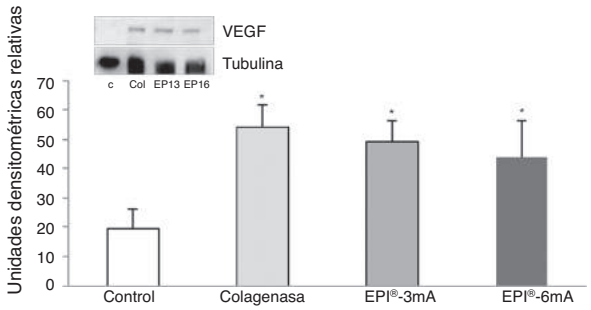

Figura 3 Histograma del análisis de la proteína VEGF. Media ± desviación estándar expresadas en unidades de densitometría relativas. El asterisco determina significación al comparar con el grupo control, y la almohadilla, al comparar con el grupo colagenasa.

La proteína Smac/Diablo (fig. 2) mostró una sobreexpresión de la misma ($p < 0,001$), detectando diferencias estadísticamente significativas al comparar los 2 grupos de tratamiento (EPI®-3 mA y EPI®-6 mA) con el grupo colagenasa ($p < 0,001$).

El análisis del VEGF (fig. 3) mostró un aumento significativo ($p < 0,001$) en todos los grupos a estudio. A su vez se detectó un aumento significativo ($p < 0,001$) del VEGFR-2 (fig. 4).

Por último, la PPAR-γ (fig. 5) presentó un aumento significativo en comparación con el grupo control ($p < 0,001$), presentando diferencias estadísticamente significativas al comparar los grupo EPI®-3 mA ($p = 0,009$) y EPI®-6 mA ($p < 0,001$) con el grupo colagenasa.

Discusión

El principal hallazgo de este trabajo fue que la técnica EPI® produjo una sobreexpresión de las proteínas citocromo C, Smac/Diablo, VEGF, VEGFR-2 y del factor de transcripción nuclear PPAR-γ.

A pesar de que actualmente no exista un tratamiento para la tendinosis considerado como estándar, se han descrito múltiples técnica destinadas a tal fin. Entre ellas se encuentra el ejercicio excéntrico, la cirugía (abierta

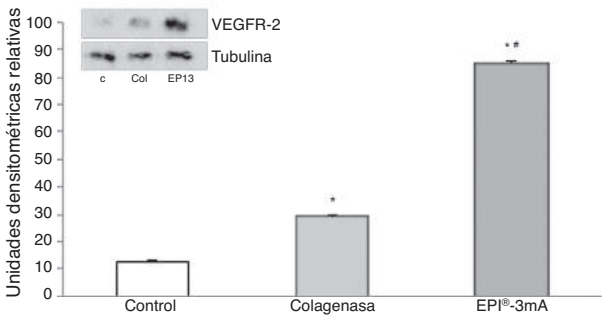

Figura 4 Histograma del análisis de la proteína VEGFR-2. Media ± desviación estándar expresadas en unidades de densitometría relativas. El asterisco determina significación al comparar con el grupo control, y la almohadilla, al comparar con el grupo colagenasa.

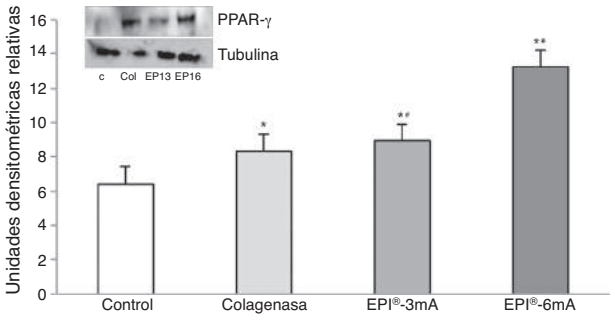

Figura 5 Histograma del análisis de la proteína PPAR-γ. Media ± desviación estándar expresadas en unidades de densitometría relativas. El asterisco determina significación al comparar con el grupo control, y la almohadilla, al comparar con el grupo colagenasa.

o artroscópica), las ondas de choque, la esclerosis de las neovascularizaciones, los antiinflamatorios no esteroideos o la aplicación de plasma rico en plaquetas o aprotina, entre otras[2,3].

La técnica EPI® es una corriente eléctrica no termal que induce una respuesta regenerativa del tejido dañado[10]. Por inestabilidad iónica se crea la formación de moléculas de hidróxido de sodio, produciendo debajo del electrodo activo o aguja catódica una modificación del pH y un aumento de la presión de oxígeno, permitiendo la fagocitosis y la activación biológica de la reparación del tendón, que se encontraba alterada por la cronicidad del proceso degenerativo[10,11].

Trabajos anteriores con terapia electrolítica, como el de Gravante et al.[14], demostraron los efectos de estas técnicas en la respuesta inflamatoria. Un metaanálisis de Gardner et al.[15] demostró que la estimulación eléctrica en heridas crónicas y úlceras de decúbito producía una curación más rápida, mientras que Zhao et al.[16] observaron cómo un campo eléctrico aplicado a cultivos de células endoteliales estimulaba la producción de VEGF, así como la elongación y migración celular, resultados que concuerdan con los mostrados en el presente trabajo. Posteriormente, Yang et al.[17] observaron que la aplicación de corriente directa en tejido blando lesionado es fundamental en la gestión y migración de células epiteliales en la respuesta de cicatrización.

La teoría de la lesión tendinosa secundaria al sobreuso parece ser la más aceptada[1]. Al igual que autores como Alfredson et al.[18] o Tan y Chan[19], consideramos la tendinosis como un proceso degenerativo más que como un proceso inflamatorio. De acuerdo con Fu et al.[20], el aumento de las proteínas VEGF, Smac/Diablo, citocromo C, VEGFR-2 y la proteína antiinflamatoria PPAR-γ está relacionado con la respuesta inflamatoria y la reparación tisular. Dado que la tendinosis es un proceso degenerativo, el tratamiento con la técnica EPI® podría estar justificado[10,11,21–23].

El presente estudio mostró una mayor capacidad de sobreexpresión del citocromo C, marcador de apoptosis relacionado con las tendinosis[5], tras la aplicación de la técnica EPI®. La proteína Smac/Diablo es exportada al citosol desde la mitocondria, produciendo apoptosis a través de la activación de caspasas[6] y daño en el ADN como resultado de la unión al receptor CD95[24]. Los datos presentados muestran cómo los grupos que recibieron tratamiento con la técnica EPI® presentaron un aumento de la expresión de esta proteína. Tal y como describieron Huang et al.[25], el aumento de la apoptosis vía las proteínas Smac/Diablo y la inducción de VEGF a través de VEGFR-2 es probablemente debido al aumento de la inhibición de las células B en el desarrollo de la médula ósea y de la diferenciación de las células T del timo.

Tras el tratamiento con la técnica EPI® se ha observado un aumento de las proteínas antiinflamatorias como la PPAR-γ[9], que tienen un papel primordial en la inhibición de la expresión de moléculas proinflamatorias secretadas por los macrófagos como el TNF-α, IL-6 e IL-1β[26], produciendo una respuesta molecular en el tejido tratado altamente beneficiosa en el transcurso de una tendinosis. A su vez, esto resulta en un aumento de la expresión del VEGF y VEGFR-2, mediadores responsables de la angiogénesis y respuesta antiinflamatoria[7,27]. La literatura identifica los receptores VEGFR-1 y VEGFR-2 como los mayor expresados en el tendón de Aquiles humano[8]. Nuestros resultados muestran un aumento del VEGFR-2 tras el tratamiento con la técnica EPI®, lo que evidencia una modificación en la vía de apoptosis celular y un aumento de la angiogénesis.

Una limitación de este estudio fue el uso de modelos experimentales en animales, por lo que los resultados obtenidos podrían no ser completamente extrapolables a humanos[28]. Sin embargo, los resultados de este estudio son alentadores y ponen de relieve la necesidad de realizar estudios adicionales que incluyan microdiálisis molecular y estudio histológico del tejido tratado[18,29]. Se debe destacar el moderado número de animales de experimentación, si bien los resultados han demostrado una adecuada potencia estadística. Otra limitación podría ser el estudio de 6 alteraciones moleculares en una dolencia tan compleja y desconocida como la que se presenta.

Conclusiones

La técnica EPI® produce, en la lesión tendinosa inducida con colagenasa tipo I en ratas, un aumento de los mecanismos moleculares antiinflamatorios y angiogénicos.

Nivel de evidencia

Nivel de evidencia I.

Responsabilidades éticas

Protección de personas y animales. Los autores declaran que los procedimientos seguidos se conformaron a las normas éticas del comité de experimentación humana responsable y de acuerdo con la Asociación Médica Mundial y la Declaración de Helsinki.

Confidencialidad de los datos. Los autores declaran que en este artículo no aparecen datos de pacientes.

Derecho a la privacidad y consentimiento informado. Los autores declaran que en este artículo no aparecen datos de pacientes.

Conflicto de intereses

El autor J.M. Sanchez-Ibáñez posee la patente de los dispositivos EPI®. Ha participado en la realización del tratamiento, así como en la redacción del manuscrito, pero no ha participado en la obtención de las muestras, el análisis molecular ni el estudio estadístico de los datos obtenidos.

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Percutaneous electrochemical debridement of the Plantaris tendon: a novel option in the treatment of midportion Achilles tendinopathy.

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Authors' contribution: GM and CM were responsible for the study concept and design. GM drafted the manuscript. All authors approved the final manuscript.

BLINDED MANUSCRIPT

TITLE

Percutaneous electrochemical debridement of the Plantaris tendon: a novel option in the treatment of midportion Achilles tendinopathy.

ABSTRACT

Plantaris tendon disorders are a well-known source of midportion Achilles tendinopathy. Plantaris tendon thickening and fibrous tissue formation between the tendons are the histological abnormalities which are typically observed. Surgical approaches (scraping of the Achilles medial and ventral paratendinous tissues and excision of the Plantaris tendon) have already shown good clinical outcomes; despite this, cost-benefit ratio of these interventions may be unfavourable and their accessibility is limited. Percutaneous needle electrolysis is a minimally invasive ablative technique of increasing consideration in the treatment of tendinopathies and associated conditions. The purpose of this article is to introduce a novel procedure to treat Plantaris tendon-related midportion Achilles tendinopathy. The procedure starts with the insertion of a non-coated needle (diameter: 0.30-0.40 millimetres; length: 30 millimetres) between the Plantaris and Achilles tendons, under ultrasound guidance. Subsequently, galvanic current (intensity: 2 mA) is locally transferred. This, in turn, induces instant non-thermal electrochemical ablation of the intertendinous tissues in close proximity to the needle, finally debriding the Plantaris tendon. In order to further promote its release, second part of the procedure involves partial tenotomy of the lateral peripheral aspects of the Plantaris tendon. Usually, the total duration of the session does not exceed thirty minutes. Percutaneous needle electrolysis may be considered as a valid alternative to surgery. The out-patient procedure presented in this article is, in fact, safe and quick to perform. Additionally, long suspension of working or sporting activities after the treatment is not required. Future investigations are needed to ascertain the short- and long-term therapeutic outcomes in the treatment of Plantaris tendon-related midportion Achilles tendinopathy, in particular by comparing them with those obtained with other mini-invasive interventions.

KEYWORDS

Ablative techniques – Electrolysis – Interventional ultrasonography – Tendon injuries

INTRODUCTION

The role of the Plantaris tendon in the etiopathogenesis of midportion Achilles tendinopathy has been certified over the last decade [1–3]. However, research of highly specific diagnostic modalities and optimal treatment strategies is still ongoing. Plantaris tendon-related midportion Achilles tendinopathy is clinically characterised by debilitating pain and swelling, which are typically localised in the medial aspects of the Achilles tendon body [2–3]. Friction and compression traumas between the tendons are likely to be the biomechanical disorders that lead to the histological changes observed in many researches, such as Plantaris tendon thickening, fibrous tissue formation between the tendons and alteration of the vascularisation and innervation patterns of the Achilles paratenon [1–4].

Surgical scraping of the Achilles medial and ventral paratendinous tissues has shown good clinical results in many trials, especially when associated with excision of the Plantaris tendon [5–8]. Despite this, cost-benefit ratio of these interventions may be unfavourable and their accessibility is relatively limited. Additionally, post-surgery rehabilitation protocols may last several months. As a consequence of this, there is need to identify new therapeutic solutions which may be as effective as surgery but without having these relevant weak points.

Thus, the main purpose of this article is to introduce the debridement of the Plantaris tendon via electrochemical ablation, induced by cathode-centred percutaneous needle electrolysis. The latter is an ultrasound-guided and minimally invasive technique which may be considered a valid alternative to surgery or, at least, a treatment option to contemplate before performing it. In support of this hypothesis, minimally invasive techniques (needle scraping or sclerosing polidocanol injections) have already shown encouraging clinical results in the treatment of Plantaris tendon-related midportion Achilles tendinopathy [9] and, on the other hand, percutaneous needle electrolysis is generally of increasing consideration in the treatment of tendinopathies and associated conditions [10–13].

PERCUTANEOUS NEEDLE ELECTROLYSIS

This study was designed and conducted according to national and international standards and in compliance with the Helsinki Declaration and the International Principles governing research on humans. Considering the typology of this article (clinically illustrated – technical note), *material and methods* and *results* sections are neither required nor presented.

Equipment

The Authors apply the technique using a specifically developed and medically certified device (EPI Advanced

Medicine®, Barcelona, Spain; directive 93/42/EEC). This instrumentation permits intratissue galvanic current transfer, at settable intensities, through an appropriate non-coated needle (diameter: 0.30-0.40 millimetres; length: 30 millimetres; same manufacturer as above). While the needle acts as the cathode, the anode can be handled by the patient or applied on the skin. The cathodic flow is the only one that is used during the procedure (cathode-centred electrolysis). When the current is transferred, the basic electrochemical process of saltwater electrolysis instantly develops, inducing the non-thermal ablation of the tissue in close proximity to the needle. The latter is inserted under ultrasound guidance in order to precisely treat the target tissue, without involving other structures. For this purpose, the Authors use the GE Healthcare® Logiq S7 Expert ultrasound equipped with the ML6-15 (50mm; 6-15 MHz) and L8-18I-D (25mm; 8-18 MHz) linear probes.

Preliminary ultrasound investigation

The patient lies on his or her side, with the medial aspects of the Achilles tendon directed upwards. The region is shaved and disinfected by applying a proper protocol. A preliminary ultrasound is carried out in order to accurately detect the portions of the Plantaris tendon in anatomical relationship with the medial aspects of the Achilles tendon body. It may be helpful to delimit the region to be treated, marking its distal and proximal limits with a sterile dermographic pencil. It is also advisable to mark the points at which the patient complains about having more pain and swelling ("critical areas") and where the major anatomical alterations are discernible (figures 1–2).

Description of the procedure

The procedure is graphically represented in figure 3. First, the needle is inserted between the Plantaris and Achilles tendons, under ultrasound guidance (figure 4). Subsequently, the galvanic current is transferred (intensity is pre-set to 2mA). Doing this, the local ablation of the fibrous intertendinous and Achilles paratenon tissues is instantaneously obtained, anatomically debriding the Plantaris tendon (figure 5). The single applications of current last 2-3 seconds.

Then, the needle is partially withdrawn and pointed toward the Plantaris tendon. In order to further promote its release, a partial tenotomy of the lateral peripheral aspects of the tendon is performed (figure 6). To this effect, the single application can have a variable duration, between 2-6 seconds, depending of the mechanical resistance offered by the tendinous tissue to the needle penetration (the lower the resistance, the shorter the application).

All the actions presented above are repeated approximatively every five millimetres (or less, in the "critical areas"; see above), in distal-proximal direction, throughout the region previously skin-marked. Typically, the total duration of the session does not exceed thirty minutes (including disinfection and dressing processes).

Tolerability of pain and side effects

The insertion of the needle typically cause minimal discomfort. By contrast, the patients may experience moderate strong pain during the applications of galvanic current. Anyway, anaesthetics are usually not locally injected before percutaneous electrolysis, since the procedure is generally well-tolerated by the patients (the single galvanic current application can be stopped at any time if the pain is not bearable) and because the use of syringes would substantially increase the overall invasiveness of the intervention. Anyway, use of anaesthetics remains a considerable option. Relevant vagal reactions during and immediately after the intervention are possible [14]. Bleeding in area of needle insertion and intervention-related discomfort in the treatment area (up to 48 hours) are the most common side effects. Infection-related issues are extremely rare, as the technique is minimally invasive and the electrolytic process has a substantial bactericidal effect.

DISCUSSION

The main purpose of this article is to introduce the debridement of the Plantaris tendon, via electrochemical ablation induced by cathode-centred percutaneous needle electrolysis, to treat Plantaris-related midportion Achilles tendinopathy. This novel procedure permits to eliminate the fibrous tissue interposed between the Plantaris and the Achilles tendons, debriding the Plantaris tendon and improving the local biomechanics.

The main practical value of this technique is the possibility of performing it in out-patient clinics, reducing considerably the costs, the waiting lists-related issue and the other implication and side effects of Achilles tendon surgery, such as suture reactions, incisional neuromas, and granuloma formation [15]. Furthermore, it should be reminded that post-surgery protocols may last several months. On the contrary, consistent with our experience, in particular with professional football (soccer) player, it is not necessary to completely suspend the sporting (or working) activities for more than 24-48 hours, after percutaneous needle electrolysis treatment. In fact, the side effects tend to be very moderate. However, many authors that use this technique, including us, find it helpful to implement a complementary protocol of active physical therapy [10–13]. Preliminary studies carried out by our research group indicate that the short-term clinical results (not yet published) after percutaneous needle electrolysis treatment in professional athletes are very promising but that it commonly necessary to conduct at least 3-5 sessions (one per week) to obtain long-lasting results. However, to date, clinical or imaging predictors of outcome are substantially unknown.

CONCLUSION

Percutaneous needle electrolysis is an ultrasound-guided and minimally invasive technique that allows specific treatment of the anatomical alterations that cause Plantaris tendon-related midportion Achilles tendinopathy. Since it is safe and quick to perform, it may be considered as a valid alternative to surgery. Future investigations are needed to ascertain the short- and long-term therapeutic outcomes in the treatment of Plantaris tendon-related midportion Achilles tendinopathy, in particular by comparing them with those obtained with other mini-invasive interventions.

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FIGURES

Figure 1. Plantaris tendon morphological abnormalities are commonly observed in case of mid-portion Achilles tendinopathy. The transversal, grey-scale, high resolution ultrasound image presented shows increasing of the thickness and width of the Plantaris tendon (indicated by the *dashed arrow*). In order to complete an accurate investigation, it is advisable to compare the tendon dimensions with those of the contralateral one and to take into high consideration the data concerning the normal morphology of the Plantaris tendon presented by Olewnik et al [1]. *Ach* = Achilles tendon; *K* = Kager's fat pad. Probe used: ML6-15 (50mm footprint).

Figure 2. Transversal, high resolution ultrasound image showing high blood flow (*filled arrows*) in the medial aspects of the Achilles tendon (*Ach*) and paratenon, between the Achilles and Plantaris tendon (indicated by the *dashed arrow*) and around the latter. In case of mid-portion Achilles tendinopathy, these signs may be discernible also in the ventral portions of the Achilles tendon [2]. Probe used: ML6-15 (50mm footprint).

Figure 3. Schematic diagram of the percutaneous needle electrolysis procedure, for the debridement of the Plantaris tendon. The needle is initially inserted between the Plantaris (*dashed arrow*) and the Achilles (*Ach*) tendons, as indicated

by the *line 1*, and, subsequently, within the lateral peripheral aspects of the Plantaris tendon, as indicated by the *dashed line 2*. *Asterisk* = tibial neurovascular bundle.

Figure 4. Ultrasound-guided insertion of the needle between the Achilles and the Plantaris tendons. Considering their anatomical relationship, the preferred approach is in posterior-to-anterior and medial-to-later direction. Inclination of the needle is variable and depends upon the specific morphological features of the tendons.

Figure 5. An iperechoic area (*arrows*) is typically observable around the needle immediately after the application of galvanic current and consequent development of the electrochemical process. This should confirm that only the intertendinous tissues have been treated, without involvement of other structures (first part of the procedure). *Dashed arrow*=Plantaris tendon; *Ach*=Achilles tendon. Probe used: L8-18I-D (25mm footprint).

Figure 6. After the ablation of the intertendinous fibrotic tissues, the needle (*asterisks*) is partially withdrawn and inserted in the lateral peripheral aspects of the Plantaris tendon (second part of the procedure). *Dashed arrow*=Plantaris tendon; *Ach*=Achilles tendon. Probe used: L8-18I-D (25mm footprint).

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Commentary Open Access

New Technique in Tendon Sport Recovery. Percutaneous Electrolysis Intratissue (EPI®)

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Based on the literature and clinical experience we know that the technique of percutaneous electrolysis intratissue (EPI®) has positive effects on the recovery of human tendinopathies. The application of the technique, together with the completion of eccentric exercise, give benefits leading to anatomical and functional recovery in the tendon that can be appreciated by ultrasound using the scale of "Victorian Institute of Sport Assessment-patellar tendon" (VISA-P). Due to clinical knowledge, damage to tendon is accompanied by increase in oxidative stress, cell death and inflammation at the damaged area. The EPI technique produced a galvanic current inside the tendon, with an acupuncture applicator, producing increase in cell death, inflammation and oxidative stress in the first days of treatment. After these days, the recovery of tendon is quickly and higher than without EPI technique used. Galvanic current is produced in a salad solution producing chemical reaction with salt decomposition (NaCl) and H_2O_2 in its chemical constituent elements. After they form new substances, such as NaOH, H_2 and Cl_2, they change the reactions inside the tendon damage. The NaOH has vital importance because it is high caustic and destroy collagen and mixed substances in tendon damage area. EPI is a basic technique giving a chemist process without boil electrocution of tissue. When EPI is used, an increase in inflammatory response of the tissue is also detected. In chronic tendon, with the unique possibility of recovery by surgery, EPI technique has recuperation of tendon without surgery. EPI technique, in European countries, has been used in the last decade with wonderfully results to recovery pathological tendons from athletes in competition. Furthermore, it is known that after recovery from injury in damaged area, neo-vascularization occurs. It is intent of tendon to obtain more energy to recover damage tissue.

Valles and its collaborators have demonstrated the molecular mechanism of action of EPI technique [1]. First of all, an increase in oxidative stress and inflammation occurs in the tendon chronic damage. After, we appreciate a neovascularization in the damage area with increase in inflammatory mediators. As we know in damage tendon, in first days of lesion, an increase in inflammation and vascularization are detected, but sometimes tendon recovery occurs with a non-excellent distribution of the tendon tissue. With the EPI technique, because the destruction produced by EPI and posterior redistribution of tendon damage, produce a more promptly recovery with a good new distribution of new tissue.

Studies with human have demonstrated the importance of this technique in sport population and also studies in rats [1,2] have shown an increase in apoptosis and necrosis, with increase in Citochrome C and SMAC/diablo, demonstrating a special pathway to recover from the damage produced by EPI [3]. Interesting, has been demonstrated in cancer A431 cells that cholesterol depletion using metil-β-ciclodextrine cause apoptosis [4]; and in human queratinocites disruption of lipid rafts by depletion of cholesterol compounds (metil-β-ciclodextrine, filipin III, colesterol oxidase or mevastatin) produce an rapid union of Fas inside lipid membranes, forming Fas-FADD complex, activation of caspase-8 and apoptosis [5]. We here want to appoint that after lesion and too destroy damage tissue or near tissue to damage tissue, a programed cell death occur inside the organism to permit the elimination and regeneration in damage tissue. SMAC/diablo is a protein principally induced in programed apoptosis.

In the clinic, we detect an increase in local angiogenesis develop after application of EPI technique. In research with rats, we have demonstrated an increase in vascular endothelial growth factor (VEGF) and its receptor VEGFR-1 and 2, demonstrating an increase in neovascularization in the damage area. Also we detect, days after application of EPI technique an increase in PPAR-γ production, anti-inflammatory protein produced after inflammation occurs in damage tissues.

With all, we want to note here the importance of this technique in the future to recover damage tendon in sport population and in football players in particular.

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Review Article Open Access

New Treatments for Degenerative Tendinopathy, focused on the Region-Specific of the Tendon

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Abstract

Tendinopathy is a common, painful, overuse disorder associated with a failure of the tendon repair process and has a low potential for healing with the usual techniques. Although many different treatment methods have been described, there is no consensus regarding the optimal treatment for this condition.

Therefore, new treatments for tendinopathies drawn from the existing literature as well as from their own experience dealing with this condition to deal with this delicate pathology have been developed over last few decades. Although some treatments like eccentric training, the EPI® technique, extra-corporeal shock wave therapy (ESWT), hyaluronic acid (HA), platelet-rich plasma (PRP) are being established as the main therapeutic models, there are still questions to be answered as well as the need for a clear treatment protocol to be established.

This brief review aims to update recent information on the treatment approaches of tendinopathy focused on the specific area of the tendon.

Keywords: Tendinopathy; EPI® technique; Treatment approaches

Introduction

The tendons play an essential role in the musculoskeletal system by transferring the tensile loads from muscle to bone so as to enable joint motion and stabilization [1]. Tendons have the ability to adapt to load changes, increasing collagen synthesis as a result of acute and prolonged physical exercise training [2,3]. Despite this ability to adapt physiological loads, tendinopathies represent a clinical problem which affects both professional and recreational athletes as well as people involved in repetitive work [4,5]. Tendinopathies overuse represents 30% to 50% of all sports injuries and result in a significant amount of morbidity and spending health cost [6]. More than 28 million patients in the United States have tendon damage annually [7]; it is estimated that they could cost the United States health system some $30 billion per annum [8].

The etiology includes lifestyle, loading pattern, biological variables (genetics, age, sex) as well as different pharmacological agents [9].

The Achilles tendon and patellar tendon are most affected, in both elite and recreational athletes, in sports that heavily load the lower extremities [10]. Achilles tendinopathy is more prevalent in the lower extremity, with a frequency of 5.9% in sedentary and about 50% for endurance athletes [10,11]. Patellar tendinopathy is most common involvement in the knee and its prevalence has been reported to be 44.6% in elite volleyball players [12] and 31.9% in elite basketball players [13] and also represents two thirds of all pathologies of the knee between these two sports [10].

The traditional model of "tendonitis" as an inflammatory process is now obsolete since the appearance of several publications, which have described the pathological process of the tendon as mainly degenerative (tendinosis) [14,15]. This is justified due to the absence of inflammatory cells, the presence of areas of collagen degeneration, myxoid degeneration and an increase in fundamental substance and is associated with a failure of the tendon repair process [14,15].

Tendinopathy is a clinical diagnosis and typically is based on medical history and clinical findings. Imaging techniques: such as color doppler sonography (CDS) and magnetic resonance imaging (MRI) are valuable tools to confirm the diagnosis and provide guidance for treatment [16].

The tendon injury can occur in the tenotendinous region, as in the Achilles tendon. However, most of the tendon pathology and pain is located in the osteotendinous, such as elbow lateral patellar tendon and the medial epicondyle tendons and tendons in the groin [17]. While osteotendinous and tenotendinous and are morphologically different region in normal state, the occurrence of extracellular matrix pathology induced cellular changes are indistinguishable [18].

Tendinopathies are in the main accompanied by an excessive nociceptive signalling from the tendon, causing pain and restricted mobility [19]. Mechanisms driving these structural and neurological changes are not fully understood. A more recent theory ascribes part of

the tendinosis changes to an increased production of biochemical agents, such as substance P (SP) [20] and NMDAR1 glutamate receptor [20-22].

Overall tendinopathies are characterized by prolonged, localized pain, associated with physical activity requiring cyclic mechanical stimuli. Patients respond poorly to most conservative treatments, however, a broad spectrum of disorders of the tendon within the concept of tendinopathy that share some common characteristics (paratendinitis, tendinitis, tendon overuse injuries, spontaneous tendon rupture, calcifying tendinitis) or gaps, often converge in the same tendon (Figure 1). In this sense, there is no single etiology and pathogenesis that can explain all these processes [17].

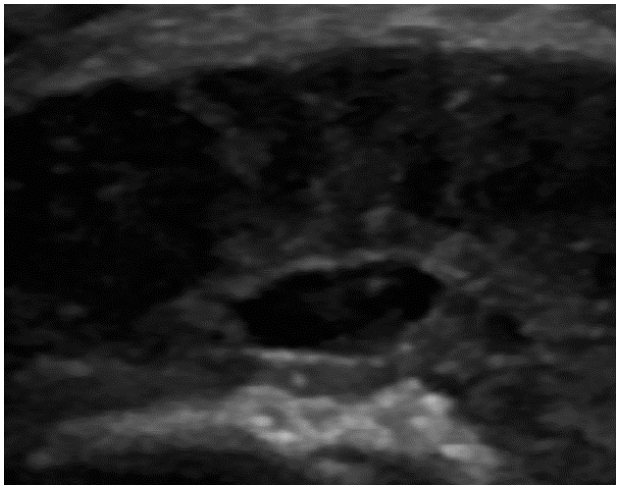

Figure 1: Transverse ultrasound of patellar tendinopathy with area of fibrillar rupture (hypoechogenic foci surrounded by connective reinforcement). Tendon degeneration in its most proximal and deep portion (critical area to receive higher tensile strength during tissue stress).

Treatment options have changed over the last decade in parallel to the pathophysiological and histopathological findings in tendinopathies. Since the underlying pathology of chronic tendinopathy can be defined as a "defective healing response", treatment should aim to encourage regeneration of the tendon, pain modulation and the restoration of the biomechanical properties [23,24].

In this paper the authors will update the knowledge about tendinopathy and current treatments focused on the region-specific of the tendon drawn from the existing literature as well as from their own experience dealing with this condition. Some of these treatments are eccentric training, the EPI® technique, extra-corporeal shock wave therapy (ESWT), hyaluronic acid (HA), platelet-rich plasma (PRP) are other treatment options [25].

Anti-inflammatory therapy

Conventional conservative treatments have generally been used empirically to reduce pain and inflammation. These treatments include relative repose or activity modification, cold, stretching, orthopedic supports, physiotherapy and biomechanical correction. They are usually employed initially in acute and the more hyperalgesic phase of tendinopathy but fail to modify the histological structure of the tendon [26,27].

The aim of non-steroidal anti-inflammatory drugs (NSAIDs) is to reduce inflammation by inhibiting the synthesis of inflammatory factors (inflammatory cells, prostaglandins, interleukins, etc.) and their use has been popular in the management of tendinopathy for years [28]. NSAIDs affect the activity of tenocytes and glycosaminoglycan synthesis [29,30]. While their use can be justified on a reactive tendinopathy, the tendon's response upon loading can be affected by a potential inhibition of collagen synthesis [31] as well as have a detrimental effect on muscle adaptation [32].

Possible mechanisms of action of corticosteroid injection include a reduction in extrinsic or intrinsic inflammation, reduction in the proliferation of tenocytes, anti-angiogenic activity, and the inhibition of scar formation, some anti-nociceptive action or a combination of these mechanisms [33].

The literature suggests that the majority of patients may experience a short-term improvement in terms of pain and/or function but in exchange for a high risk of relapse in the medium term and with side effects that may even lead to a rupture of the tendon [34]. Two recent systematic reviews showed worse results from the use of glucocorticoids in comparison to other treatments and the placebo group in the medium and long-term [35,36].

Konsgaard et al. [37] reported that heavy slow resistance training also resulted in significant improvement compared with corticosteroid injections.

Eccentric exercises

Eccentric exercise has shown to cause an upregulation of insulin-like growth factor (IGF-I). This upregulation of IGF-I is associated with cellular proliferation and matrix remodelling within the tendon [38].

Programs of eccentric exercise have been proposed as a key element in strength training in rehabilitation because they can supposedly counteract the response of defective healing that apparently underlies tendinopathy by promoting the creation of collagen fibers within the tendon [39,40]. The literature places increasing emphasis on the importance of a proper choice of the load used [41].

The continuum model in tendinopathy (reactive tendinopathy, tendon dysrepair and degenerative tendinopathy) provides a reasoned basis for believing that the protocol to be performed depends on the current clinical presentation [17]. The protocol proposed by Alfredson et al. is generally used [39]. It consists of three sets of 15 repetitions, performed twice a day, seven days a week for 12 weeks.

Ohberg et al. [42] examined tendon structure by grey-scale ultrasound in 26 tendons with Achilles tendinosis, which had been treated with eccentric exercise. Remarkably, after a mean follow up of 3.8 years, 19 of 26 tendons had a more normalised structure, as gauged by their thickness and by the reduction of hypoechoic areas.

Visnes et al. [43] suggested that eccentric training had a positive effect on patellar tendinopathy and recommended that athletes suspend sports activity during rehabilitation.

The gradual progression from eccentric-concentric to eccentric followed by a faster loading can benefit patients with Achilles tendinopathy cannot start with a program proposed by eccentric

Alfredson et al. [39] due to pain or weakness of the sural triceps muscle [44].

Isoinertial eccentric training (YoYoTechnology AB, Stockholm, Sweden) resulted in an improvement of muscle function and reduced pain in patients with patellar tendinopathy [45]. The combination of EPI® technique and isoinertial eccentric exercise offers good results in the treatment patellar tendinopathy [46].

EPI® technique

In recent years, the intratissue percutaneous electrolysis (EPI®) technique has become more relevant in the scientific literature [46-48] given the good results yielded in the treatment of patellar degenerative tendinopathy in comparison to other previous conservative treatments.

This technique, created by Sánchez-Ibáñez [49,50] and who have over 15 years' experience in its use, uses a flow of cathodic current directed exclusively to the area of degenerated tendon through an ultrasound-guided needle that brings about an organic reaction that leads to rapid regeneration of the degenerated tendon.

The application of ultrasound-guided EPI® technique produces a non-thermal electrochemical reaction centered on degenerated tissue (tendinosis). This leads to a controlled local inflammatory reaction that leads to the regeneration of damaged tissue [48,51].

In experimental studies with human tendon injury, there has been a disproportionate expression of certain cytokines and matrix metalloproteinase (MMPs), prostaglandin E2 (PGE2), interleukin-6 (IL-6) and interleukin-1b (IL-1b) [52,53]. IL-1b in turn increases the production of matrix metalloproteinase-1 (MMP-1), matrix metalloproteinase-3 (MMP-3) and prostaglandin E2 (PGE-2) [53].

A recent experimental study [48] showed that with the use of EPI® technique in patellar tendinopathy increase of anti-inflammatory proteins, like peroxisome proliferator-activated receptor gamma (PPAR-γ). These proteins play a key role in the inhibition of expression of proinflammatory molecules secreted by macrophages, such as tumor necrosis factor alpha (TNF-α), IL-6 and IL-1β, thus producing in the treated tissue a highly beneficial molecular response during degenerative tendinopathy. This, in turn, results in an increase of the expression of vascular endothelial growth factor (VEGF) and vascular endothelial growth factor receptor 2 (VEGFR-2), mediators responsible for angiogenesis anti-inflammatory response. The EPI® technique makes for the activation of molecular and cellular mechanisms of the tendon responsible for phagocytosis and the regeneration of degenerated tissue.

In recent research to evaluate the therapeutic effects EPI® technique on the patellar tendinopathy [46]. The results documented were good and stable with the Victorian Institute of Sport Assessment-Patella (VISA-P) score, Tegner scores and Roles and Maudsley score, and terms of clinical and functional improvement in patellar tendinopathy and providing a follow-up of 10 year.

The EPI® technique (Figure 2) achieves a much localized organic reaction in the clinical focus by using a specially designed device for this purpose (EPI Advanced Medicine®, Barcelona, Spain. EPI® technique videos online: www.epiadvanced.com), which leads to the rapid regeneration of degenerated tissue. This leads to the production of new immature collagen fibers that become mature by means of eccentric stimulus [47], thereby obtaining good results in the short and long-term in terms of pain and function.

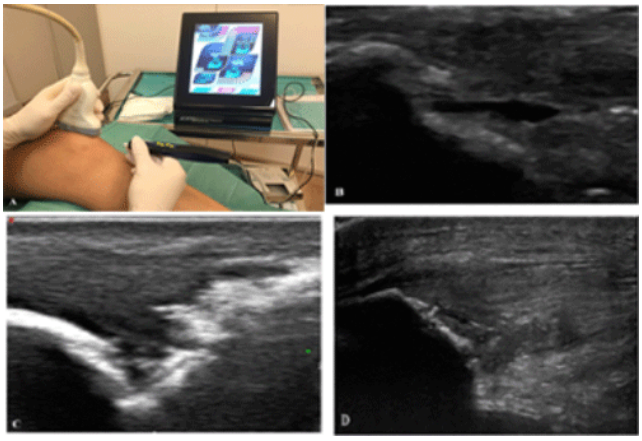

Figure 2: A) Treatment of patellar tendinopathy with ultrasound-guided EPI®- MTR device (EPI Advanced Medicine®, Barcelona, Spain). B) Ultrasound longitudinal view of patellar tendinopathy with area of fibrillar rupture. C) Treatment is directed exclusively to the area of tendon injury. Note the electrochemical reaction (white area) produced on the tip of the needle, just in the area of damaged tissue. D) Longitudinal ultrasound view of patellar tendinopathy, three weeks post-treatment with EPI® technique. Note that the area of fibrillary rupture has been replaced by new connective tissue.

Extra-corporeal shock wave therapy (ESWT)

Several clinical trials have evaluated the use of extra-corporeal shock waves therapy (ESWT) for the treatment of patients with chronic tendinopathy with divergent results [28,54,55]. Multiple variables are associated with this therapy, the type of shock wave generator (electrohydraulic, electromagnetic or piezoelectric), the wave type (radial or focal), the intensity (total energy per shock waves/session), the frequency and the protocol of application and repetitions [56].

Some of the effects of ESWT on tendinopathies like the inhibition of nociception with the release of substances which inhibit pain (endorphins), the increase in the permeability of cell membranes of neurons and cellular damage that could create immediate analgesia have been described [25].

Other biological effects of ESWT described, are the induction of specific growth factors (TGF-β1 and IGF-1) which play an important anabolic and mitogen role, increased blood flow, mediators of the inflammatory process, and increased release of hydroxyproline tenocytes of proliferation and collagen synthesis [57].

However, evidence of the effectiveness of ESWT in the treatment of tendinopathy is inconsistent, still so, it is widely used in sports medicine and physiotherapy [58]. It appears that the combination of treatments may have a synergistic effect and lead to better results. In this sense, a study showed better results by combining the ESWT and eccentric exercises than by performing eccentric exercises alone [59, 60].

Platelet-rich plasma (PRP)

Platelets are nonnucleated cytoplasmic bodies derived from megakaryocyte precursors. They play a pivotal role in hemostasis and wound healing via the formation of fibrin clots. Therefore, increasing platelet concentration in injured tissue and may result in an exponential release of diverse bioactive factors and, subsequently, enhance the healing process [61].

Injections with platelet rich plasma (PRP) has been used for the treatment of tendinopathy with the aim of providing cellular and humoral mediators to induce healing in areas of degeneration. Despite the long road ahead toward establishing an agreed protocol on the use of PRP [62,63], it is a widespread treatment option for the treatment of chronic tendon injuries and its beneficial effects have been demonstrated in several studies [70].

A recent experimental study showed that with the use of PRP in patellar tendinopathy, there was an increase in fibroblasts and bone marrow stem cells inside of and around the injury. Cell proliferation was twice as high and the PRP-treated group also showed a significant increase in type I and III collagen when compared to the control group [64]. Another in vitro study in humans showed that following the application of PRP, there was increased cellular proliferation, collagen production in tenocytes, an overexpression of the receptor of vascular endothelial growth factor-A (VEGF-A) and an increase in the concentration of transforming growth factor beta (TGF-B), indicating an increase in the production of type I and III collagen [65]. Despite everything described, it should be noted that there are different techniques for the preparation of PRP, thus obtaining different volumes and concentrations of platelets [66,67].

Filardo et al. [68] evaluate the therapeutic effects of multiple PRP injections on the healing of chronic refractory patellar tendinopathy. The results documented were good and stable with the VISA-P score. The ultrasound measurements showed that tendon thickness and neovascularization level gradually decrease over time, despite an initial increase after the injection cycle.

Dallaudiére et al. [69] also aimed to assess the efficacy and tolerance of intratendinous injection of PRP to treat tendinopathy. This study included 41 patients had patellar tendinopathy. The average WOMAC scores of 41 patients with patellar tendinopathy improved from 38 to 16 at the 6-week follow-up and more improved (6 scores) at 32-month follow-up. No clinical complication was reported during follow-up. This study demonstrates that the ultrasound-guided injection of PRP allows rapid healing of tendon with good tolerance.

Another study of randomised control trials (RCT) by Dragoo et al. [70] compared a regimen of eccentric exercises combined with either ultrasound-guided PRP injection or ultrasound-guided dry needling alone in the treatment of patellar tendinopathy. The PRP group showed significantly better improvement than the dry needling group in VISA-P score at 12 weeks. However, at 26-week follow-up, the difference between the PRP and dry needling groups dissipated in all assessed scores, such as VISA-P, Tegner, VAS, and short form-12 (SF-12) scores.

Sclerosant injections (polidocanol)

Based on the theory that neovascularization are associated with an underlying mechanism due to overuse in tendinopathies. The randomized, double-blind trial by Alfredson and Öhberg focused on the potential benefit of the sclerosing substance polidocanol on chronic tendinopathies. The VAS pain and the patient's satisfaction at 3 months of those who were injected, compared with those of whom received injections of local anesthetics only, supported the superiority of the tested treatment, with significant differences in the values recorded ($p<0.005$) [71].

The use of polidocanol (a vascular sclerosing agent) has been put forth for the treatment of the same [72]. Polidocanol is used to sclerose areas of high intratendinous blood flow, which is sometimes called "neovascularization", visible histopathologically [73] and in vivo by means of high-resolution ultrasound with color doppler.

Some studies have reported effects using polidocanol for patellar tendinopathy, tennis elbow or Achilles tendinopathy [72,74,75].

Studies that associate sclerosing injections and eccentric training have shown a decrease in pain during eccentric training, resulting in complete resolution of pain in the short term Achilles tendinopathy [26].

Zeisig et al. [76] they reported that maintained sclerosis neovascularization in lateral elbow epicondylitis was a good predictor of positive clinical effect at 2 years follow-up.

High-volume image guided injection (HVIGI)

Different methodologies have been described when applying HVIGI. In one study in athletes with achilles tendinopathy, patients were treated with 10 ml of 0.5% bupivacaine hydrochloride injection plus 40 ml saline solution and 25 mg of aprotinin. The HVIGI with aprotinin showed a significant improvement in pain and function in both the short and long term follow up of 12 months [77].

Study groups like those of Chan et al. [78] reported good results with the use of high volume image-guided injections (HVIGI) in the treatment of tendinopathy mainly of the Achilles and patellar tendon, claiming that they significantly reduce pain and improve function.

This intervention uses large volume injections of saline solution, corticosteroids or an anesthetic that make the neovessels stretch, break or occlude. Occlusion or interruption of neovessels supposedly also affects the innervation that it accompanies [79].

Hyaluronic acid (HA)

Possible biological effects of hyaluronic acid (HA) in tendinopathies be related with an anti-inflammatory activity, enhanced cell proliferation, and collagen deposition, besides the lubricating action on the sliding surface of the tendon.

Study groups like those of Petrella et al. [80] determined the efficacy of periarticular HA injections in patients with chronic lateral epicondylosis. Pain, both at rest and after grip testing, was significantly reduced in the study group compared to controls.

Muneta et al. [81] reported good results with the use of HA in the treatment of patellar tendinopathy. After treatment, 94% of patients were rated in excellent in good conditions complained of some degree of limitation.

Injections of the MMP-inhibitor (Aprotinin)

Tendinopathies, are characterized by changes in expression and activity of various metalloproteinase enzymes that degrade the matrix which are consistent with increased proteolytic activity in the degenerate tendons [25].

Aprotinin is a broad spectrum inhibitor of matrix metalloproteinase (MMPs) [82]. It is suggested that by inhibiting the enzymes that break down or degrade tendons, the healing response may be promoted.

In a study by Orchard et al. [83] with 430 patients suffering from patellar and Achilles tendinopathy treated with local injections of aprotinin, the results showed that, at a minimum follow-up of 3 months (range 3-54 months), 76% of patients improved clinically and functionally.

Brown et al. [84] conducted a randomized control trial study (RCT) the use of aprotinin in the treatment of Achilles tendinopathy, 26 patients divided into 2 groups, one group with aprotinin injection and another group with saline (placebo). There were no significant difference scores in VISA-A (p=0.946) at 52 weeks of follow-up.

Stem cells

In the last few decades, several emerging strategies including with mesenchymal stem cells (MSC) have been proposed to enhance tendon healing. Stem cells are undifferentiated cells with ability of self-renewing and differentiating in progenitor or precursor cells. The latter are committed cells for a specific cell lineage, but are not able to self-renew [85].

Human MSCs have been isolated from adipose tissue, umbilical cord, placenta, peripheral blood, connective tissues of the dermis and skeletal muscle [86-91].

A stem cell population has been recently identified in human tendons, residing in a unique tendon extracellular matrix (ECM) niche [92].

Tendon stem cells (TSCs) have been described in 2007 by Bi et al. [92]. These stem cells present in mature tendon have multi-differentiation and self-renewal potential [92]. They can differentiate into other cell types, like muscle or fat cells. These cells have been implicated as possible cause of chronic tendinopathy because of the erroneous differentiation into abnormal matrix components causing fatty degeneration and calcification. These cells are still in the preclinical experimentation stage but have great potential for tendon therapy in the future [93].

TCSs could be involved in tendon homeostasis, remodelling, and repair, by ensuring replacement of mature cells lost, or in the pathogenesis of tendinopathy, as this tendon disorder is associated with chondroid and fatty degeneration, and ossification [94].

Since the tendon cell rate is low like its biological turnover, it has recently been proposed that adult stem cells would be good candidates for the regeneration of the tendon [95]. However, the exact role in the healing process of stem cells implanted into the tendon remains uncertain. One possibility is that they differentiate into tenocytes and are involved in healing by producing collagen and remodeling. It has also been suggested that the mononuclear bone marrow stem cells (BM-MNC) can aid in healing by acting as "growth factor pumps" rather than through terminal differentiation [96].

In vitro research has shown encouraging results with the use of stem cells for the treatment of degenerative diseases, like tendinopathy, of the musculoskeletal system [97].

Bone marrow mesenchymal cells (BMSCs) have been shown effective in the management of superficial digital flexor tendon injuries in horses; BMSCs were inoculated in the injured tendons leading to lower of re-injury rate compared with the re-injury rate obtained with the conventional non cellular based management [98,99].

An experimental study conducted by Lacitignola et al. [100] showed in an in vivo collagenase-induced superficial digital flexor tendinopathy study of horses, that when injected with autologous BMSCs intratendinous it produced a regeneration effect on the tendon.

Also adipose derived stem cells were showed to be effective in the treatment of equine tendinopathies leading to normal horse activity recovery [101].

Obaid et al. [102] perform a RCT study of 40 human patients diagnosed with Achilles tendinosis, a group that was treated with autologous stem cells derived from skin and other serum group saline (placebo). Clinical outcomes were assessed with VAS and VISA-A questionnaire at 3 and 6 months follow-up. Significant improvements in the experimental group compared to the placebo group in VISA-A (p=0.02) and VAS (p<0.001) scores were found.

In theory, pluripotent stem cells can be isolated and then be integrated into an area of need of the tendon. Once stem cells are at the desired location, either by local signaling or by the addition of exogenous factors, they can lead pluripotent cells to differentiating into the desired cell line [25].

Surgery

Historically, surgery has been proposed as a salvage technique if other treatments fail [103,104], showing similar functional results using an open or arthroscopic technique [105], and the latter with less comorbidity. With surgery, the removal of the degenerated tissue or calcifications in order to promote the tissue response is generally sought.

Lorbach et al. [106] performed a prospective study to evaluate the clinical results of arthroscopic resection of the lower patellar pole in patients with patellar tendinopathy. The main conclusion was that arthroscopic resection of the lower patellar pole as a minimal invasive method to treat patellar tendinopathy provides satisfactory clinical results in knee function and pain reduction with fast recovery and return to sport activities.

Kelly examined the results of arthroscopic tendon debridement with excision of the distal pole of the patella for refractory patellar tendinopathy [107]. He concluded that arthroscopic excision of the distal patellar pole with tendon debridement holds promise for the treatment of refractory patellar tendinopathy.

Shelbourne et al. [108] reported that surgical removal of necrotic tissue, surgical stimulation of remaining tendon, and aggressive rehabilitation after patellar tendonectomy could allow athletes to return to sports. Overall, tendonectomy, surgical tendon stimulation, and aggressive post-operative rehabilitation were found to be a safe, effective way to return high-level athletes to their sports.

Analysis of the surgical treatments is complicated given the differences between both techniques, as well as the heterogeneity of the samples and the different protocols used postoperatively [105].

Discussion

Treatment of tendon injuries is a subject of frequent debate in sports medicine and physiotherapy. Multiple techniques have been described for their treatment and although some of them [46,56,71,106,107].

To date, there is no consensus on the optimal treatment of tendinopathies. It has been suggested that the incomplete understanding of the underlying mechanisms (etiology of the condition), limits the ability to develop effective treatment strategies [108]. Are emerging as the most accepted treatment option, more RCT's are still needed to clearly establish what the therapeutic protocol therapeutic to follow should be.

Doubts have mainly centered on the fact that there are few controlled prospective studies that analyze all aspects of tendinosis, and few studies that investigate the early stages of these processes and their healing mechanisms. The exact mechanism by which tendinopathy develops in humans remains the target of numerous investigations. A variety of degenerative characteristics associated tendinopathies, including accumulation glycosaminoglycan (GAG), calcification and lipid accumulation nerve damage and hyperinnervation, is one of the theories whose publications are scarce, despite its special interest in explaining the possible pathophysiological mechanisms of pain in tendinopathy [109].

In several studies it has been shown that there is a correlation between tendinopathy and hyperinnervation, citing that the production of nerve growth factor (NGF) and the corresponding hyperinnervation could be induced by repetitive ischemic crisis in osteotendinous union [110,111]. This growth of nerve fibers, which causes chronic pain, could be part of a process of abnormal tissue repair, preceded by repetitive micro trauma [112].

Despite its prevalence, the precise pathogenic mechanisms of tendinopathy are not clear and, as a result, current treatments of tendinopathies are largely empirical and not always efficient [17,113]. The continuum model of tendon pathology was proposed to provide a model for the staging of tendon pathology and to assist clinicians in managing this often complex condition. The model presents clinical, histological and imaging evidence for the progression of tendon pathology as a three-stage continuum: reactive tendinopathy, tendon disrepair and degenerative tendinopathy [17].

The use corticosteroids are by far the most utilized treatment in all painful tendinopathy. Da Cruz et al. [114] investigated the role of corticosteroid injections in Achilles tendinopathy, at final follow-up (12 weeks), they were not able to find a significant higher improvement within the intervention group in any of the primary outcomes measured.

Others authors [115] consider that in the absence of an inflammatory process, there is no rational basis for the use of NSAIDs in chronic tendinopathy.

Chen et al. [116] believe that local infiltration of corticosteroids is associated with an increased risk of spontaneous tendon rupture.

A review study conducted by Dean et al. [117] reported that the effects of corticosteroid injection, reduce cell viability, cell proliferation is reduced, degrades collagen, produces higher tendon necrosis, decreases the mechanical properties of the tendon, and it produces significant long-term tissue damage and tendon cells.

One of the clinical effects that eccentric exercises might have in tendinopathy is in pain modulation due to changes in glutamate content or in the central nervous system with increased activation of inhibitory neurons and cortical reorganization [71,118]. There is little evidence that isolated eccentric exercise reduces pain in tendinopathy compared with concentric exercise [119].

It is considered that hypoxia could be responsible for neovascularization in tendinopathies, capillary flow and post-capillary pressure decreased following 12 weeks of eccentric loading [120].

In the treatment of tendinopathy, there is conflicting evidence that eccentric exercises are superior to other load programs [119]. Eccentric work on an inclined plane did not improve functional outcomes when it was done during a competitive season in volleyball [121]. In another study, continuous sporting activity did not compromise clinical outcomes at 12 months, as long as the sport was introduced incrementally ensuring minimal pain during and after loading [122]. Eccentric decline squat training and heavy slow resistance training showed good long-term clinical results, and heavy slow resistance training also resulted in advantages in pathological improvement and increased collagen turnover [37].

Some authors have demonstrated better results with eccentric exercise on corporeal tendinopathies in comparison with enthesopathies [35].

Further studies are needed to assess the unique effects of an eccentric strengthening program. Eccentric loading should be considered in conjunction with the concentric rather than just eccentric loading in Achilles and patellar tendinopathy. Patients with marked muscle weakness may benefit from a program of progressive eccentric-concentric loading [122]. On the other hand, maximal eccentric loading may be best for some groups of patients and permit adaptive changes in the tendon [45].

Despite the fact that the eccentric muscle workout has become the dominant conservative strategy in treating Achilles and patellar tendinopathy, up to 45% of patients do not respond to this treatment [123].

A recent study suggests that sedentary subjects with Achilles tendinopathy may show less promising results with eccentric exercise therapy compared to athletic subjects [124].

In the treatment of chronic lateral epicondylalgia where they were randomly assigned to three groups, one assigned to a stretching program, another to eccentric strengthening and the last to eccentric strengthening with stretching, no significant difference was observed either in the evaluation of strength or the visual analog pain scale [125].

Despite some good results reported with eccentric programmes [123,126], it is still unclear as to the more effective exercise protocol, its frequency, load and dosage.

Despite over 15 years of experience in the use of the EPI® technique and its widespread deployment in sporting clubs around the world, this technique has grown in relative to scientific dissemination in recent years [46].

An experimental study showed that after application of the degenerated tendon EPI® technique, an increase in anti-inflammatory proteins, like PPAR-γ has been observed after treatment with the EPI® technique. These proteins play a key role in the inhibition of expression of proinflammatory molecules secreted by macrophages, such as TNF-α, IL-6 and IL-1β [127] thus producing in the treated tissue a highly beneficial molecular response during tendinopathy. This, in turn, results in an increase of the expression of VEGF and VEGFR-2, mediators responsible for angiogenesis anti-inflammatory response [128,129].

In another recent study by Sánchez-Ibàñez and co-workers [46] it has been illustrated that when treatment with the US-guided EPI® technique and eccentric exercises in patellar tendinopathy it resulted in extensive improvement in the knee function and a rapid return to the previous level of activity after few sessions. The limitation of this study is the absence of a control group of subjects.

References to the use of the EPI® technique in combination with eccentric exercise can be found in the literature. In those cases the EPI® technique focuses on biological tissue recovery, leaving the functional recovery of tissue biomechanics to eccentric exercise.

The EPI® technique is mainly contraindicated in patients with tumors, articular or systemic infection and bleeding disorders [49].

Regarding the effectiveness of extra-corporeal shock waves therapy (ESWT) for tendinopathy, according to published studies, conclusive results cannot be drawn because the clinical effects are unclear [130,131]. The effectiveness of ESWT may depend on the stage of tendinopathy, it seems more appropriate in degenerative tendinopathy and where conservative treatment has little or no effect [17].

The mechanisms of the therapeutic effect of ESWT in tendinopathy with calcification are also uncertain. It has been proposed that the increased pressure within the therapeutic focus produces a fragmentation and cavitation effect within calcifications and leads to the disruption and disintegration of calcium deposit [132].

Some studies have shown that ESWT is as effective as surgery, but cheaper, and this treatment seems to be a supplement for the treatment of those tendinopathies who are refractory to conventional therapies [133]. In this sense, studies using high-energy ESWT do better in the tendinopathies than those using low-energy ESWT [54]. This is consistent with a recent study that showed ESWT had no effect in athletes with patellar tendinopathy who actively compete [130]. Currently, there is a controversy relative to the utilization of ESWT in the treatment of patellar tendinopathy [134] as well as in Achilles tendinopathy [54].

With the use of the platelet-rich plasma (PRP), the intention is to enhance the natural healing process at the site of injury through the action of growth factors (PDGF, IGF-1, VEGF, bFGF, TGF-β1, EGF, etc.) to promote matrix synthesis and the healing of injured tissue [135]. It should be noted that the delicate balance between these growth factors may have important implications in the control of angiogenesis and fibrosis [135].

Although many studies have been reported positive results using PRP [136,137], others have shown the same effect in comparison with a placebo [138,139]. De Vos et al. [139] found no significant differences between the group of patients with Achilles tendinopathy treated with PRP and the group treated with saline (placebo) to kept under review 24 weeks; these results agree with de Jonge et al. [138].

At the same time, many questions are raised about what the optimal concentration of platelets should be, in which phase of the injury is it better to do infiltration or how it should be prepared [66]. Caution is warranted when comparing different PRP studies, different types of PRP or PRP-derived products have been used, with a variety of platelet concentrations, inclusion of leucocytes, the use of anticoagulant and the use of activating agents.

Through the present research, it is hard to draw a clear conclusion for the effectiveness of PRP treatment on tendinopathy.

PRP injections should be avoided in patients suffering from infection, tumoral disease, coagulation disorders and changes in the number of platelets [135].

The use of polidocanol injection is based on the belief that neovascularizations are associated with the mechanism underlying tendinopathy due to overuse. Although it is unclear whether this is a causal agent in the pathophysiology of tendinopathy [140]. In fact, these "neovessels" may be associated with the ingrowth of nerves in the areas of pathological tendons [141] and it is possible that nerve fibers are the pain generators in chronic tendinopathy [142]. A priori, polidocanol injections may not only sclerose the veins, but may also eliminate the pain nerve fibers [25]. Although polidocanol injections appear to provide pain relief, it is unclear what role they can play in tendon healing in tendinopathy.

Hoksrud et al. [74] reported reduced pain after ultrasound-guided sclerosing in patients with patellar tendinopathy, contradictory results were recently presented in a retrospective study [143] in which sclerosing injections in 48 patients with chronic Achilles tendinopathy revealed less promising results than expected [143]. Even though capilliary blood flow may decrease by around 25% [144] some authors say that there is no relationship between changes shown in ultrasound and tendon function after sclerosing treatment.

Willberg et al. [145] compared the clinical effects in patellar tendinopathy after treatment with sclerosing polidocanol injections and arthroscopic shaving. After treatment, the patients treated with arthroscopic shaving had a significantly lower visual analogue score (VAS) score at rest and during activity, and were significantly more satisfied compared with the patients in the sclerosing injection group.

Prospective comparative studies involved small numbers of patients: polidocanol injections were superior to lidocaine injections [75], and similar results were found when compared with patients undergoing mini-open surgery [146].

Although some studies that associate sclerosing injections with eccentric training have shown a decrease in pain [26], further studies to evaluate its safety (possible nerve damage) and effectiveness, to determine the injection protocol (volume/concentration) and its combination with other therapies are needed [141].

Avoid injection of polidocanol in patients who previously had an allergic reaction to polidocanol or diagnosed with a blood clotting disorder. Nor it is recommended in pregnant or latency [141].

While some authors advocate the use of high-volume image guided injection (HVIGI) in treating refractory tendinopathy [77,147]. Preliminary studies have shown that a HVIGI with normal saline, local anaesthetic and corticosteroid can significantly reduce pain and improve short- and long-term function in patients with Achilles tendinopathy [77,78,147] reported results are not conclusive nor homogeneous enough to establish a protocol for use.

HVIGI adverse effects are similar to those of other injection techniques. Caution must be exercised with the administration of the diluted corticosteroid, for possible risk of tendon rupture and should not be injected into the ducts inside and outside the tendon [77].

Hyaluronic acid (HA) is actively secreted by the tendon sheath it is an important component of the synovial fluid, which allows a smooth tendon gliding, and provides nutrition to tendon itself [148]. Moreover, it is an important component of tendon structure, being largely present in extracellular space.

Several studies have been performed to evaluate the efficacy of HA on adhesions, gliding resistance, and tendon healing [149-152].

Despite the promising results of HA injections for treating tendinopathy in most of the studies the joint space has been injected and not into the tendon, and it could be that the modification of the synovial fluid exerts a positive effect on the tendon [153].

Avoid introduction of HA into the tendon and the peritendinous fat to avoid delete rating effects [81].

Aprotinin injections have been shown to provide clinical improvement in tendinopathies, most successful in patients with Achilles tendinopathy or with patellar tendinopathy [55,82]. Also better results have been obtained with aprotinin injections with corticosteroid injections or saline [82].

Moreover, in 7% of cases systemic allergic reactions occurred when aprotinin injections were applied at intervals of 2 to 4 weeks, but if applied every 6 weeks the reactions of systemic allergy was reduced significantly to 0-9%. Positive IgG antibodies against aprotinin patients most at risk of an anaphylactic reaction during treatment with this; therefore the authors recommend that if this type of technique is to be used the necessary equipment to treat anaphylaxis should be present [152].

Brown et al. [84] investigated whether aprotinin could achieve better improvement than the usual rehabilitation protocol adopted to treat Achilles tendinopathy in their RCT. They recorded VISA-A scores, tenderness, satisfaction and other clinical parameters and demonstrated no significant statistical differences.

It has been suggested that the efficacy of stem cells is related to its state of differentiation, i.e., the greater the state of differentiation the more effective will the effect be in the healing of the tissues in which they are implanted [154]. Keeping this statement in mind, it should be remembered that the cells that are better able to differentiate have lower telomere length and therefore a greater degree of aging during wound healing and therefore may not be able to complete the necessary steps in the process of regeneration and produce a useful and sufficient cellular matrix [155].

Another important aspect concerning the use of stem cells is their viability during the inflammatory phase of the tendon [154]. During the inflammatory phase, different types of cytokines, cytotoxic proteins and inflammatory factors are released by necrotic tissue and inflammatory cells reduce the possibilities of viability of stem cells in the host [97,154].

Stem cells are promising candidate for the management of tendinopathies and tendon rupture. However, these cell-based strategies have been investigated only in preclinical studies and the role of stem cells needs to be confirmed. Tendon stem cells have been hypothesized to have a crucial role in the development of calcifying tendinopathy due to the erroneous differentiation of tendon stem cells (TSCs) to chondrocytes or osteoblasts. For this reason it was hypothesized that the re-direction of the differentiation of resident TSCs or supplementation of mesenchymal stem cells (MSCs) programmed for tenogenic differentiation may be appealing targets for the treatment of tendinopathy in the future [156].

The use of stem cells is in the early stage of clinical application in humans. There is only one clinical study performed on human subjects showing that inoculation of bone marrow mononuclear cells (BMMNC) in tendinopathy patellar has good mid-term clinically and ultrasound results [155]. As demonstrated by these preliminary studies, management of tendinopathies with stem cells is promising even though more clinical studies are needed to validate this treatment approach.

Despite the growing interest in this type of therapy and its expected potential, there are still many open questions to answer in order to implement these techniques in the tendinopathy treatment protocol. Further research is required to identify mechanisms involved in tendon regeneration and in survival, proliferation, and differentiation of stem cells.

Although the results shown by some authors with the surgical treatment of tendinopathy [157-159] showed that surgery did not show advantages over eccentric exercise in their RCT. In addition, the low predictability of the results obtainable through surgery make it such that this technique should be put forward only in selected cases and after other conservative options fail.

It is commonly accepted that surgical treatment must be indicated in motivated patients if carefully followed conservative treatment is unsuccessful after 3-6 months [103,104]. The literature, however, does not clarify which surgical technique is more effective.

Conclusion

In this report, a brief review of treatment approaches of tendinopathy was conducted. Tendinopathy is a condition that causes significant pain and disability in many patients. Currently, the etiology of tendinopathy is still unclear, it is multifactorial, and influenced by intrinsic and extrinsic factors. Tendinopathy often becomes chronic because the exact pathogenesis remains largely unknown. The continuum model of tendon pathology was proposed to provide a model for the staging of tendon pathology. Physicians and physiotherapist have a variety of therapeutic options available to treat tendinopathies but, in each case, there is a lack of evidence supporting their use as the gold standard treatment. Larger randomized controlled trials on the various treatment options and even comparative studies between them are needed to determine the treatment of choice (Gold Standard) for tendinopathies.

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Author Contributions

Wrote the first draft of the manuscript: JMS, MEF, JCM, AAD, JSG, JSS. Contributed to the writing of the manuscript: JMS, MEF, JCM, AAD, JSG, JSS. Agree with manuscript results and conclusions: JMS, MEF, JCM, AAD, JSG, JSS. Jointly developed the structure and arguments for the paper: JMS, MEF, JCM, AAD, JSG, JSS. Made critical revisions and approved final version: JMS, MEF, JCM, AAD, JSG, JSS. All authors reviewed and approved the final manuscript.

Disclosures and Ethics

The authors declare that one author has the patent for the EPI devices® and one author is the creator of the EPI® technique.

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Review

Treatment Techniques

Patellar tendinopathy: a critical review of current therapeutic options

F Abat[1]*, JM Sanchez-Ibañez[2]

Abstract

Introduction

The treatment of patellar tendinopathy remains a subject of ongoing debate in the field of sports medicine. It was initially thought that the tendon injury produced was characterised as an inflammatory process, but this thinking has evolved to reasoning it as a cellular degenerative process so as to explain the poor evolution that tendon injuries generally show. Traditionally, conservative treatment by means of eccentric exercise was advocated, going on to surgery when good results were not obtained. The use of minimally invasive techniques has grown in popularity over recent years. Currently, there is a significant therapeutic arsenal at our disposal in clinical practice that ranges from the use of shock waves, growth factors, sclerosis of neovessels using polidocanol or techniques such as intratissue percutaneous electrolysis (EPI®). Despite the abundance of literature on the treatment of tendinopathy, there are few studies of high scientific evidence. Thus, the choice of a therapeutic method as a gold standard remains a point of debate. This present critical review, focused on the treatment of patellar tendinopathy, aims to shine a light on the different studies of each of these treatment options by analysing each ones level of scientific evidence.

Conclusion

Larger randomised controlled trials on the various treatment options and even comparative studies between them are needed to determine what the treatment of choice for patellar tendinopathy should be.

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Introduction

Patellar tendinopathy, with a prevalence rate that may reach 40% in high demand functional athletes[1,2], is a disease that is especially problematic for the patient as it is usually a chronic injury which can mean the end of a career in sports in severe cases[3].

Historically, patellar tendinopathy was considered an inflammatory process, but it is now known that this affectation is characterised as a degenerative process that may be associated with inflammation of the paratenon in some cases[4]. During the course of the tendon lesion, healing mechanisms are altered as a result of a faulty repair process that produces a degeneration of collagen fibres of the tendon as well as vascular changes[5,6]. There are multi-factor causes for the onset of patellar tendinitis[3], presenting repetitive microtraumatisms that bring about cyclical tendon overload as the common denominator. Secondarily, as a result of inadequate healing and insufficient recovery time, the tendon will initiate a degenerative process of the collagen fibres[3–6].

Many therapeutic techniques have been described in the literature. However, none has emerged as the gold standard[7] and that is probably due to lack of sufficient scientific evidence. Eccentric exercise has gained recognition within the scientific literature as first-line therapy[8], but when it fails or is ineffective there is no consensus as to which therapy to use.

Among the therapies most used currently, there are open or arthroscopic surgery[9,10], extracorporeal shockwave therapy (ESWT)[11], the intratissue percutaneous electrolysis technique (EPI®)[12] and the use of polidocanol injections[13] or platelet-rich plasma (PRP)[14].

This critical review, focused on patellar tendinopathy, studies these therapeutic methods by analysing the extent of scientific evidence.

Discussion

The authors have referenced some of their own studies in this review. These referenced studies have been conducted in accordance with the Declaration of Helsinki (1964) and the protocols of these studies have been approved by the relevant ethics committees related to the institution in which they were performed. All human subjects, in these referenced studies, gave informed consent to participate in these studies.

The great difficulty that the treatment of patellar tendinopathy presents, given their high rate of chronicity and sport disability, has made this disease a great battlefield in traumatology and sports medicine today. At present, the literature does not present a clear treatment as the gold standard. The ones with the most widespread use are eccentric exercises and, if those should fail, the surgical option.

Establishing which should be the method of choice when treating patellar tendinopathy after failed conservative treatment is currently very

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difficult given the fact that there are very few randomised controlled trials (RCTs) or high quality studies, there mostly being prospective or retrospective studies of case series or low level of evidence comparative studies. Therefore, the present review aims to show the most relevant studies within each therapeutic option.

Historically, eccentric exercises have been considered a good treatment for tendinopathy although some authors argue that their strength is founded more in prevention than in the treatment of fully established lesions[2]. While some authors have argued for this therapeutic means[15,16], others indicate that there are no significant differences upon comparing them with control groups[17,18].

Although eccentric exercise is a good therapeutic tool, the type of exercises to use, the frequency, the load and the dosage of the same require further research so as to establish a clear protocol to follow.

Surgery has been positioned as the option of choice when other less invasive treatments have no effect[10]. A recent meta-analysis[19] reported that open surgery obtains results comparable to those obtained with arthroscopic surgery, being therefore up to the surgeon as to what must be the most suitable approach to treating this condition while producing the least comorbidity.

Analysing the works on the treatment of patellar tendinopathy with surgery is very difficult given the great heterogeneity of the samples studied, the various types of functional analysis and the fact that the postoperative rehabilitation protocol is detailed in few studies. This might clearly influence the clinical and functional outcomes[19].

Authors such as Pascarella et al.[9] or Willberg et al.[19] who advocate the use of arthroscopy or others such as Cucurulo et al.[10] or Shelbourne et al.[20] who advocate open surgery can be found in the current literature. Despite these results, authors such as Bahr et al.[15], in their RCT, showed that there was no advantage to patellar tenotomy versus eccentric exercise, opening a big question about the potential benefit of putting the patient through a surgical procedure.

These findings along with the low prediction of the results obtained with the surgical option for patellar tendinopathy[10] emphasise the importance of reserving surgery for those carefully selected patients who have undergone very controlled conservative treatment. It must be remembered that in any of these cases, it would result in a significant delay in the return to sporting activities.

Some authors have presented the ESWT as a valid option in cases in which conventional therapies have proven ineffective in the treatment of tendinopathy[11]. It supposedly provides benefits in reducing pain by suppressing the substance P neurotransmitters and the calcitonin gene-related peptide as well as by destroying unmyelinated nerve fibres[11].

An important multi-centre RCT showed that shock waves obtained the same results as the application of a placebo in a population of active broad-jump athletes with patellar tendinopathy[21]. In parallel, other studies such as the Wang et al.[22] study showed positive results with the use of ESWT. Notably, the participants continued their high level of physical activity throughout the study process in the study of Zwerver et al.[21]. This may have interfered in the results, while the Wang et al.[22] group did not allow patients to perform heavy activities.

A major weakness of the technique is the lack of consensus as to what the protocol for the application of ESWT should be in terms of dose, time or mode of application[23].

Intratissue percutaneous electrolysis (EPI®) is a technique that is performed under ultrasound guidance by which a non-thermal electrolytic ablation induces a controlled inflammatory response of injured tissue. Experimental studies have shown that the EPI® technique permits the activation of the cellular mechanisms involved in phagocytosis and the regeneration of damaged soft tissue[24].

This technique, created by Sanchez-Ibañez et al.[12,24] and who have over 10 years experience in its use[12], uses a flow of cathodic current directed exclusively to the area of degenerated tendon through an ultrasound guided needle that brings about an organic reaction that leads to rapid regeneration of the degenerated tendon. The EPI® technique combined with eccentric exercises has shown excellent results in the treatment of refractory tendinopathies over conventional treatment[12,25].

Despite being one of the few studies that follows the rules of the functional assessment of patellar tendinopathy by means of the validated Victorian Institute of Sport Assessment-Patella questionnaire and providing a follow-up of 10 years, the study has some important limitations for being a prospective study of a case series[12,25].

The combination of different techniques with eccentric exercise is a common practice in studies of tendinopathy as eccentric exercises provide physical support for the proper maturation of collagen fibres. Recent work by authors such as de Vos et al.[26] and Filardo et al.[27] reported so, therefore, the fact of using eccentric exercises in combination with other techniques when exercise alone has failed does not limit the results obtained in these studies.

If the aetiological hypothesis of tendinopathies that defends hypervacularisation as the cause of the pain is accepted as valid, the use of sclerosis of neovessels using polidocanol may be justified[13]. Some authors such as Hoksrud et al. advocate this technique[13], whereas authors such as Willberg et al.[28], in a randomised controlled study, demonstrated that patients treated with polidocanol in-

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jections showed no better functional outcomes than those treated with arthroscopic surgery.

The use of PRP is based on the hypothesis that it has the potential to cause changes in the production and degradation of collagen fibres by acting at the level of matrix regulating enzymes[14]. In spite of the many laboratory studies that suggest the great potential of this technique[29], the fact that healthy or surgically injured tendons are used represents a difficulty in extrapolating clinical data.

There are studies that show significant improvements in both pain and function when using PRP. Nevertheless, most of them are without significant differences when compared with controls groups[30].

Regardless of the great potential of this technique, the main limitation is currently in the lack of conclusive studies on the quantity of growth factors that are obtained with different systems of cell separation, what the optimal mixture is, which conditions the patient must meet prior to blood collection or what the volume and frequency of injections should be[14]. Similarly, it remains unclear as to whether the activation of platelets prior to infiltration is required[14,30].

Conclusion

Larger RCTs on the various treatment options and even comparative studies between them are needed to determine what the treatment of choice for patellar tendinopathy should be.

Abbreviations list

ESWT, extracorporeal shockwave therapy; PRP, platelet-rich plasma; RCT, randomised controlled trial.

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1 CLINICAL RESULTS AFTER EPI® AND ECCENTRIC EXERCISE IN PATELLAR TENDINOPATHY AT 10 YEARS FOLLOW-UP

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Aims To investigate the outcome of ultrasound-guided Intratissue percutaneous electrolysis (EPI®) [Abat, 2014] and eccentric exercise [Romero-Rodriguez, 2011; Malliaras, 2013; Larsson, 2012] in the treatment of patellar tendinopathy during a long-term follow-up.

Methods Forty patients with patellar tendinopathy [Maffulli, 1998] were prospectively evaluated over a 10-year follow-up period. Pain and function were evaluated before treatment and at 3 months and 2, 5 and 10 years with the Victorian Institute of Sport Assessment–Patella (VISA-P) score [Visentini, 1998], the Tegner score and Blazina's classification. According to VISA-P score at baseline, patients were also dichotomized into Group 1 (<50 points) and Group 2 (≥50 points). There were 21 patients in Group 1 and 19 in Group 2. Patient satisfaction was measured according to the Roles and Maudsley score.

Results The VISA-P score improved globally by 41.2 points ($p < 0.01$) after a mean 4.1 procedures. In Group 1, VISA-P score improved from 33.1 ± 13 to 78.9 ± 14.4 at 3 months and to 88.8 ± 10.1 at 10 years follow-up ($p < 0.001$). In Group 2, VISA-P score improved from 69.3 ± 10.5 to 84.9 ± 9 at 3 months and to 96.0 ± 4.3 at 10 years follow-up ($p < 0.001$). After 10 years, 91.2% of the patients had a VISA-P score > 80 points. The same level (80% of patients) or a Tegner score at no more than one level lower (20% of patients) was restored and 97.5% of the patients were satisfied with the procedure.

Conclusion Treatment with the US-guided EPI® technique and eccentric exercises in patellar tendinopathy resulted in a great improvement in knee function and a rapid return to the previous level of activity after few sessions. The procedure has proven to be safe with no recurrences on a long-term basis.

Abstract 1 Table 1 Patients' characteristics at baseline

	Group 1 $n = 21$ (52.5 %)	Group 2 $n = 19$ (47.5 %)	p value
Age (years)			
Mean ± SD	26.0 ± 8.49	25.7 ± 8.12	n.s.
Gender % (n)			
Male	81.0 (17)	94.7 (18)	n.s.
Female	19.0 (4)	5.3 (1)	
Dominant extremity % (n)			
Right	81.0 (17)	89.5 (17)	n.s.
Left	19.0 (4)	10.5 (2)	
Injured knee % (n)			
Right	38.1 (8)	15.8 (3)	n.s.
Left	47.6 (10)	68.4 (13)	
Bilateral	14.3 (3)	15.8 (3)	
Baseline VISA-P			
Mean ± SD	32.5 ± 12	69.5 ± 10.05	<0.001

Values expressed as mean ± SD or frequencies and percentages

Abstract 1 Table 2 Victorian Institute of Sport Assessment-Patella (VISA-P) values during follow-up

Time	VISA-P score			Tegner score		
	Group 1	Group 2	Global	Group 1	Group 2	Global
Baseline ($n = 40$)	33.1 (±13)	69.3 (±10.5)	51.2 (±21.7)	8.1 (6–10)	7.8 (4–9)	7.9 (4–10)
3 months ($n = 40$)	78.9* (±14.4)	84.9* (±9)	81.9* (±12.2)	7.7 (4–10)	7.6 (3–9)	7.7 (3–10)
2 years ($n = 40$)	83.2 (±13.6)	88.6 (±7.4)	85.9 (±11.1)	8.1 (5–10)	7.7 (4–9)	7.8 (4–10)
5 years ($n = 37$)	85.2 (±12.2)	91.9 (±5.6)	88.6 (±10)	7.9 (5–10)	7.6 (4–9)	7.8 (4–10)
10 years ($n = 34$)	88.8 (±10.1)	96.0 (±4.3)	92.4 (±8.5)	7.7 (5–10)	7.3 (4–9)	7.5 (4–10)

Victorian Institute of Sport Assessment–Patella (VISA-P) values expressed as mean (±SD). Tegner values are expressed as median (range)
* $p < 0.001$. No statistically significant differences were observed in the results between any intermediate outcome measurements other than from baseline

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2 THE EFFECT OF EARLY AND STANDARD WEIGHTBEARING ON FUNCTION 8 WEEKS AFTER ACHILLES TENDON RUPTURE

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Introduction The incidence of Achilles tendon rupture (ATR) is steadily increasing, yet the exact treatment and rehabilitation of this traumatic injury is still debated [Chiodo, 2010]. Early weight bearing (WB) after ATR repair potentially yields better functional outcomes compared to immobilised patients, although re-rupture can occur at a higher rate [Costa, 2006]. Though WB has been often compared to immobilisation, it is currently unclear if early WB yields benefits in early ankle function compared to standard WB. We hypothesised that compared to standard WB, patients undergoing early WB would have higher plantarflexion moments in the injured side during gait, which would yield a longer tendon length 8 weeks after surgery. Furthermore, we hypothesised that early WB patients will show less intrapatient asymmetry than standard WB.

Methods A total of fourteen patients were randomised to either early (full WB in 2nd week, n = 6) or standard WB (n = 8) after percutaneous ATR repair by the same surgeon (SM). Kinematic (f = 120 Hz) and kinetic (f = 960 Hz) data of the lower limbs were collected using 22 reflective markers, 10 infrared cameras (VICON, Oxford, UK) and two force plates (AMTI, Watertown, USA) for a minimum of five barefoot walking trials at a self-selected speed. ISB-recommended conventions determined ankle angles and inverse dynamics calculated ankle moments. B-mode ultrasonography (f = 25 Hz, Esoate, Genoa, Italy) noninvasively assessed the resting Achilles tendon length *in vivo*, with the knee outstretched and the ankle in 20° of plantarflexion. Plantarflexion moments and tendon lengths were compared both within patients and between early and standard WB. Statistical differences were calculated in SPSS (IBM, Armonk, USA) using paired t-tests (within patients) or one-way ANOVAs (WB comparison).

1 Clinical Results After EPI® and Eccentric Exercise in Patellar Tendinopathy at 10 Years Follow-Up

Ferran Abat, Pablo-Eduardo Gelber, Fernando Polidori, et al.

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MANIPULO EPI® ALPHA	MANIPULO EPI® ALPHA	1	250,00	0,00		250,00
ELECTRODOS	ELECTRODOS CON CABLE 5X5	4	4,00	0,00		16,00

Suma Importes	Base	Portes	% IVA	Total IVA
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TOTAL

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ORIGINAL ARTICLE

Intratissue percutaneous electolysis combined with active physical therapy for the treatment of adductor longus enthesopathy-related groin pain: a randomized trial

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ABSTRACT

BACKGROUND: *Adductor longus* enthesopathy-related groin pain (ALErGP) is the most common cause of groin pain in soccer players. The aim of this study was to evaluate the therapeutic utility of intratissue percutaneous electrolysis (EPI®) technique in combination with an active physical therapy (APT) program to treat ALErGP.
METHODS: Twenty-four non-professional male soccer players diagnosed with ALErGP were included in this study and randomly divided into two groups. Group A was treated with EPI® technique in combination with a standardized APT program. Group B only underwent the APT program. The Numeric Rating Scale (NRS) and the Patient Specific Functional Scale (PSFS) were used to assess the effectiveness of the two interventions. The follow-up covered a 6-month period.
RESULTS: Both groups significantly improved pain and functional scores after treatment and maintained this therapeutic result throughout the follow-up. The combined intervention of APT program and EPI® ensured a greater and faster reduction of pain in group A. In addition, functional recovery tended to be greater in group A than B after the treatment and throughout the follow-up by 7.8±3.8% (P=0.093).
CONCLUSIONS: EPI® treatment in association with APT ensured a greater and more rapid reduction of pain and tended to promote greater functional recovery in soccer players with ALErGP compared to APT only. This positive therapeutic result lasted for at least 6 months after the end of the treatment. These findings support the combined use of EPI® and APT to treat ALErGP.

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Key words: Tendinopathy - Soccer - Electrolysis - Ultrasonography.

Groin pain (GP) can generally be defined as a syndrome characterized by pain in the pubic and inguinal regions,[1] which results in a functional deficit that can lead to severe impairment of different motor tasks, such as kicking and twisting movements while running,[2] and to the suspension of athletic activities.[3] In soccer, the incidence of this condition ranges between 10% and 18% of all time-loss injuries with relapse rates as high as 30%.[3, 4] In fact, the term "longstanding" GP is often used to describe the impact of the syndrome in the long term.[5] The anatomy of the region is extremely complex and many different conditions provoking GP can be factors into a differential diagnosis.[1, 6-8] Hence, the identification of the primary cause of GP can be challenging. Despite the difficulties in diagnosis, adductor-related GP has been identified as the most common clinical pattern of GP in soccer players.[9] This is clinically characterized by pain that is exacerbated by the palpation of the inser-

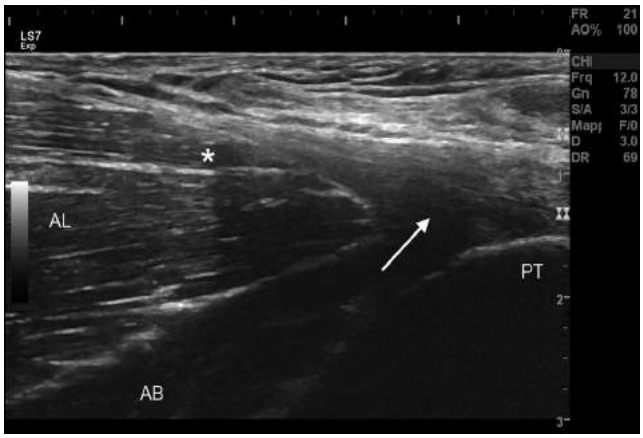

Figure 1.—Longitudinal ultrasound section of the *adductor longus* (AL). The tendon insertion on the pubic tubercle (PT) is recognized as a hypoechoic area (arrow). Additionally, the intramuscular tendon, or central aponeurosis, of the *adductor longus* (the hyper-echoic horizontal structure indicated by an asterisk), and the *adductor brevis* (AB) can also be seen.

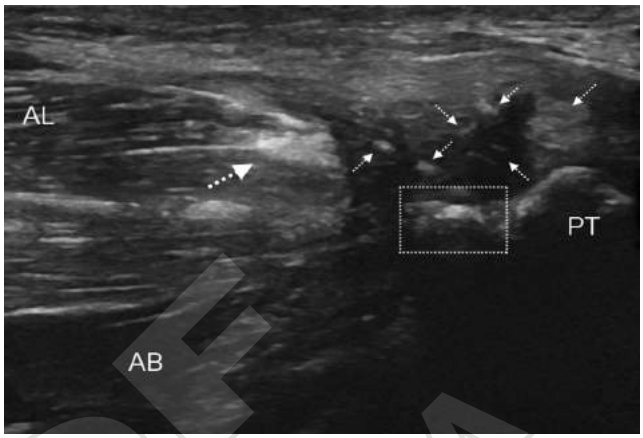

Figure 2.—Anatomic changes of the proximal tendon/enthesis of the *adductor longus (*AL) in the ultrasound examination. In the vicinity of the pubic tubercle (PT) the presence of significant calcification of the tendon can be seen (dotted box), as well as many fibrotic areas at the level of the enthesis (small arrows), which appears to be clearly deconstructed. Furthermore, it is possible to identify significant fibrotic thickening near the myotendinous unit of the muscle (thick arrow). AB: adductor brevis.

tion of the *adductor longus* (AL) on the pubic tubercle (unilaterally or bilaterally), as well as by the counter-resistance contraction of the muscle.[1, 9] This clinical condition is often associated with AL enthesopathy, which involves also alterations of the tendon portion in close proximity to its insertion (Figure 1),[10] and is recognized as the most common disease in athletes with pain localized in the proximity of the pubic symphysis.[6, 11] Therefore, *adductor longus* enthesopathy-related GP (ALErGP) is identified as one of the main causes of GP in soccer players. Etiopathogenesis of AL enthesis degeneration is associated with repeated functional overloading, as the fibrocartilaginous enthesis is vulnerable to prolonged biomechanical stimuli over time.[12, 13] Repeated functional overloading results in the progressive manifestation of histological and anatomical alterations, detectable with ultrasound and MRI.[11, 14-17] The fibrosis and the formation of calcifications (Figure 2) are compatible with a chronic failure of the physiological processes of adaptation and healing, resulting in ineffective microcycles of injury repair.[12, 13] Also, histological alterations of the enthesis contribute to the progressive loss of the biomechanical properties of the tissue and finally to the onset of symptoms and functional deficits typical of an overuse injury.[1, 11, 15]

Physiotherapy is usually preferred over surgical intervention to treat GP. On the other hand, surgery is considered when the rehabilitative programs are unsuccessful.[18] The more conservative treatments usually involve: rest (or restriction of activities); passive physiotherapy (*i.e.* massage, laser and transcutaneous electrical nerve stimulation) [19] to recover the joint mobility of the hip, sacroiliac joints, and lumbar spine, as well as the restoration of the visco-elastic properties of the muscles (the adductors, in particular); active physiotherapy targeted at improving the stabilizing ability of the abdominal and pelvic muscles, especially the *Transversus Abdominis*.[2, 20-23] It has been shown that a program of active physiotherapy is more effective than one of exclusively passive physiotherapy in the care of Adductor-related GP,[19] and that a multimodal program promotes even faster results than active physical therapy *per se*.[24] The physical therapy interventions usually last for 6 to 8 weeks.[25]

In addition to the abovementioned interventions, another therapeutic approach to consider is intratissue percutaneous electolysis (EPI®), a novel technique that plays a role in the treatment of tendinopathy, enthesopathy, and fibrosis.[26-28] Furthermore, a recent study reported the use of this technique for the treatment of muscular lesions as well.[29] EPI® is an ultrasound-guided minimally invasive technique that makes it possible to degrade the diseased tissue through the electrolytic action of EPI® (electrochemical ablation), as well as to develop an extremely localized inflammatory process that can induce the heal-

TABLE I.—*Enrollment phase: inclusion and exclusion criteria.*

	Inclusion criteria	Exclusion criteria
General criteria	Non-professional soccer players	Previous Groin/Hip surgery
	Age 18-35 years	
Clinical criteria	Presence of pain upon palpation of the enthesis of the *adductor longus* (unilaterally or bilaterally)	Adductor-related Groin Pain is not the primary clinical entity
	Presence of pain upon contraction against resistance (Adductor Squeeze Test) of the enthesis of the *adductor longus* (unilaterally or bilaterally)	
Imaging criteria	The ultrasound testing revealed anatomical alterations of the proximal tendon/enthesis of the adductor longus, which was painful during clinical examination	The ultrasound and MRI showed and absence of anatomical alterations of the enthesis of the *adductor longus*, which was painful during clinical examination
		Presence of major pathologies revealed by the MRI
After randomization		Consumption of NSAIDs or local infiltration during treatment
		Absence from more than 20% of scheduled physiotherapy sessions or absence from more than one scheduled EPI® session.

ing process in the treated structure (indirect reparative action).[29] Other works described the therapeutic benefits of EPI® technique in the treatment of patellar tendinopathy and how this technique, in conjunction with a program of active physical therapy — eccentric exercises in particular — can promote considerable structural and functional benefits that are maintained in the long term.[26, 27] However, further studies are still needed to evaluate the usefulness of this technique in the treatment of other tendinopathies and enthesopathies.

The aim of this study was to evaluate the therapeutic utility of the EPI® technique in combination with an APT program to treat ALErGP, while comparing the results achieved solely from the APT program in a group of non-professional soccer players. We hypothesized that 1) the combination of EPI® and APT can promote greater and faster clinical and functional improvements than treatment relying solely on an APT program; and that 2) the functional improvements obtained in the study group will be more solidly maintained over time compared to the control group that underwent APT program alone.

Materials and methods

Participants and sample size

Between February and July 2014, 37 male soccer players affected by generic GP were clinically and instrumentally evaluated (see below). These athletes usually performed 2 to 4 training sessions per week, thus were considered non-professional players.[24] Twenty-

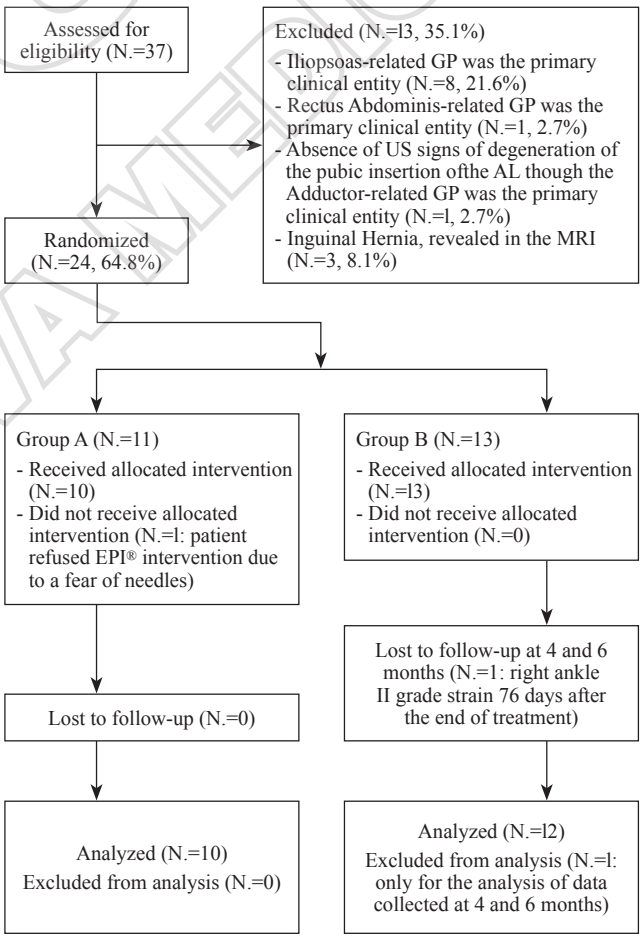

Figure 3.—Study profile.

four of these athletes (age: 26.0±4.7 year; stature: 178.7±8.0 cm; body mass: 73.9±6.9 kg) were diagnosed with ALErGP, satisfied the inclusion and exclusion criteria (Table I) and thus were initially enrolled in the study (Figure 3). Two subjects did not complete the study protocol; hence, data recorded from 22 players were taken into account for further analysis.

The study was ethically designed and conducted according to national and international standards. The research reported in the paper was undertaken in compliance with the Helsinki Declaration and the International Principles governing research on humans. All participants were informed of the experimental risk and gave written informed consent. In addition, the present study was designed taking into consideration the guidelines on reporting standards for clinical research on groin pain in athletes indicated by Delahunt *et al.*[30]

Patients initially took part in a medical interview. Their anthropometric data were collected, as well as sport-specific (level of activity, position, dominant foot) and GP-specific (laterality and duration of the symptoms) information. The final part of the interview involved the registration of Patient-Specific Functional Scale (PSFS) values. This was followed by the clinical evaluation, including recordings of the Numeric Rating Scale (NRS) values. After this evaluation, an ultrasound examination was administered. If the inclusion criteria were met, the patient was asked to undergo an MRI scan. Based on an analysis of the final report, a decision was made whether to enrol the subject. MRI scans were performed by a private clinical facility, while all other assessments and therapeutic interventions were performed within the facilities of the "Friuli" Stadium, in Udine (Italy), the sporting venue of Udinese Football Club.

Clinical evaluations

For the clinical evaluation, a standardized assessment protocol was used for athletes with GP.[31] This protocol was shown to be particularly valuable because it was subject to limited variation between operators. All the clinical assessments were performed by a well-trained physiotherapist who followed precisely the protocol details found in the appendix "Examination techniques for the evaluation of GP in athletes" used in the intra-observer and interobserver reliability study.[31] The assessor was not aware of the treatment type received by every subject.

Pain assessment

The NRS Scale,[32-34] which showed high test-retest reliability,[32] was selected among the available scales for pain assessment in adults. The patient was asked to verbally assign a value to his pain, ranging from 0 (total absence of pain) to 10 (the most intense pain imaginable). The NRS values were collected to assess the pain: upon palpation of the insertion of the AL into the pubic tubercle (NRSpalp) (if pain is present bilaterally, the highest value was always recorded); upon bilateral isometric contraction against resistance (NRScontr). The values were recorded at enrolment, at the end of treatment, and at 2, 4, and 6 months after treatment (follow-up).

Functional assessment

As suggested by Hedegus et al.,[33] the PSFS was chosen to assess the functional level of subjects with GP. The patient was asked to select the activities with a reduced level of performance and to assign them with increasing values from 0 to 10, representing a complete deficit in the performance of the activity and the ability to perform the activity at the highest level of performance, respectively. To ensure uniform assessment in the sample, the authors selected 10 activities to which the patient was asked to assign a performance level, 6 non-sport specific and 4 sport specific (SS): linear running; linear sprinting; rapid braking in a sprint; twisting movements; jumping, pulling with dominant foot; jumping, pulling with the non-dominant foot; passing with the dominant foot (SS); passing with the non-dominant foot (SS); kicking with the dominant foot (SS); and kicking with the non-dominant foot (SS). The sum of the values obtained could range from 0 to 100, where 100 is the maximum level of athletic performance. The values were recorded at enrolment, at the end of treatment, and at 2, 4, and 6 months after treatment (follow-up). PSFS showed also high test-retest reliability for evaluation of the functional level for chronic syndromes such as low back pain and chronic lateral epicondylitis.[35]

Instrumental evaluations

Ultrasound assessment was performed by a well-trained operator (more than 10 years of experience in evaluating the lower limb muscle-skeletal system in professional and non-professional soccer players) us-

ing the GE Healthcare Logiq S7 Expert ultrasound (GE Healthcare®, Milwaukee, WI, USA) with a linear probe (6-15 MHz). Ultrasound assessment was performed only before the intervention; it was aimed at evaluating any eventual anatomical alterations of the proximal tendon and enthesis of the *adductor longus*, which was painful during clinical examination, in order to define the inclusion/exclusion criteria (Table I). The assessor was neither aware of the clinical evaluation results nor the type of treatment that the subject would have received.

Ultrasound evaluation was followed by an MRI of the pubic region which was necessary to confirm the diagnosis and to rule out any other condition: subjects with significant comorbidities (such as inguinal hernia, muscle injuries, femoroacetabular impingement, visceral diseases, etc.) were excluded from the study.

Treatment protocols

Two randomized groups were created: the study group, or group A, and the control group, or group B. In group A, the EPI® technique was used along with a standardized APT program, whereas group B only underwent the APT program. To randomize the groups, the following tool was used: "Create a blocked randomization list" (Sealed Envelope Ltd. 2014), available online from: https://www.sealedenvelope.com/simple-randomiser/v1/lists. The block size was set at 10 subjects (1:1 allocation). The tool also generated a unique randomization code. After the assessments, each subject included in the study was given their personal code assigning them to one of the two groups. The code was enclosed in sealed envelopes (numbered to identify the block).

Eco-guided EPI® intervention

The patient was placed in a supine position, with the limb in slight abduction and external rotation of the hip in order to better expose the enthesis of the AL to be treated. The entire pubic and inguinal region was previously disinfected with isopropyl alcohol. The treatment was performed by a well-trained operator (more than 10 years of experience in applying this technique for ALErGP in professional and non-professional soccer players) using a specifically developed medically

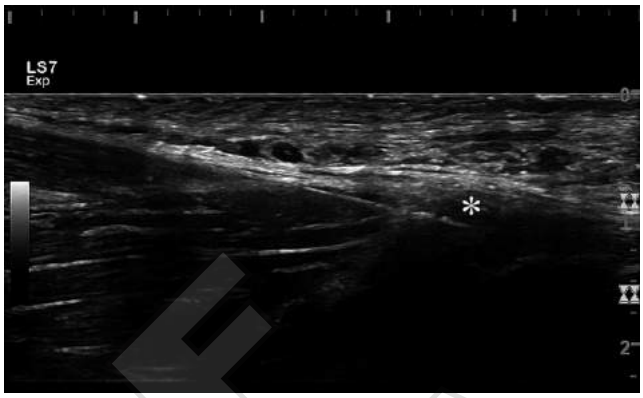

Figure 4.—Ultrasound-guided intratissue percutaneous electrolysis. The operator inserts the needle (asterisk) into the treatment area.

certified (Directive 93/42/EEC) device (EPI Advanced Medicine®, Barcelona, Spain). The chemical process of electrolysis is induced by the modulated galvanic current generated by the device. The current is transferred to the tissue to be treated using an appropriate needle (0.33x50 mm); its insertion is ultrasound-guided in order to reach precisely the targeted area. In the present study, the GE Healthcare Logiq S7 Expert® ultrasound with a linear probe (6-15 MHz) was used to guide the insertion of the needle (Figure 4). Group A subjects received EPI® intervention during Phase 1 of the APT program. EPI® intervention protocol was similar to that reported by Abat *et al.*[26, 27] for the treatment of patellar tendinopathy. In particular, two treatment sessions were held each week during Phase 1 of the APT program (EPI® intervention was completed 15 minutes prior to the start of the physical therapy session). The pre-set program "Adductors Tendinopathy" was used, with the device set at 3mA (current intensity). Each session consisted of 3 applications (3 right + 3 left if the ALErGP was present bilaterally), with a duration of 5 seconds each. Each session had a maximum duration of 10 minutes.

EPI® intervention was overall well tolerated by the subjects. Some of them experienced minor discomfort during needle insertion. In addition, the electrolytic treatment caused moderate to moderately strong pain in some of the participants; however, the short duration of every stimulus, 5 seconds, resulted in a tolerable pain. Indeed, none of the subjects asked to pause or stop the treatment, being these options available after every single 5-second stimulus. Furthermore, no adverse events

TABLE II.—*The standardized Active Physical Therapy program: description of the exercises and method of administration.*

Phase 1	1) Bilateral isometric contraction of the AL: patient in supine position. Isometric adduction against a fit ball (Ø=30cm) positioned between the knees.	10 s of holding (+20 s pause) for 8 repetitions
	2) Bilateral isometric contraction of the AL: patient in supine position, hips flexed at 45°. Isometric adduction against a fit ball (Ø=30 cm) positioned between the knees.	10 s of holding (+20 s pause) for 8 repetitions
	3) Unilateral eccentric contraction of the AL: patient in supine position, hip in neutral position. The physiotherapist slowly abducts the hip up to 45° and the patient is asked to slow down the muscle elongation.	5 s of contraction (+5 s pause) for 8 repetitions for 4 sets (2 for each leg)
	4) Bilateral eccentric contraction of the AL: patient in supine position, hips flexed at 45° and fully adducted. The physiotherapist slowly abducts both hips up to 30°, while the patient is asked to slow down the muscle elongation.	5 s of contraction (+10 s pause) for 8 repetitions for 2 sets
Phase 2	1) Spinning bike (warm up).	10 min
	2) Bilateral eccentric contraction of the AL: patient in supine position, hips flexed at 45° and fully adducted. The physiotherapist slowly abducts both hips up to 30°, while the patient is asked to slow down the muscle elongation (warm up).	5 s of contraction (+10 s pause) for 8 repetitions for 4 sets
	3) Isoinertial eccentric training for AL: patient in supine position. Overload: 2 Kg (Concentric + Eccentric phases duration: ~3 s).	6 repetitions for 4 sets (2 for each leg)
	4) Isoinertial eccentric training for AL: patient in upright position. Overload: 4 Kg (Concentric + Eccentric phases duration: ~3 s).	6 repetitions for 4 sets (2 for each leg)
Phase 3	1) Spinning bike (warm up)	10 min
	2) Bilateral eccentric contraction of the AL: patient in supine position, hips flexed at 45° and fully adducted. The physiotherapist slowly abducts both hips up to 30°, while the patient is asked to slow down the muscle elongation (warm up).	5s of contraction (+10s pause) for 8 repetitions for 4 sets
	3) Isoinertial eccentric training for AL: patient in supine position. Overload: 3 kg (concentric + eccentric phases duration: ~3 s).	6 repetitions for 4 sets (2 for each leg).
	4) Isoinertial eccentric training for AL: patient in supine position. Overload: 4 kg (concentric + eccentric phases duration: ~6 s).	4 repetitions for 4 sets (2 for each leg).
	5) Isoinertial eccentric training for AL: patient in upright position. Overload: 4 kg (concentric + eccentric phases duration: ~3 s).	6 repetitions for 4 sets (2 for each leg).
	6) Isoinertial eccentric training for AL: patient in upright position. Overload: 6 kg (concentric + eccentric phases duration: ~6 s).	4 repetitions for 4 sets (2 for each leg).

AL: adductor longus.

such as fainting or nausea occurred during the treatment. Some patients reported minor pain in the treated location up to 12 hours after the end of EPI® intervention.

The standardized active physical therapy program

For all participants, the program began within 10 days of enrolment and was performed under the constant supervision of a physical therapist, who did not know which subjects were also treated with Eco-Guided EPI® intervention. Table II specifically shows the therapeutic proposals of each of the 3 phases comprising the treatment. The APT protocol was defined taking into consideration: 1) previous studies that investigated the effects of active physiotherapy (*i.e.* isometric and eccentric muscle contractions performed against manual resistance) on GP;[19, 24]; 2) previous studies aimed at examining the combined effects of EPI® technique and isoinertial eccentric exercises on the treatment of patellar tendinopathy;[27] 3) previous studies that examined the effects of isoinertial eccentric exercises on muscle function in healthy athletes;[36, 37] 4) pilot studies carried out by our research group. The duration of each phase depended on the functional and symptomatic improvement shown by each individual. In particular, the achievement of specific NRSpalp, NRScontr and PSFS threshold values (see below) resulted in the phase completion. However, each subject was required to perform at least 1 week of training for each phase.

PHASE 1

The aim of this phase was to reduce the ALErGP symptoms. Subjects were required to completely suspend all sport-related activities and perform three rehabilitative sessions per week, which included isometric

lower limb adductions and AL eccentric contractions performed against manual resistance (Table II). The duration of each session was about 30 minutes. At the beginning of each session, NRSpalp and NRScontr tests were replicated. When the values of both tests were ≤3/10, subjects advanced to Phase 2.

Phase 2

The objective was non-sport specific functional recovery. As in the previous phase, 3 sessions per week (30 minutes/session) were performed by the subjects. Phase 2 involved the use of a machine (Element Sport™, Sevilla, Spain; Figure 5) for performing isoinertial eccentric exercises. This isoinertial machine was equipped with a 7 kg flywheel (moment inertia: 0.09 kg/m^2) and additional overloads (between 3 and 6 kg) that were appropriately set by the operator (Table II), and was very similar to those described in other studies that used isoinertial exercise as an intervention.[27, 36, 37] In particular, an important feature of this machine is that the concentric-eccentric phase transition is extremely fast (*i.e.* the isometric phase is negligible). During the concentric contraction phase, the kinetic energy is transmitted to the spinning cone (flywheel) through the extraction of the nylon cord wrapped around it. When the cord is completely extended, the stored energy causes the cone to continue its rotation through inertia, in turn rewinding of the cord. At this point the subject is required to perform an eccentric contraction (proportional to the effort exerted during the concentric phase) in order to break and stop the rotation of the cone, thereby completing the repetition. During APT phase 2 (as well as phase 3), the two initial exercises were proposed as controlled warm-up activity (Table II). The initial 3 repetitions of each of the subsequent exercises were performed by the subjects at a lower intensity because they were aimed at familiarizing with the isoinertial equipment. It is worth noting that eccentric exercise was reported to be effective as an "active stretching" intervention for tendon tissue.[38] In addition, isoinertial eccentric exercise was shown to be effective for increasing muscle mass and improving muscle function.[36, 37] At the beginning of each session, the PSFS was assessed for the non-sport specific activities. When the score of this test was ≥8, subjects advanced to phase 3.

During phase 2, subjects were also allowed to perform

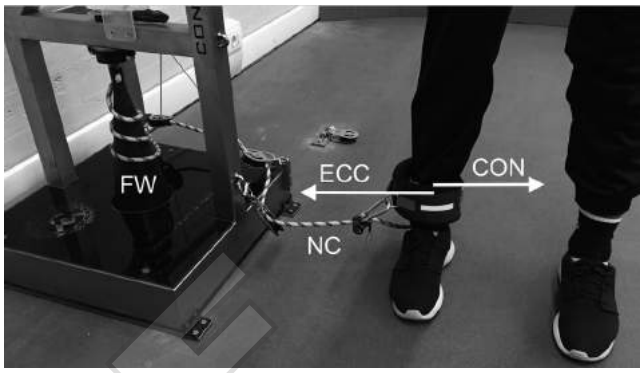

Figure 5.—Isoinertial machine. The nylon cord (NC) is wrapped around the flywheel (FW) and secured at the athlete's ankle. A concentric contraction (CON) of the adductor muscles results in the initiation of FW rotation while unwinding the NC. Once the pushing CON phase has been completed, the NC rewinds because of the kinetic energy of the FW and pulls the lower limb toward the machine. Hence, the athlete is required to perform an eccentric contraction (proportional to the effort exerted during the concentric phase) in order to break and stop the rotation of the FW, thereby completing the repetition. After bringing the FW to a stop, a subsequent CON muscle contraction is instantly initiated.

up to two unsupervised training sessions per week, performing linear running, sprinting, twisting movements and jumping; during these sessions, the use of the ball was not allowed. The duration of the first unsupervised training sessions was 10 minutes; if no adverse events occurred, the subject was allowed to increase the duration of the subsequent session by 10 minutes. Duration increments were allowed in order to reach a maximum session length of 40 minutes. In addition, subjects were required to limit the exercise intensity during the unsupervised training sessions. In particular, the perceived exertion should have been lesser than 3/10 (moderate exertion) referring to the Borg CR-10 Scale, which is commonly used for rating the perceived exertion in male soccer players.[39]

Phase 3

The goal was to restore a level of physical performance sufficient for participating consistently in subsequent full training sessions as well as soccer matches. The endeavors started in phase 2 were continued, while increasing the sessions load. Each session lasted up to 40 minutes, and was performed twice a week. In order to achieve the goal of this phase and complete the APT program, preliminary observations carried out by our team suggested that the player was required to obtain

TABLE III.—*Baseline characteristics of the participants.*

	Group A	Group B	P value
Age (years) (mean±SD)	26.9±4.5	25.2±4.9	0.384
Stature (cm) (mean±SD)	176.3±7.9	180.7±7.8	0.164
Body mass (kg) (mean±SD)	74.5±8.3	73.4±5.7	0.816
Position			
Goalkeeper	1	1	
Defender	2	5	
Midfielder	3	4	
Striker	5	3	
Dominant foot			
Right	7	11	
Left	4	2	
Athletic activity/week			
<6 hours	1	2	
>6, <10 hours	7	7	
>10 hours	3	4	
Activity status			
Normal	5	6	
Restricted	3	3	
Suspended	3	4	
Duration of the symptoms			
0-4 weeks	5	6	
4-10 weeks	4	3	
10-26 weeks	2	3	
>26 weeks	0	1	
Groin pain			
First case	0	3	
Recurrent	11	10	
ALErGP laterality			
Right	7	7	
Left	1	2	
Bilateral	3	4	

ALErGP: *adductor longus* enthesopathy-related groin pain.

at least 80 points on the PSFS, assigning each of the sport specific and non-sport specific activities a score of ≥8. We did not set a "complete recovery" threshold (100/100) because this would have exponentially delayed the restart of individual soccer activities, conceivably impairing the compliance to the study protocol and increasing dropout.

During phase 3, subjects were allowed to perform two unsupervised soccer-specific training sessions per week, the maximal duration of which was set as 60 minutes. Similar to phase 2, the maximal duration of the first unsupervised training sessions was 20 minutes; if no adverse events occurred, subjects were allowed to increase the duration of the subsequent session by 20 minutes. Also, the perceived exertion of each session was required to be equal or lesser than 5/10 (hard exertion) referring to the Borg CR-10 Scale.[39] During these soccer-specific training sessions, subjects were allowed to perform passing and kicking as well as running, sprinting, twisting movements and jumping.

FOLLOW-UP

From the end of APT program to the end of the follow-up period (6 months), subjects were allowed to perform up to 3 soccer-specific training sessions (duration: 60 minutes) and one official game every week.

Statistical analysis

Data are reported as means±standard deviation (SD). The distribution of quantitative variables was tested for normality using the Kolmogorov-Smirnov Test with the Lilliefors correction to apply a parametric or non-parametric test for group comparison. Since the assumption of normality distribution for the investigated variables was not met, the differences between independent samples were analyzed using the non-parametric Mann-Whitney *U* test, and the differences between related samples were analyzed using the non-parametric Friedman Test and Kendall Coefficient of concordance. Alpha level for all of these analyses was set at $P<0.05$ (two-tail test). Data were analyzed using SPSS 13.0 (SPSS Inc., Chicago, IL, USA).

Results

Characteristics of the participants

Group A and B presented similar characteristics at baseline. Age, stature and body mass were not significantly different between the two groups (Table III). Also, when the medical interview occurred, soccer-related activities were already restricted or suspended for 6 players (group A) and 7 players (group B). In addition, GP was recurrent in all group A subjects and in 10 out of 13 players enrolled in group B.

Pain and functional assessments

Both Groups significantly improved pain and functional scores after treatment ($P<0.001$, Table IV). Furthermore, NRSpalp, NRScontr, and PSFS values recorded after treatment were similar to those recorded throughout the follow-up in both groups ($P>0.05$).

TABLE IV.—*Numeric Rating Scale (NRS) and Patient Specific Functional Scale (PSFS) values registered at the end of treatment and during the follow-up (2, 4, and 6 months).*

		Pre	End	2 months	4 months	6 months	Time	Group	Time x group
NRSpalp	Group A	7.5±1.9 #	1.6±1.1	0.7±0.8 **	1.0±0.9 **	1.1±0.9	<0.001	0.010	0.457
	Group B	8.1±1.9 #	2.5±1.5	2.4±1.3	2.3±0.9	2.0±1.5			
NRScontr	Group A	8.5±1.4 #	1.3±0.9 *	1.3±1.1 *	0.7±0.7 *	0.5±0.7 *	<0.001	0.011	0.013
	Group B	8.0±1.6 #	2.2±1.7	2.8±1.6	2.2±1.4	1.6±1.3			
PSFS	Group A	55.5±22.2 #	91.6±3.8	93.7±3.6	93.8±4.2	95.4±4.1	<0.001	0.093	0.200
	Group B	56.7±20.6 #	87.5±5.6	81.5±10.8	86.3±7.5	89.9±6.8			

NRSpalp: Numeric Rating Scale: pain upon palpation of the insertion of the adductor longus. Scale: 0-10; lower score indicates better outcome.
NRScontr: Numeric Rating Scale: pain upon bilateral isometric adductor longus contraction against resistance. Scale: 0-10; lower score indicates better outcome.
PSFS: Patient Specific Functional Scale: 0-100; higher score indicates better outcome.
Time effects. Values recorded at Pre were significantly different (P<0.01) than those recorded at the other time points; *Significant differences between the two groups; *P<0.05; **P<0.01.

TABLE V.—*Active physical therapy program duration.*

	Group A	Group B	P value
Phase 1 (days)	11.9±4.7	20.7±9.3	0.048
Phase 2 (days)	14.8±4.8	16.0±4.2	0.948
Phase 3 (days)	11.0±3.8	12.7±3.3	0.512
Total duration (days)	37.9±8.5	48.8±9.4	0.098

When comparing the two groups, baseline values of NRSpalp and NRScontr were also similar between group A and B (P=0.442 and P=0.505, respectively; Table IV). However, at the end of the APT program, NRScontr was significantly lower in group A (0.9 points, P=0.047). Lower NRScontr values in group A were also recorded at the three follow-up time points (P<0.05). Furthermore, time x group interaction was also significant for this parameter (P=0.013, Table IV). NRSpalp showed a trend similar to NRScontr, with values that tended to be lower in group A than group B at the end of treatment and follow-up (Table IV); however, statistical significance was achieved only at the 2- and 4-month follow-up (P=0.003 and P=0.005, respectively).

On the other hand, no significant difference for PSFS between the two groups was found (P=0.093, Table IV). However, while the PSFS baseline value was very similar between group A and B (55.5±22.2 and 56.7±20.6, respectively), it tended to be greater in group A after treatment and throughout the follow-up by 7.8±3.8%.

It is also worth noting that the duration of Phase 1 was on average 8.8 days shorter in group A (P=0.048). The same trend, without statistical significance, was also shown by Phase 2, 3 and total duration (Table V).

Discussion

This study investigated the therapeutic utility of the EPI® technique in combination with a standardized APT program to treat ALErGP in non-professional soccer players. The assessment of pain- and functional-related outcomes in the experimental group (A), who underwent the APT program in combination with EPI® treatment, and in the control group (B), who underwent the APT program only, revealed that: 1) both groups significantly improved pain and functional scores after treatment and maintained this therapeutic result throughout the 6 months after treatment; 2) the combined intervention of APT program and EPI® ensured a greater and faster reduction of pain compared to the APT programme alone; 3) functional recovery was not significantly different between the two groups, although it tended to be greater in group A after the treatment and throughout the follow-up.

APT program with and without EPI® effectively reduced pain and improved functional recovery

High quality studies on non-surgical treatment of long-standing adductor-related GP are rather scanty.[40] For example, Hölmich *et al.*[19] showed that 79% of the patients with adductor-related GP that were treated with exercise therapy (static and dynamic exercises aimed to improve strength and coordination of the pelvic muscles) resumed their usual physical activity without symptoms. On the other hand, in the study conducted by Weir *et al.*,[24] the success rate of an active physiotherapy programme aimed at the strengthening of adduc-

tor and core muscles, associated to a return-to-running programme, decreased to 50%. The present study supports the view that an active physiotherapy programme that promotes significant eccentric muscle contraction of the AL via isoinertial eccentric training is conceivably a valuable intervention for long-lasting pain reduction and functional improvement. Indeed, both group A and B significantly improved pain and functional scores after the treatment. Generally, the time course of these improvements throughout the ATP program was related to the initial GP symptoms of each individual: the more severe the symptoms, the longer the duration phases. Also, pain and functional scores were similar at the end of the ATP program and throughout the subsequent 6-month follow-up.

The positive effects of active physiotherapy on adductor-related GP can be related to the connective tissue remodeling that occurs physiologically as a result of the mechanical stimulation exerted by the exercise.[38, 41] In particular, Apostolakos *et al.*[12] emphasized that biological factors are important for the proper modulation and regulation of collagen production, while mechanical stimuli are crucial for the proper collagen fibers orientation; thus, both factors are essential for the proper healing of the degenerated enthesis. For this reason, eccentric exercise represents one of the most considered therapeutic solutions in the treatment of collagen-rich tissues pathologies,[38, 41-43] and isoinertial eccentric training one of the effective methods to perform eccentric exercise.[27, 36, 37]

The integration of EPI® and APT interventions promoted greater and faster pain reduction compared to APT intervention alone

The pain-related clinical testing proposed in the present study showed substantial differences between group A and group B after the treatment and during the 6-month follow up. In particular, the scores of the active test form proposed in the present study (NRScontr) were significantly lower in group A than group B at the end of the treatment and for the entire duration of the follow-up. The "time x group" interaction was also significant for this parameter. In addition, NRSpalp values tended also to be lower in Group A after the treatment, and significantly lower at the 2-month and 4-month follow up. Interestingly, Mosler *et al.*[44] supported the view that NRScontr is better than NRSpalp for evaluating and quantifying GP in athletes.

The relevant effect of EPI® treatment integration with the APT intervention on GP was also underlined by the fact that the duration of phase I of the APT programme, which was focused on pain reduction, was significantly shorter (-8.8 days) in group A than in group B. These results support the view that the combination of EPI® and APT interventions was more effective than APT intervention alone for reducing AL enthesopathy-related symptoms. It is plausible that EPI® electrolytic action promoted the removal of excessive deposits of connective tissue (fibrosis), so decreasing the tendon tissue tension [28] and consequently reducing GP. It is worth noting that EPI® intervention initially induces a local and controlled inflammatory process that subsequently promotes the histological enthesis healing process,[28] the duration of which is reported to be longer than 14 days.[12] Hence, a proper protocol of active exercises should be proposed as a parallel intervention to the EPI® treatment in order to ensure that the new production of collagen (resulting from the inflammatory process) develops adequately from a biomechanical point of view.[40] With this respect, the association of EPI® intervention and isoinertial eccentric exercises has already produced encouraging results in the treatment of patellar tendinopathy, and in particular for the tendon tissue repair.[26, 27]

Effects of EPI® intervention on functional recovery

In the present study, functional recovery was evaluated by PSFS, which consisted of 10 motor tasks (see Methods) that did not require a selective, sustained and maximal AL muscle contraction. For example, maximal effort soccer kick requires a substantial level of AL activation during a limited part of the kicking swing phase (30% to 45%);[45] furthermore, AL activation is primarily aimed at controlling the hip extension rather than contributing substantially to hip flexion and to completing this complex motor task.[45] In addition, Delmore *et al.*[46] underlined that AL activation intensity recorded by EMG during twisting movements was about half of that observed during Adductor Squeeze Test. In the present study, the experimental group that underwent EPI® intervention and APT programme tended to achieve greater functional recovery after treatment and throughout the follow up (+7.8±3.8%) compared to the control

group that underwent APT programme only. However, this difference was not statistically significant. The fact that PSFS lacks in motor tasks that specifically and substantially involve AL activation is conceivably one of the main causes of this finding. The total duration of the treatment was also not significantly different between the two groups, although it tended to be shorter (-10.9 days) in group A. These data suggest that further studies are required to better assess the effectiveness of EPI® treatment on functional recovery in soccer players suffering from ALErGP. It is also worth noting that an intrinsic limit of the non-surgical treatments is that they reduce only to some extent the anatomical alterations of the enthesis. Therefore, while the functional recovery and symptoms reduction can be achieved by these non-surgical treatments, the connective tissue alteration often persists,[15] even in asymptomatic patients.[17] As a consequence, these residual anatomical alterations of the enthesis might result more likely in a premorbid condition. From this perspective, further studies should investigate whether the substantial reduction of the enthesis anatomical alteration brought about by EPI® intervention may eliminate or reduce such premorbid condition.

Limitations of the study

One of the limitations of this study is the lack of a graduation in the severity of the ultrasound imaging of the proximal tendon of the AL: we differentiated between "tendons with anatomical changes" and "healthy tendons". However, we hypothesize that a worse ultrasound image could potentially be associated with a lower expectation of therapeutic success, regardless of the intervention. In addition: 1) the EPI® intervention protocol lacks validation (the technique has recently been developed); 2) research participants were not blinded with respect to the treatment received; thus, placebo effect could have played a role in the subjective scoring, especially in the earlier stage of the study protocol. On the other hand, it is less likely that any eventual EPI®-related placebo effect could have lasted throughout the follow-up; 3) the copresence of GP secondary clinical patterns (*i.e. iliopsoas*-related GP, *rectus abdominis*-related GP) or comorbility (snapping *iliopsoas*, hip arthrosis, ilioinguinal nerve entrapment) could have potentially played the role of confounding variables. Finally, 5) the subjects of this study resumed independent soccer-related activities without supervision after the end of the treatment. So, different factors such as amount and characteristics of the physical activity performed by each individual could also have influenced the follow-up results.

Conclusions

EPI® treatment in association with active physiotherapy ensured a greater and more rapid reduction of pain and tended to promote greater functional recovery in soccer players with ALErGP compared to active physiotherapy only. This positive therapeutic result lasted for at least 6 months after the end of the treatment. This finding, together with the fact that EPI® treatment is minimally invasive and was overall well tolerated by the patients, support the combined use of EPI® and active physiotherapy in soccer players with GP syndrome. Further studies on the effects of EPI® treatment on functional recovery in ALErGP and on clinical conditions similar to ALErGP (*i.e. rectus abdominis* enthesopathy and tendinopathy, *gracilis* enthesopathy, degenerative pubic symphysis, *iliopsoas* syndrome, *rectus femoris* aphophysitis) are needed to gain more insight into the effectiveness of EPI® treatment on GP syndromes.

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