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LATERAL EPINCONDYLITIS – NEW THERAPEUTIC OPTIONS IN REFRACTORY AND CHRONIC CASES

Daniela Poenaru*

PhD, MD, lecturer Rehabilitation Departament, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania.

***Corresponding Author: Dr. Daniela Poenaru**

PhD, MD, lecturer Rehabilitation Departament, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania.

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ABSTRACT

Lateral epicondylitis is associated with overuse from either sport activity or overuse in work and home environement. It has an incidence of 1 – 3% in general population, it is prevalent in the forth and fifth decades, in professionaly active population and has a high rate of recurrence or chronic course. Despite the actual denomination, which suppose an inflammatory substrate, the main morhopathologic process is degenerative, eith tendon microtears and angiofibrotic proliferation. For the acute stage, whose symptoms last under 3 months, conservative treatment consists in nonsteroidal antiinflammatory drugs, rest, bracing, physiotherapy and therapeutic exercise. Corticosteroids provide rapid analgesic effect but carry the risk of rupture and recidive. The chronic stage necesitates therapies oriented toward tendon regeneration. Research was performed on extracorporeal shock wave therapy, regenerative therapies, prolotherapy, botulinum toxin injection. Musculoskeletal ultrasound is largely used for diagnostic and treatment purpose, improving the injection techniques.

KEYWORDS: lateral epincondylitis, corticosteroids, ESWT, PRP, ABI, prolotherapy, botulinum toxin.

INTRODUCTION

Lateral epicondylitis (LE) may be found through literature under many denominantions: Epicondylitis humeri radialis (Writers cramp named by Runge), Lawn tennis elbow or simply, Tennis elbow. Once thought to occur mostly in tennis players in the dominant upper limb, today it is associated, beside sport activity, with overuse in work and home environement.

It has an incidence of 1 – 3% in the adult population and of 15% in manual workers. Peak incidence is between 40 and 50 years of age.

From the common extensor tendon, extensor carpi radialis brevis (ECRB) occupies the deep and anterior aspect and is the most frequently affected. As it inserts at the base of the third metacarpal bone, an important diagnostic sign is the painful third digit extension against resistence. The next tendon involved is extensor digitorum communis, whose involvement is documented with painful fingers extension.

Mechanical factors are determinants, as highly repetitive activities, implying supination and extension of the forearm and wrist and power grip. Risk factors for tendinopathies may promote the occurence of LE, as diabetes, hyperuricemia, dysthyroidism, certain drugs intake (quinolones, statins, corticosteroids either orally or locally). Smoking, alcohol and obesity have been identified as risk factors by some scholars.[1] Tennis players are at risk especially when their technique is inadequate. On the whole, only 5% of tennis players are diagnosed with lateral epicondylitis, which is a rather small incidence.

Although the term of epicondylitis suggests inflammation, morphopathologic studies revealed absence of inflammatory cells. There are tendon microtears, collagen degeneration and angiofibrotic proliferation. Terms like tendinosis or tendinopathy are preffered as they describe more accurate the underlying degenerative process.

Natural course, equivalent with an ”wait-and-see” atittude, is self limitative, in a frametime of 6 months to 2 years. An evolution of under 3 months may be considered acute. Frequent recurrence and chronic evolution accentuate the disability. Treatment stratification is based on physician experience and scientific research and may vary according to technique availabilities and costs of the intervention.

First treatment option is based on traditionally conservative methods: rest and bracing, oral non-steroidal anti-inflammatory drugs (NSAIDs), physiotherapy and therapeutic exercise.

BRACING

Elbow straps with special padding belong to counterforce bracing, they apply pressure on the proximal extensor muscles, ECRB being the most targeted muscle.

Two mechanism of action of local constriction are presumed: inhibition of muscle contraction followed by lowering the tension proximally and creation of a compressive adhesion or a secondary origin to unload the anatomic origin on the lateral epicondyle.[2] Electromyographic studies confirmed reduction of electrical activity in the forearm muscles under bracing.[3]

The recommendation is to find the most painful spot along the muscle belly, usually at about 5 cm below the elbow crease and apply the foammy pad on it. The strap is tightened until the pressure is comfortable and motion in elbow and wrist is permited. The orthosis is used during daytime and removed when showering and nightime. The orthosis has to be worn for a long time, at least 6 months, since it doesn′t restrict motion. The researchers admit that pain and recovery are accelerated on short term (2 weeks) and mentained on long term (6 months). Despite these facts, patients adherence to wrist brace is rather poor, with a drop-out rate varying between 66% and 71%.[4] It is important to add other therapeutical modalities to accelerate healing.

Wrist resting orthosis with a dorsiflexion of 15 – 20^0 immobilises the forearm extensors in resting position and offers a constant reminder to protect the forearm. It has to be worn during daytime, excepting shower and physical therapy. Some researchers reported better result on pain after 6 weeks, although functionality improved in the same amount as with the counterforce brace.[5] Whereas other researchers found equal improvement between the two types of orthosis, with a dropout rate of 5:1 for the wrist resting splint, as it interferes with daily activities.[6]

Physiotherapy includes low level laser therapy, sonophoresis, iontophoresis, ice-packs.[7] On a short therm both cryoultrasound and extracorporeal shock waves (ESWT) reduced pain; the difference became significative on long term (12 months) in the favor of ESWT.[8]

Sometimes the above mentioned traditionally modalities offer a short period of improvement followed by a relapse; the pain and limitation reappear and the course becomes chronic. The patient has to attempt many sessions for therapy and its adherence may be reduced over time.

PHYSICAL EXERCISE

It is important to emphasize that physical exercise is a main component of most therapeutic schemes. In the acute stage, rest for a short period of time (maximum 2 weeks), must be followed by kinetotherapy. It consists in stretching and strenghtening, especially with eccentric contractions, under medical surveillance. Practice may be done in medical settings exclusively or in a mixed medical environement and home based program. Every effort is important to increase patient participation

For the refractory or recurrent cases there are new therapies under extensive research, all of them being followed by therapeutic exercise.

CORTICOSTEROIDS

For a number of musculoskeletal disorders, local corticosteroids represent a common approach to pain control.

On short time (4 to 6 weeks) and acute LE, one single corticosteroid injection provided more analgesia than placebo or other therapies (extracorporeal shockwave therapy ESWT and autologous blood injection ABI). After 8 weeks, corticosteroids were simillar with placebo; on long term (12, 26 and 52 weeks) the analgesic effect declines, being surpassed by other therapies.

For chronic LE corticosteroids may provide analgesia for short term (4 weeks), but the effect decreases on medium and long term, being surpassed by other therapies (ESWT, ABI).[9,10,11,12] As the pathophysiologic mechanism of tendinopathy are the degenerative changes and the failure of healing respons, the corticosteroids do not find place.[13] The risk of recidive or of tendon rupture is increased with corticosteroids, due to at least two factors: the local inhibition of migration and proliferation of cells with healing delay and the analgesic effect which fails to limit the overuse of the tendon.[14,15]

Side effects are of moderate intensity: skin atrophy, tendon rupture, cutaneous rash, postinjection pain and, rarely, serious and systemic effects in specific groups of patients.

A rationale for corticosteroids use may be a peritendinous injection to provide analgesia and comfort for the patient to join the therapeutic sessions.

New treatment methods focused on tendon regeneration are investigated with the aim of reducing the recurrence and the chronic evolution.

Extracorporeal Shock Wave Therapy (Eswt)

There are various clasiffications of ESWT according to energy level; most of researchers define low level energy under 0,12 mJ/mm^2 and high energy level above the afore mentioned level. There is general opinion that effects vary proportionally to level of energy; the high energy ESWT is a painful procedure.[16]

Many protocols use low energy (0,06 – 0,09 mJ/mm^2), 3 weekly sessions (sometimes 4) with 2000 pulses/session.

As a first line therapy for acute LE, ESWT didn′t provide significative better results than corticosteroids or sham therapy for short term (4 weeks), although on medium

term (8 weeks) and long term (6 months) the results were in favor of ESWT.[17,18]

For chronic LE, ESWT produced significative pain and disability reduction on short and long term (3, 6, 12, 24 weeks).[19,20,21] A few studies found an analgesic effect of ESWT comparable with sham therapy, presumably due to placebo.[3,22,23,24,25] Some of ESWT applications were performed under local anesthesia, which may alter the effect of ESWT. It is supposed that local anesthetic inhibits the C-fibers activity and alters the biological response to ESWT.[26]

There are reasons to consider local anesthesia to have an inhibitory effect on ESWT treatment. The pathway may be represented by the stimulation of nociceptive C-fibers, which posess also a trophic function through various neuropeptides. Local anesthetics abolish nociception and also the neuropeptides release, interfering with the trophic effect of ESWT.

The effect on nociceptive C-fibers of ESWT is dose-dependent. The application of local anesthetic, under the form of lidocaine patch, reduces the pain at stimulation, the subsequent neurogenic flare and release of trophic neuropeptides. Therefore, there is a strong recommendation against local anesthesia when applying ESWT.[27] Some researchers applied high energy ESWT under conscious sedation analgesia to achieve better results in the context of dose-dependency effect.

ESWT may be a good choice before surgical therapy (tenotomy). Applying one session of high energy ESWT (0,22 mJ/mm^2) under conscious sedation anesthesia provided comparable results on pain reductions, grip strength and overall rating of disease state as percutaneous release of common tendon.[28] Thus, it seems reasonable to prescribe a conservative method to reduce the number of patients candidates to surgery.

Side effects of ESWT are rare and of minor importance. Local reactions are mild, transient and didn′t modify the course of therapy: reddening of the skin (especially on high energy level), petechias, haematomas and small cutaneous hemorrhagies (inconstant, presumably associated with the urologycal device), local pain during the procedure itself or persisting one week after, local dysesthesias. General reactions are infrequent: migraine attacks and vasovagal syncopes, both mentioned for musculoskeletal and urologic devices. On the whole, the procedure is safe and well tolerated.[29,30]

One ethical consideration deserves attention. Some studies revealed a rather simillar effect on pain and disability for short and medium term (6 weeks, 3 months) between corticosteroids and ESWT; the fact that the cost of corticosteroids is about one hundred times lower than ESWT and the risk of adverse effects is considerable higher is an important issue to be discussed with the patient.[31]

REGENERATIVE GROUP OF THERAPIES

It includes autologous blood injections, platelet rich plasma and prolotherapy. They aim at initiating maturation and proliferation within the tendon, through stimulation of cellular activity.

Autologous blood injection

The structural alteration in the tendon is described under the term of angiofibroblastic hyperplasia, a degenerative process. In the aim of modifying its course researchers used chemical modifiers of cellular activity from autologous blood, known to be mitomorphogenic, that may initiate the healing cascade.[32]

A small amount of venous blood (about 2 ml) is drawn, mixed with 1 ml of local anesthetic and injected extraarticulary, into the common tendon, either blindly or under sonographic guidance. The procedure is safe, easy to prepare and inject, inexpensive and with minimum risk of adverse effects. It can be administered in multiple shots, according to the clinical response. Technically, it requiers short time immobilisation of the elbow (40^0 flexion). Patients must refrain from anti-inflammatory medication.

The injection may be unique or may be repeated until three times, at 6 weeks interval.[33]

Another technique of injection is derived from dry-needling, peppering the autologous blood into the tendon with one single skin puncture and multiple tendon shootings, changing the needle position. It requires ultrasound guidance.[34]

After the procedure, a short period of rest (about five days) would support the initial healing phase. The patient would refrain from duties with the involved upper limb or would wear a wrist splint, in neutral to 10^0 extension. Afterwards, a rehabilitation program based on physical exercise is provided.

Researchers reported improvement of pain and disability scores over medium and long term (8, 26 and 52 weeks), comparative with corticosteroids. On short time the results were either simillar or weaker than corticosteroids.[11,35,36,37]

Side effects are rare and mild: many patients experience local pain, some of them transient skin reaction. None of these was dangerous. The risks of the procedure itself are infection when local asepsia is poor and nerve damage (on the radial side of the elbow resides the radial nerve and its bifurcation).

Platelet rich plasma PRP

Recently, PRP is considered by many authors an important tool in treating chronic tendinopathies.

The final product has a baseline platelet concentration of three to five times greater than baseline or a platelet

count of at least 1 000 000/µl; white blood cell count and cytokine concetration may vary, as there no standardized method to obtain PRP.

The alpha-granules of platelets release a number of growth factors to enhance the recruitment, proliferation and differention of cells involved in tissue regeneration.[38] From the pool of cytokines, transforming growth factor-beta (TGF-β) was correlated with functional improvement and MRI structural improvement. TGF-β and vascular endothelial growth factor (VEGF) were found to correlate with the degree of improvement of MRI tendon structure.[39]

In a small study, contrast-enhanced ultrasound showed changes in the morhology and vascularity of the tendon, at the myotendinous junction and footprint in the timelapse of one to six months after PRP injection. This new technique opens the field for further research on PRP mechanism of action.[40]

Literature is controversial and inhomogenous about the technique and clinical results of PRP in lateral epicondylitis.

As two types of PRP can be obtained, leucocyte-rich (L-PRP) and leucocyte free PRP (simple PRP) compete for the optimal therapeutic approach.

Some researchers found that L-PRP offered significative relief of pain, increase in function and reduces the number of cases to undergo surgical procedure, estimating a number to treat PRP injections of 1,3 to avoid one surgery.[41,42] As leucocytes are known to have inflammatory local response, they may be responsible for side effects as pain; there is suggestion that a more persistent inflammation (promoted by leucocytes) may alter tendon healing.[43] Despite this presumption, studies failed to notice differences between leucocyte-poor and leucocyte-rich PRP in side effects occurence (pain and redness).[44]

In an important number of studies there no approximation of leucocyte number in PRP products, being difficult to make an assuption on what type of PRP was used.

Research on PRP versus placebo used as control procedure the local injection with saline, which was presumed not to have local effects. However, a meta-analysis revealed significant measurable improvements in pain and function scores at 6 months after single saline injection, suggesting that saline injection may have clinically relevant effect.[45]

Applying local anesthetic together with PRP, as performed in some treatment protocols, may compromise the therapeutic potential of PRP by reducing local pH and inhibiting platelet degranulation.[46]

On the number of injections, it seems that one injection would be sufficient; there is no significative difference between one and two injections at 4 weeks interval.[47] The volume of injected material within the tendon varied between 2 and 3 mL.

Post-injection pain as a side effect may be a normal occurence since the local mechanism is based on inflammatory reaction which promotes healing. It is of short duration and necesitates local cryotherapy and simple analgesics. Avoidance of NSAIDs for 21 days after the procedure is important as they inhibit the PRP effect. After the procedure, immobility is recommended for 15 minutes, followed by 24 hours rest and beginning of the physical exercise program. After 4 – 6 weeks sport activity may be resumed with functional bracing.

The technology of musculoskeletal ultrasound allowes guided infiltration of the exact point of maximum structural alteration and lesion follow-up. One single PRP injection produced at 6 months structural improvement of the tendon, as graded on ultrasound images, together with pain reduction and functional improvement.[48] Another injection technique consists in peppering within the common tendon, with a single skin insertion and deep peripheral multiple sites of injection, changing the position of the needle.

Comparing PRP injection with ultrasound-guided percutaneous tenotomy, both procedures were successful in producing clinical and statistically significant improvement in pain, function and quality of life.[49]

Comparison between different procedures is useful to standardize them.
On short term (4 weeks), one single injection of ABI or PRP produces a significant improvement in pain and function. At 8 weeks, PRP but not ABI continued to offer improvement of pain and disability.[50,51] A recent study found no diference between one single injection of ABI, PRP and saline at 4, 8, 12, 26 and 52 weeks for elbow pain and function.[52] It is noteworthy the saline was used as control, which may be a bias.

PRP was found to have fewer adverse effects (local pain and skin reaction).[53,54] The ethical aspects of the two procedures point to the fact that PRP is a more expensive technique than ABI.
At 2 years, ESWT and PRP offered significant comparable pain and disability reduction, with a faster recovery in the case of PRP.[55]

For chronic LE corticosteroids offer rapid improvement of pain, as noted at 4 weeks evaluation, but were significantly surpassed on long term (26 weeks and one year) by PRP.[56,57]

PROLOTHERAPY

Prolotherapy uses local injection of specific substances, with osmotic, irritant effect (dextrose and polidocanol) or

chemotactic effect (sodium morrhuate) to promote inflammation and healing.[58] Inflammatory response is triggered by osmotic rupture of local cells, by local cellular irritation and sclerosing of neovascularity. Prolotherapy may stimulate the release of growth factors to accelerate healing.[59]

As a technique, prolotherapy can be delivered through one single punction, on anatomic landmarks or under sonographic guidance or as a peppering technique, with multiple tendon punctures under one skin penetration. The volume of injected substance may vary between 2 and 3 mL and the concentration of dextrose between 10 to 16%. After the treatment, patients are advised to apply cold or ice massage for 5 to 10 min, to use acetaminophen as pain killer, to avoid NSAIDs and to wear functional bracing.

A research on a combination between dextrose (10,7%), sodium morrhuate (14,7%) and local anesthetic, administred in three injections at 4 weeks interval reported significant reduction of pain and improvement of function in refractory LE, as compared to placebo.[60] Separatedly, simple hypertonic dextrose and mixture of hypertonic dextrose and sodium morrhuate, in the same 3 injections schedule, offered both significant clinical improvement versus ”wait-and-see” control group. Simple hypertonic dextrose acted quicker and with less pain as an adverse effect. Results were recorded at 16 and 32 weeks.[61]

Corticosteroids provided more rapid analgesic effect but inferior long-term efficacy versus prolotherapy.[62]

BOTULINUM TOXIN

The rationale for use of botulinum toxin resides in temporary blocade of acetylcholine receptors and muscle paralysis, which stops further overuse and allows healing. Another rationale may be the antialgic effect of botulinum toxin on the myofascial trigger points within the extensor muscles; these trigger points could be a source of pain.[63] The antialgic effect was suggested to be a decrease of pain perception due to release of cellular mediators (substance P, calcitonin gene-related peptide, glutamate and bradykinin).

Different techniques of administration were used: intratendinous (deeply into the subcutaneous tissue and muscle, 1 cm from the lateral epicondyle, toward the most tender spot) or intramuscular (the muscle bellies of extensor digitorum communis and extensor carpi radialis brevis on anatomic landmarks, at a distance from lateral epicondyle of 1/3 from the forearm lenght or on electrodiagnostic detection).

Administration of 60 UI botulinum toxin A was superior to placebo for pain reduction at 12 and 16 weeks. Transient weakness of finger extension and grip strenght decrease were the most common side effects.[64,65] Reduction of grip strenght may be due to loss of wrist stabilization role of extensor muscles. The procedure has to be recommended for patients whose professional activity doesn′t imply hands or digit extension.[66]

There is scarce information about studies comparing botulinum toxin with other therapies. In an acute or subacute stage of LE, steroids proved to reduce the pain more than botulinum toxin at 4 weeks, but the differences between the groups were not significant at 8 and 12 weeks, with a decreasing tendency of the botulinum toxin group for pain scoring. A small reduction of grip strenght was noted at 4 and 8 weeks for botulinum toxin; it disappeared at 12 weeks.[67] For the chronic LE, botulinum toxin and surgery had comparable results on pain and function at 1 and 2 years follow up.[68]

CONCLUSION

In the acute stage of lateral epincondylitis conservative treatment is recommended; it consists in rest, bracing, physiotherapy and therapeutic exercise. In this case, corticosteroids provide rapid analgesic effect, on condition of continuing the treatment schedule and avoid overuse and heavy workout.

For the chronic and recurrent cases, corticosteroids may add short analgesic effect, which diminishes after 4 weeks and is surpassed by other therapies. The new lines of treatment aim at reversing the degenerative tendon process and reducing pain and disability. Extracorporeal shock wave therapy, blood derivates injection, prolotherapy and botulinum toxin injection are proposed therapies to act on long therm. Results are controversial, every new treatment prescribtion is followed by contradictory studies. As scientific papers and clinical experience accumulate, the need of treatment standardization and stratification would be fulfilled.

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