Pain Medicine, 0(0), 2019, 1–5
doi: 10.1093/pm/pny303
Original Research

Prolotherapy vs Radial Extracorporeal Shock Wave Therapy in the Short-term Treatment of Lateral Epicondylosis: A Randomized Clinical Trial

Tannaz Ahadi, MD,* Maryam Esmaeili Jamkarani, MD,† Gholam Reza Raissi, MD,* Korosh Mansoori, MD,† Seyede Zahra Emami Razavi, MD,‡ and Simin Sajadi, MD†

*Neuromusculoskeletal Research Centre, Firoozgar Hospital, †Neuromusculoskeletal Research Centre, and ‡Physical medicine and rehabilitation department, Tehran University of Medical Sciences, Tehran, Iran

Correspondence to: Simin Sajadi, MD, Neuromusculoskeletal Research Centre, Shafa Yahyaian Hospital, Baharestan Square, Tehran 1157637131, Islamic Republic of Iran. Tel: (+98) 21-33542001; Fax: (+98) 21-33542020; E-mail: dr.sajadi_pmr@yahoo.com.

Funding sources: This study had no financial support.

Conflicts of interest: The authors declare no conflicts of interest.

Abstract

Objective. The aim of this study was to compare the efficacy of prolotherapy with hypertonic dextrose and radial shock wave therapy in chronic lateral epicondilosis. **Design**. Prospective single-blind randomized clinical trial. **Setting**. Physical medicine and rehabilitation clinic. **Subjects**. Thirty-three patients with at least three months of signs and symptoms of lateral epicondilosis, as well as failure of at least one of the conservative treatments, randomly allocated into two groups. **Methods**. Sixteen patients received three sessions of shock wave therapy, and 17 received one session prolotherapy. Severity of pain via visual analog scale (VAS), grip strength via Baseline Pneumatic Dynamometer, pressure pain threshold (PPT) by algometer and Disabilities of Arm, Shoulder, and Hand quick questionnaire (Quick DASH) were assessed at baseline, four weeks, and eight weeks after the intervention. **Results**. Within-group analysis showed that in both groups, differences between all of the outcome measures were significant after four and also eight weeks. Between-group analysis after four and eight weeks showed that the VAS and Quick DASH had significantly more improvement in the shock wave group. However, the two groups were similar regarding grip strength and PPT. No complication was observed in the two groups. **Conclusions**. Based on the results of this study, a regiment of three sessions (weekly) of radial extracorporeal shock wave therapy is significantly more effective than one session of prolotherapy with 20% dextrose regarding pain and function in the management of chronic lateral epicondylosis in short-term follow-up.

Key Words: Extracorporeal Shock Wave Therapy; Prolotherapy; Lateral Epicondilosis; Tennis Elbow

Introduction

Chronic lateral epicondylosis (CLE), or tennis elbow, is a painful enthesopathy of the common extensor tendon at the lateral part of the elbow [1]. It is a common, debilitating, and expensive condition, accounting for four to seven of every 1000 primary care office visits annually [2]. The disorder develops insidiously and is usually related to repetitive and strenuous physical activity [3]. This is a self-limited disorder in most cases, and the typical duration of symptoms is six months to years [4]. Histopathologic evidence of patients with CLE shows that it is not an acute inflammatory condition but rather a failure of the normal tendon repair process characterized by collagen degeneration, fibroblast proliferation, mucoid degeneration, and neovascularization [5]. Although many nonsurgical therapies have been suggested for CLE refractory to conservative treatment, none have been shown to be uniformly effective in the long term [6].

Prolotherapy is an injection-based technique for the treatment of chronic musculoskeletal pain. It is an iatrogenic stimulation of wound healing and tissue repair by

injection of an irritant solution into damaged ligaments and tendons [7].

Previous studies have shown benefit of prolotherapy in the treatment of tendinopathies [8,9]. Preliminary findings have also demonstrated the potential of prolotherapy in the management of CLE [10–12]. On the other hand, extracorporeal shock wave therapy (ESWT), which was first used in the treatment of urinary stones, has recently been used in the treatment of orthopedic conditions. It has a dose-related analgesic effect [13,14]. The biologic effect of ESWT is not clear. However, an inhibitory effect on nociceptors and some hyperstimulation mechanism have been suggested [15]. In vitro studies have shown that an optimal dose of shock wave stimulates cell proliferation. Proliferative morphologic changes and functional effects on neovascularization and collagen synthesis, as well as effects on the expression of some genes, suggest that shock wave therapy can enhance healing of the tendons [16]. Data about the therapeutic effect of ESWT on function and pain in patients with CLE are conflicting [17–22].

Considering the paucity of prolotherapy studies (which also lack a control group), the contradictory results of ESWT studies on the treatment of CLE, and that the proposed mechanism of action of both prolotherapy and ESWT is through cell proliferation and the healing process of tendons, this study was conducted to compare the effectiveness of prolotherapy with hypertonic dextrose and radial ESWT in CLE.

Methods

Study Setting

This study was an eight-week, single-blind randomized study of patients with signs and symptoms of CLE who were referred to our physical medicine and rehabilitation clinic during 2015.

Participants

Eligible participants in the study were 33 patients (10 men and 23 women) aged 18–70 years, diagnosed with CLE by having a history of at least three months of pain, having tenderness over the lateral epicondyle on palpation, having resisted wrist extension during physical examination, and having confirmatory hypoechoic lesions on ultrasonography. All the patients had pain with visual analog scale (VAS) score >4 and failure of at least one of the conservative treatments for CLE (nonsteroidal anti-inflammatory drugs [NSAIDs], physiotherapy, or steroid injection). Patients were not included in the study if they had history of steroid injection in the past three months, history of prolotherapy, radicular neck pain, coagulation disorder or on anticoagulant treatment, pregnancy, coexisting pathology or history of any surgery on the upper limb, taking opioids, allergy to local anesthetics, diabetes, any history or active rheumatologic disorder, or fibromyalgia.

The study was performed in accordance with the Declaration of Helsinki. This study was approved by the local ethics committee. All patients signed written informed consent before entering into the study.

Intervention

Patients were allocated to two groups by block randomization: 16 patients to three sessions of shock wave therapy weekly and 17 patients to one session of prolotherapy. In the prolotherapy group, after subcutaneous anesthesia with 2 cc of lidocaine 2%, under aseptic conditions and using a 25-gauge 1.5-inch needle, 3 cc of dextrose 20% was injected deeply, with the needle touching bone, into the maximal tenderness point and ultrasound-documented pathology of extensor muscle tendons insertion. A peppering technique was not used. The ultrasonography MINDRAY machine DP-6600 (Shenzhen, China) with a 5–10-Hz linear probe was used in this study. In the shock wave group, patients received three sessions of shock wave therapy at a weekly interval. The shock wave machine BTL6000 (2010, Baltimore, UK) was used for all patients, and in each session, 2000J shocks with an intensity of 1.5 bars and a frequency of 10 Hz were exerted. All patients were recommended to return to normal activity and to avoid pain-enhancing activities. They were prohibited to use braces, physiotherapy, NSAIDs, or steroids during the study. Three hundred twenty-five–milligram acetaminophen tablets were prescribed for patients to take in the case of severe pain. Patients were assessed by a blinded physiatrist at baseline and then four and eight weeks after the intervention.

Grip strength was evaluated via dynamometer. Pain-free grip strength is a commonly used objective measure of CLE-related disability with high reliability and validity [23]. In this study, we used a Baseline Pneumatic Dynamometer with 30 pounds per square inch. Patients were asked to sit, adduct the shoulder, flex the elbow to 90° and put their forearm in a neutral position, then squeeze the dynamometer for three to five seconds. This test was conducted three times with 60-second intervals for each patient, and the mean patient grip strength was recorded [11]. Pressure pain threshold (PPT) was also assessed in this study. PPT is an exact and reliable method for evaluating pain [24]. An algometer is a device for measuring the degree of exerting pressure on a surface of 1 cm^2 that can cause pain and is comprised of a gauge attached to a hard rubber tip. We used the FDX (Wagner Instruments, Greenwich, CT, USA) algometer in this study. In each evaluation session, two points with an interval of 2 cm on the lateral epicondyle were evaluated, and the mean (expressed as kg/cm^2) was recorded as the PPT. Each point was tested three times with at least a two-minute interval.

Outcome

Patients expressed their most severe pain in the last 24 hours via the VAS, a measurement instrument for pain (0–10; 0 = no pain, 10 = worst severe pain).

A Persian validated version of the Disabilities of Arm, Shoulder, and Hand quick questionnaire (Quick DASH), consisting of 11 items from the original 30-item DASH, was completed by patients before and after therapy in every evaluation session [25].

Statistical Analysis

Data were entered and analyzed by SPSS. P values <0.05 were considered significant.

The Kolmogorov-Smirnov test revealed normal distribution of data. To compare the demographic data between the two groups, the Fisher exact test and t test were used. Differences between the two groups at baseline and at four and eight weeks were tested by unpaired Student t tests. Paired t tests were used for within-group analyses. Intention-to-treat (ITT) analysis with a last observation carried forward (LOCF) procedure was performed.

Results

Of 53 assessed patients, 33 met eligibility and agreed to participate in the study. These 33 patients were randomized to two intervention groups. During the trial, two patients from the prolotherapy group and one patient from the shock wave group dropped out of the study. The mean age of patients (range) was 46.94 ± 8.3 (29–68) years, and 23 (69.6%) participants were female. In 24 patients (72.7%), the dominant hand was affected. No significant differences were identified between demographic and clinical characteristic of the two groups (Table 1). Within-group analysis showed that in both the shock wave group and the prolotherapy group, differences between all the outcome measures (VAS, grip strength, PPT, and Quick DASH score) were significant after four and also eight weeks (Table 2).

Between-group analysis showed that after four and eight weeks of follow-up, the VAS ($P = 0.01$ and $P = 0.008$, respectively) and Quick DASH ($P = 0.003$ and $P = 0.009$, respectively) had significantly more improvement in the shock wave group. However, significant differences were not observed between the two groups with respect to grip strength ($P = 0.94$ and $P = 0.77$, respectively) and PPT ($P = 0.14$ and $P = 0.08$, respectively). No noticeable adverse effects of the treatment were reported in either group.

Discussion

Prolotherapy is the injection of an irritant material that triggers the inflammatory cascade, fibroblast hyperplasia, and collagen synthesis, leading to strengthening of the ligaments and tendons [26]. Similarly, an optimal dose of shock wave stimulates cell proliferation and induces the healing process [19].

Previous studies have shown efficacy of prolotherapy in the treatment of tendinopathies other than CLE [8,9]. Recent studies also have confirmed ESWT as an effective therapy in rotator cuff calcified tendinitis and plantar fasciitis [27–29]. However, few studies have assessed the efficacy of prolotherapy on CLE [10–12], and studies about the benefit of ESWT in treatment of CLE are contradictory [17–22].

In the present single-blind randomized clinical trial, although both groups showed significant improvements in VAS, grip strength, PPT, and Quick DASH score during the eight-week trial, patients in the shock wave group had significantly greater improvement in VAS and Quick DASH scores. Similar to this study, the therapeutic effect of prolotherapy on CLE has been shown by previous clinical trials. The therapeutic benefit of three sessions of prolotherapy with monthly intervals (dextrose 50% injection) over placebo (0.9% saline injection) on VAS and grip strength of 24 randomized patients with CLE was shown by Scarpone et al. in a clinical trial [12]. In another randomized clinical trial [10], 17 patients with CLE were randomized to receive two monthly sessions of either prolotherapy (eight patients) or corticosteroid (nine patients). The authors concluded that although evaluation of patients three and six months after intervention showed no significant differences between the two groups in terms of VAS, Quick DASH, or grip strength scores, the small sample size precluded determining whether one therapy was superior to the other. A three-arm randomized clinical trial on 32 patients with CLE [11] revealed that patients receiving prolotherapy with dextrose and prolotherapy with dextrose-morrhuate had better results compared with controls (wait and see) in terms of Patient-Rated Tennis Elbow Evaluation (PRTEE) questionnaire scores during 32 weeks of follow-up. Patients in the prolotherapy group with dextrose showed greater grip strength compared with the other two groups.

Data about the therapeutic effect of ESWT over sham treatment in patients with CLE are conflicting [17–22]. Some previous studies concluded that ESWT is significantly more effective than placebo in the treatment of CLE [17–19], contrary to other studies [20–22].

Two randomized controlled trials that compared three sessions of ESWT with steroids demonstrated benefit of steroids over ESWT at follow-up [13,15]. Haru Multu et al. [15] compared three sessions (weekly) of ESWT and steroid injection in CLE patients. After a long follow-up (seven to 40 months), they concluded that both ESWT and steroids can be successfully used for treatment of tennis elbow. However, steroid injection has better results in pain reduction, improvement of function, and patient satisfaction. In another randomized controlled trial on 93 patients with CLE, the treatment group received three sessions (weekly) of ESWT and the control group

Table 1. Baseline characteristics of the SW and PrT groups

	SW (n = 16)	PrT (n = 17)	*P* Value
Age	47.25	46.65	0.83*
Duration of pain, mean (SE), mo	4.13 (0.37)	6.82 (1.39)	0.07*
Gender	75% female	64.7% female	0.70†
Dominant hand	100% right-handed	94.1% right-handed	1†
Affected hand	81.3% right	64.7% right	0.43†
VAS, mean (SE)	6.13 (0.32)	7.35 (0.47)	0.06*
Grip strength, mean (SE)	7.28 (0.52)	7.02 (0.64)	0.74*
Pressure pain threshold, mean (SE)	2.26 (0.10)	2.13 (0.12)	0.38*
Quick DASH, mean (SE)	41.84 (3.04)	47.82 (4.78)	0.25*

PrT = prolotherapy; Quick DASH = Disabilities of the Arm, Shoulder, and Hand quick questionnaire; SW = shock wave; VAS = visual analog scale.
*Independent-samples *t* test.
†Fisher exact test.

Table 2. Outcomes at 4 and 8 weeks after treatment with SW and PrT

		VAS	Grip Strength	Pressure Pain Threshold	Quick DASH
SW	4 wk mean (SE)	3.19 (0.50)	8.31 (0.49)	2.64 (0.11)	22.25 (3.57)
	8 wk mean (SE)	2.60 (0.40)	8.36 (0.50)	2.71 (0.13)	23.13 (3.20)
	P value* (baseline vs 4 wk)	0.00	0.002	0.001	0.00
	P value* (baseline vs 8 wk)	0.00	0.001	0.001	0.00
PrT	4 wk mean (SE)	5.71 (0.50)	8.02 (0.64)	2.34 (0.14)	39.67 (4.30)
	8 wk mean (SE)	5.47 (0.53)	8.00 (0.64)	2.35 (0.14)	37.39 (4.40)
	P value* (baseline vs 4 wk)	0.00	0.006	0.008	0.00
	P value* (baseline vs 8 wk)	0.001	0.007	0.008	0.00

*Paired-samples *t* test.
PrT = prolotherapy; Quick DASH = Disabilities of the Arm, Shoulder, and Hand quick questionnaire; SW = shock wave; VAS = visual analog scale.

received an injection of 20 mg of triamcinolone. In this study, patients in both groups showed significant improvement, while steroids had a better result of ~50% reduction in pain. However, due to the considerable number of dropsout in the steroid group after randomization, the interpretation of the results of this study is difficult [13]. A recent nonrandomized and noncontrolled study showed a benefit of three sessions of ESWT with a monthly interval in three major tendon diseases, calcific tendonitis of the shoulder (129 patients), chronic Achilles tendinopathy (102 patients), and lateral epicondylitis of the elbow (80 patients) during one year of follow-up [30]. Different protocols employed in previous studies, especially in terms of intensity of ESWT, may be one reason for the contradictory results [20,21]. To the best of our knowledge, this is the first study comparing prolotherapy with shock wave therapy. In this study, the VAS and Quick DASH questionnaire showed shock wave therapy to be significantly more effective.

However, our study showed no differences between the two groups in objective items (PPT and grip strength). The inhibitory effect of ESWT on nociceptors and a hyperstimulation mechanism of action besides its effect on the healing process may partially explain the greater effect of ESWT on pain reduction. Although the local anesthesia (lidocaine) before injection was administered subcutaneusely in this study, it might have affected our results as a toxic effect of lidicaine on tenocytes has been shown recently [31]. A single session of prolotherapy vs three sessions of ESWT could also be a cause of differences between the ESWT and prolotherapy groups in this study. The small sample size and short period of follow-up are the main limitations of this study; therefore, further studies with more injections, larger sample sizes, and longer duration of follow-up are needed.

References

1. Leadbetter W. Soft tissue athletic injuries. In: Fu FH, Stone DA, eds. Sports Injuries: Mechanisms, Prevention, Treatment. Baltimore: Williams & Wilkins; 1994:733–80.
2. Silverstein B, Viikari-Juntura E, Kalat J. Use of a prevention index to identify industries at high risk for work-related musculoskeletal disorders of the neck, back, and upper extremity in Washington state, 1990–1998. Am J Ind Med 2002;41(3):149–69.
3. Kraushaar BS, Nirschl RP. Tendinosis of the elbow (tennis elbow): clinical features and findings of histological, immunohistochemical, and electron microscopy studies. J Bone Joint Surg Am 1999;81 (2):259–78.
4. Hudak PL, Cole DC, Haines AT. Understanding prognosis to improve rehabilitation: The example of lateral elbow pain. Arch Phys Med Rehabil 1996;77 (6):586–93.

5. Jobe FW, Ciccotti MG. Lateral and medial epicondylitis of the elbow. J Am Acad Orthop Surg 1994;2 (1):1–8.
6. Smidt N, van der Windt DAWM, Assendelft WJJ, et al. Corticosteroid injections, physiotherapy, or a wait-and-see policy for lateral epicondylitis: A randomised controlled trial. Lancet 2002;359 (9307):657–62.
7. Rabago D, Best TM, Beamsley M, Patterson J. A systematic review of prolotherapy for chronic musculoskeletal pain. Clin J Sport Med 2005;5:376–80.
8. Maxwell NJ, Ryan MB, Taunton JE, Gillies JH, Wong AD. Sonographically guided intratendinous injection of hyperosmolar dextrose to treat chronic tendinosis of the Achilles tendon: A pilot study. Am J Roentgenol 2007;189(4):W215–20.
9. Topol GA, Reeves KD, Hassanein KM. Efficacy of dextrose prolotherapy in elite male kicking-sport athletes with chronic groin pain. Arch Phys Med Rehabil 2005;86(4):697–702.
10. Carayannopoulos A, Borg-Stein J, Sokolof J, Meleger A, Rosenberg D. Prolotherapy versus corticosteroid injections for the treatment of lateral epicondylosis: A randomized controlled trial. PM R 2011;3 (8):706–15.
11. Rabago D, Lee KS, Ryan M, et al. Hypertonic dextrose and morrhuate sodium injections (prolotherapy) for lateral epicondylosis (tennis elbow): Results of a single-blind, pilot-level, randomized controlled trial. Am J Phys Med Rehabil 2013;92:587–96.
12. Scarpone M, Rabago DP, Zgierska A, Arbogast G, Snell E. The efficacy of prolotherapy for lateral epicondylosis: A pilot study. Clin J Sport Med 2008;18 (3):248–54.
13. Crowther MA, Bannister GC, Huma H, Rooker GD. A prospective, randomised study to compare extracorporeal shock-wave therapy and injection of steroid for the treatment of tennis elbow. J Bone Joint Surg Br 2002;84(5):678–9.
14. Haupt G. Review article: Use of extracorporeal shock waves in the treatment of pseudarthrosis, tendinopathy and other orthopaedic diseases. J Urol 1997;158 (1):4–11.
15. Mutlu H, Mutlu S, Ozkazanli G, Fidan F, Kilic M. Treatment of lateral epicondylitis: Steroid injection versus extra-corporeal shock wave therapy. JAREM 2014;4(2):58–61.
16. Visco V, Vulpiani MC, Torrisi MR, et al. Experimental studies on the biological effects of extra corporeal shock wave therapy on tendon models. A review of the literature. Muscles Ligaments Tendons J 2014;4:357–61.
17. Pettrone F, McCall B. Extracorporeal shock wave therapy without local anaesthesia for chronic lateral epicondylitis. J Bone Joint Surg Am 2005;87: 1297–304.
18. Rompe JD, Hope C, Küllmer K, Heine J, Bürger R. Analgesic effect of extra corporeal shock wave therapy on chronic tennis elbow. J Bone Joint Surg Br 1996;78(2):233–7.
19. Spacca G, Necozione S, Cacchio A. Radial shock wave therapy for lateral epicondylitis: A prospective randomised controlled single-blind study. Eura Medicophys 2005;41:17–25.
20. Haake M, König IR, Decker T, et al. Extracorporeal shock wave therapy in the treatment of lateral epicondylitis: A randomized multicenter trial. J Bone Joint Surg Am 2002;84(11):1982–91.
21. Speed CA, Nichols D, Richards C, et al. Extracorporeal shock wave therapy for lateral epicondylitis—a double blind randomised controlled trial. J Orthop Res 2002;20(5):895–8.
22. Capan N, Esmaeilzadeh S, Oral A, et al. Radial extracorporeal shock wave therapy is not more effective than placebo in the management of lateral epicondylitis: a double-blind, randomized, placebo-controlled trial. Am J Phys Med Rehabil 2016;95(7):495–506.
23. Mathiowetz V, Weber K, Volland G, Kashman N. Reliability and validity of grip and pinch strength evaluations. J Hand Surg Am 1984;9(2):222–6.
24. Fischer AA. Algometry in diagnosis of musculoskeletal pain and evaluation of treatment outcome: An update. J Musculoske Pain 1998;6(1):5–32.
25. Ebrahimzadeh MH, Moradi A, Vahedi E, Kachooei AR, Birjandinejad A. Validity and reliability of the Persian version of shortened Disabilities of the Arm, Shoulder and Hand questionnaire (quick-DASH). Int J Prev Med 2015;6:59.
26. Maynard JA, Pedrini VA, Pedrini-Mille A, Romanus B, Ohlerking F. Morphological and biochemical effects of sodium morrhuate on tendons. J Orthop Res 1985;3(2):236–48.
27. Speed CA. Extracorporeal shock-wave therapy in the management of chronic soft-tissue conditions. J Bone Joint Surg Br 2004;86(2):165–71.
28. Lou J, Wang S, Liu S, Xing G. Effectiveness of extracorporeal shock wave therapy without local anesthesia in patients with recalcitrant plantar fasciitis: A meta-analysis of randomized controlled trials. Am J Phys Med Rehabil 2017;96(8):529–34.
29. Eslamian F, Shakouri SK, Jahanjoo F, Hajialiloo M, Notghi F. Extracorporeal shock wave therapy versus local corticosteroid injection in the treatment of chronic plantar fasciitis, a single blinded randomized clinical trial. Pain Med 2016;17(9):1722–31.
30. Carulli C, Tonelli F, Innocenti M, et al. Effectiveness of extracorporeal shockwave therapy in three major tendon diseases. J Orthop Traumatol 2016;17 (1):15–20.
31. Piper SL, Laron D, Manzano G, et al. Effects of lidocaine on torn rotator cuff tendons. J Orthop Res 2016;34:1620–7.