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Original Research Paper

Health Science

EFFICACY OF ESWT AND NUTRACEUTICAL SUPPLEMENTATION VS ESWT-ONLY IN THE TREATMENT OF CHRONIC LATERAL EPICONDYLITIS: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Introduction: Tendinopathy is common in professional athletes as well as in sedentary people. It occurs 30% -50% of all sports related injuries. Injection of autologous blood has been reported beneficial for the treatment of tendinopathy. It is hypothesized that transforming growth factor- and basic fibroblast growth factor carried in the blood will act as humoral mediators to induce the healing cascade. Musculoskeletal ultrasound can document the pathology prior to the injection and accurately identify the site for injection. It also helps in monitoring tendon healing. **Materials And Methods:** This randomized controlled trial was carried out after obtaining permission from Research EthicsBoard between September 2023 to August 2024 in the Department of Physical Medicine and Rehabilitation (PMR), IGM Hospital, Agartala. A total of 30 patients with lateral epicondylitiswere included in this study using block of four randomization technique. The independent variable considered were age, sex, occupation, duration and side of affection. The intervention group received ESWT and nutraceutical supplementation whereas the control group received ESWT only. **Results And Observations:** Out of 30 patients recruited, 18 patients were female (60%) and 12 were males (40%). The intervention group consisted of 8 females and 7 males with a mean age group of 47.20±10.06 years while the control group consisted of 10 females and 5 males with a mean age group of 46.20±8.79 years. There was significant improvement in VAS and PRTEE score in ESWT and nutraceutical supplementation group compared to control group in 6 months follow up. There were also significant improvement in neovascular, echotexture grading and tendon size in ESWT and nutraceutical supplementation group compared to the control group in 6 months follow-up. **Conclusion:** The study showed that ESWT and nutraceutical supplementation is significantly more effective in reducing pain and disability in resistant lateral epicondylitis at 6 months as compared to ESWT only. This study also confirmed that there was significant improvement of ultrasound parameters in ESWT and nutraceutical supplementation group compared to ESWT only group and may be considered as an alternative to surgery in resistant lateral epicondylits.

KEYWORDS : Tendinopathy, Lateral epicondylitis, Extracorporeal shock wave therapy(ESWT) Patient Rated Tennis Elbow Evaluation (PRTEE), Musculoskeletal ultrasonography.

INTRODUCTION

Tendon pain is common in professional athletes as well as in sedentary people. It occurs 30% -50% of all sports related injuries.[1]Tendinopathy (often called tendonitis or tendinosis) is the most common tendon disorder. It is characterized by activity related pain, focal tenderness and decreased range of movement in the affected area. Tendinopathy can occur in any tendon. Tendinopathy is not characterized by an inflammatory response but rather infiltration of fibroblasts and vessels ensuing chronic cycle of tendon degeneration and repair resulting in a weakened tendon.[2]Lateral epicondylitis also known as the tennis elbow is a term used to describe myriad of symptoms around the lateral aspect of the elbow which occurs more frequently in nonathletes than athletes.[3] The disorder arises as a result of repetitive movements of the involved muscles particularly in the working age group. The disease imparts significant disability in terms of the quantity and quality of work done. Tennis elbow may also cause significant weakness of grip strength particularly with the elbow in extension.[4]Incidence of injury has been reported in various forms. For instance, in club gymnastics injury rates vary between 2 to 4 and 39.9 per 100 school children per year.[5]The peak incidence is in the early fifth decade and a nearly equal gender incidence is seen.[6]The pathology of lateral epicondylitis results from overuse of the extensor muscles leading to degenerative pathology of the involved tendons.[7] Although it is known as a tendonitis, histopathologic studies have shown that it is associated with few inflammatory cells but more associated with hypertrophy of fibroblasts, abundant disorganized collagen, hyperplasia of vascular elements, apoptosis and extracellular matrix breakdown.[8]

The diagnosis of tennis elbow is usually made clinically by localizing discomfort at the origin of the extensor carpi radialis brevis. Tenderness is present over the lateral epicondyle approximately 5 mm distal and anterior to the midpoint of the lateral epicondyle. Pain usually is exacerbated by dorsiflexion of wrist against resistance and forearm supination and on grasping objects.[3]Resistant lateral epicondylitis will be diagnosed if there is persistent pain and tenderness on or near lateral epicondyle despite all conservative treatments spanning for a minimum period of 6 months along with 2 of 3 pain provocative tests- gripping, Cozen's test and Mill's manoeuvre.[9] Numerous different methods have been proposed to treat tendinopathy, such as eccentric training, the injection of corticosteroids and sclerosants, prolotherapy, extracorporeal shockwave therapy and glyceryltrinitrate patches[10]. Corticosteroid injection has been shown to provide short term relief but relapse rates are high.Recent literature suggests that corticosteroid injections may actually have deleterious effects after their short-term pain relief.[11]Currently, eccentric training is the first choice of treatment of most practitioners, although the methodological quality of the studies suggesting efficacy has recently been questioned.[12,13]

It has been demonstrated that ESWT is effective for tendinopathy, leading to a success rate ranging from 55–90%. In particular, recovery is achieved in 83% of calcific tendonitis of the shoulder, 55% of sub-acromial impingements, 76% of epicondylitis, 74% of plantar fasciitis, 90% of pertrochanteric bursitis, 82% of Achilles tendinopathy, and 86% of patellar tendinopathy .[14]

ESWT stimulates soft-tissue healing through inhibition of afferent pain-receptor function, down regulation of expression of inflammatory cytokines, improvement of cellular proliferation, synthesis of extracellular matrix, and enhanced angiogenesis.

Recently several clinical studies have demonstrated that exogenous supplementation with micronutrients can facilitate recovery of tendinopathies.[15–17] The main substances essential for tendon healing include arginine, polyphenols (Vinitrox™ Bio Serae Laboratories SAS, Bram, France), collagen, methyl-sulfonyl-methane (MSM), vitamin C, and bromelain.[18]

The goal of this study was to assess the effects of our synergistic therapy using clinical and functional recovery indexes to assess patients affected by lateral elbow tendinopathy.

AIMS AND OBJECTS

1. To study the efficacy of ESWT and nutraceutical supplementation vs ESWT-only in the treatment of lateral epicondylitis
2. To assess the tendon healing by musculoskeletal ultrasonography after the procedure.

MATERIAL AND METHODS

This randomized controlled trial was carried out after obtaining permission from Research EthicsBoard between September 2023 to August 2024in the Department of Physical Medicine and Rehabilitation (PMR), IGM Hospital, Agartala. A total of 30 patients with lateral epicondylitiswere included in this study using block of four randomization technique.

Inclusion Criteria:

- Tendinopathy more than 6 months
- Ultrasound features of tendinopathy
- Pain severity with minimum score of ≥5 based on 10 scale VAS (Visual Analogue Scale)
- Willingness to comply with the treatment and follow-up assessments

Exclusion Criteria:

- Prior tendon rupture or surgery
- History of steroid injection in last 6 weeks
- History of any malignancy
- Systemic illnesses including ischemic heart disease, diabetes, rheumatoid arthritis, hepatitis
- Any fracture, bony malformation, articular lesions at elbow
- Patients who showed contra-indications to ESWT (Pacemaker, pregnancy, systemic or in-situ neoplasia, local infection, history of epilepsy, severe coagulopathies)

Procedure

Patient's baseline complete haemogram and musculoskeletal ultrasonography of the affected elbow was taken before the intervention.

1. For each condition, the patients were sub-dividedinto a control group, treated with ESWT, and an experimental group, treated with a combination of ESWT and the dietary supplement (DS). Dietary Supplement (DS) containing methylsulfonylmethane (MSM), hydrolyzed swine collagen(Type I and Type II), L-arginine and L -lysine, vitamin C, Condroitin Sulfate, Glucosamine, Curcuma longa extracted toobtain curcuminoids, dry Boswellia serrata extracted to obtainacetyl-11-keto-b-boswellic acid (AKBA). The diet-ary supplement was consumed twice a day for 1 month,then once a day for an additional month. We advised patients to take the dietary supplement at roughly the same time every day on an empty stomach in order to increase its bioavailability. VAS was selected to measure the perceived pain intensity, by asking the patient to report a value between 0–10 cm along a horizontal line (10 ¼ severe pain;0 ¼ no pain). A two-centimetre change was considered clinic-ally relevant6 . The PRTEE, formerly known as the Patient-Rated Forearm Evaluation Questionnaire (PRFEQ), is a 15-item questionnaire designed to measure forearm pain and disability in patients with lateral epicondylitis. It consists of two subscales (pain and function). The sensitivity and specificity values associated with the PRTEE were 0.94 (95% CI=0.83–0.98) and 0.78 (95% CI=0.58–0.91) respectively.[19]All 30 patients were subjected to one cycle of three high-energy Extracorporeal Shock Wave Therapy sessions, per-formed once a week for three consecutive weeks, with1,700–2,000 shocks applied with a flux energy density of0.12–0.35- mJ/mm 2 using a Storz Medical Duolith SD1a machine.

Insert Figure No 1 And 2 Here

Outcome variables were measured at baseline (i.ebefore intervention) and follow up assessment were done at 2weeks, 3 months and 6 months after the injection. But ultra sonography examination was carried out at baseline, 3 months and 6 months follow-up.

The outcome measures considered in this study were
1. Visual Analogue Scale (VAS)
2. Patient Rated Tennis Elbow Evaluation (PRTEE)
3. Ultrasnographic assessments

2. Visual Analogue Scale (VAS)[20]for pain is a 100 cm horizontal line on which the patient's pain intensity is represented by a point between the extremes of "no pain at all" and "worst pain imaginable". The patient marks on the line the point that they feel represents their perception of their current state. The VAS score is determined by measuring in centimeters from the left hand end of the line to the point that the patient marks.

3. Patient Rated Tennis Elbow Evaluation (PRTEE)[21]**:-** The PRTEE, formerly known as the Patient-Rated Forearm Evaluation Questionnaire (PRFEQ), is a 15-item questionnaire designed to measure forearm pain and disability in patients with lateral epicondylitis. It consists of two subscales (pain and function). The sensitivity and specificity values associated with the PRTEE were 0.94 (95% CI=0.83–0.98) and 0.78 (95% CI=0.58–0.91) respectively.[21]

4. Sonographicassessment[22]

I. Echotexture grading scale
0 Normal
1a Hypoechogenicity less than one third of the tendon
1b Hypoechogenicity in between one third to two third of the tendon
1c Hypoechogenicity in more than two third of the tendon
2 Partial thickness tear
3 Full thickness tear

II. Neovascularization grading scale-
0 No neovascularization
1 Neovessels on the tendon surface
2 1 or 2 intratendinousneovessels
3 3 or more intratendinousneovessels

III. Tendon size- In milimeter.

IV. Calcification-

Insert image no 3, 4, and 5 here

Statistical analysis:

Data were collected in a pre-tested proforma. Analysis was done using Statistical Package for the Social Sciences, SPSS 21 version. For descriptive statistics, mean and standard deviation was used. For continuous variable Student's t-test was used. Chi-square and Fisher' exact test were used for categorical variables. P-value < 0.05 was taken as statistically significant.

RESULTS

Table 1 shows the baseline characteristics of the study participants. 18 patients were females which constituted 60% of total patients and 12 were males constituting 40% of total sample size. The ESWT and nutraceutical supplementation group consisted of 8 females and 7 males with a mean age group of 47.20±10.06 years while the control group (ESWT only group) consisted of 10 females and 5 males with a mean age group of 46.20±8.79 years. The baseline characteristics of

both the groups were shown in Table1 and showed no statistically significant difference in both the groups. As far the side of involvement is concerned, majority of patients in both the groups had right sided involvement. The mean duration of symptoms in ESWT and nutraceutical supplementation group was 8.47±2.31 months and where as in the ESWT-only group it was 7.81±2.93 months.

Inset Table No 1 Here

Table 2 shows the mean improvement of VAS score which was found to be statistically significant ($p<0.05$) in the ESWT plus nutraceutical and ESWT only groups. At 2 weeks and 3 months follow-up, ESWT only group showed more improvement compared to the group receiving ESWT plus nutraceutical. But at 6 months follow-up, ESWT plus nutraceutical group showed more improvement of VAS score compared to the ESWT-only group and which was statistically significant ($p<0.001$).

Insert table no 2 here

Table 3 shows the mean improvement of PRTEE score which was found to be statistically significant in both the groups at 2 weeks and 6 months follow-up. But ESWT plus nutraceutical group showed more improvement of PRTEE score compared to the ESWT-only group at 6 months follow-up ($p<0.001$).

Insert table no 3 here

Table 4 shows echotexture improvement in both the group having normal echotexture pattern that is grade 0 at the end of three months follow-up however the group receiving ESWT-only group showed more improvement compared to the group receiving ABI in terms of echotexture grading improvement ($p<0.001$). But at the end of 6 month improvement in term of normal echotexture grading pattern was more significant in the group receiving ESWT plus nutraceutical as compared to the group receiving ESWT-only ($p=0.000$).

Insert table no 4 here

Table 5 shows that there were improvement in terms of neovascularization in both the groups at 3 month and 6 month follow-up but at the end of 6 month ESWT plus nutraceutical group showed more improvement compared with the group receiving ESWT-only with nostatistical significance ($p>0.05$)

Insert table no 5 here

Table 6 shows that the mean reduction in tendon size were found to be statistically significant ($p<0.05$) in both the ESWT plus nutraceutical and ESWT-only group. But ESWT plus nutraceutical group showed more improvement at 6 month compared to the ESWT-only group.

Insert Table No 6 Here

DISCUSSION

Tennis elbow is a common tendinopathy that can be quite resistant to treatment and often affect the daily activities of the people. Many conservative treatment strategies have been used in treatment of lateral epicondylitis as first line but the treatment response is often inadequate. Conservative management like activity restrictions, orthotics and splints, NSAIDs, physical modalities has been tried. A recent Cochrane review[23]concluded that steroid injection has only short term effect and has poor outcome in long term.Surgical treatment remains a last option and many a times it involves considerable cost, morbidity and complications. Most of the people refuse to opt for surgical treatment because of fear and ignorance. Thus there is a question for effective alternative conservative therapies. Growth factors have shown promising results in field of tendon injury and repair. These are usually given in form of whole blood, platelet rich plasma or bone marrow aspirate injection. According to recent report by Jindal et al, autologous blood injection showed marked improvement in patients with chronic refractory lateral epicondylitis.[24]

ESWT, initially introduced for the treatment of nephroli-thiasis, has become a viable option for the treatment ofdifferent soft-tissue disorders8 such as calcific tendinopathyof the rotator cuff, lateral elbow tendinopathy, and inser-tional Achilles tendinopathy. ESWT modifies cell membraneand cytoplasm organelles, resulting in nucleus stimulation.All of these changes lead to synthesis of proteins, nitricoxide (NO), and specific growth factors (GF) which activateseveral biological processes.[25] Erroi et al. demonstratedthat both ESWT and platelet-rich plasma (PRP) injectionsare effective in the treatment of insertional Achilles ten-dinopathy in people who participate in sports. PRP is aconcentrate of platelet-rich plasma protein derived fromthe patient's own blood containing growth factors, withhealing, regeneration, and anti-inflammatory effects21–23 .Lee et al. have reported optimal outcomes after ESWTin the treatment of chronic refractory Achillestendinopathy.Frassanito et al.[26] stated that a treatment of kinesio tap-ing, followed by ESWT, can be an effective treatment inpatients affected by calcific shoulder tendinopathy. Kinesiotaping indeed can be considered an adjuvant therapy, whichimproves the regenerative effects of ESWT.Li et al have demonstrated the effectiveness of ESWT inshoulder pain relief in patients affected by chronic rotatorcuff tendinopathy.Moreover, Vulpiani et al.[27]showed that ESWT had betterclinical outcomes at 6 and 12 months follow-up when compared to Cryo-US in the treatment of symptomaticchronic lateral epicondylitis.

A more recent retrospective study, conducted by Chouet al.[28] underlined the effectiveness of performing ESWT inthe management of chronic rotator cuff tendinitis or partialtears of the rotator cuff before undergoing surgery. Theycompared two groups of patients, an athletic group and anon-athletic group, and observed a faster recovery with arate of satisfaction greater than 50% in both groups.

Gumina et al[29] demonstrated that an oral supplement containing methylsulfonylmethane, arginine L-alpha-ketoglu-tarate, hydrolyzed type I collagen bromelain, and grape juice(Tenosan), could reduce shoulder pain and improve healingof large rotator cuff tears after arthroscopic repair.Merolla et al.[30]used a dietary supplement containing Boswellia serrata and Curcumalonga (Tendisulfur, LaborestSpA, Nerviano, Italy), which showed short-termeffectiveness in post-operatively reducing pain after rotatorcuff tear repair surgery.Notarnicola et al.[6]evaluated the efficacy of combinedtreatment with ESWT and arginine supplementation inpatients with Achilles tendinopathy, observing an improve-ment of the therapeutic response. Another interesting study was conducted by Baliuset al.[31]who evaluated the effects of an oral supplement composed by mucopolysaccharides, type I collagen, and vita-min C in the treatment of Achilles tendinopathy. Their resultsshow that the combination of the aforementioned supple-ment and either eccentric training or passive stretching pro-vides further benefits compared to physical therapy alone.Considering the wide consensus of ESWT in the literature,we believe that ESWT represents the best physical therapy toprovide an effective recovery for tendinopathies, andTendisulfur Forte may be useful in reducing inflammation andthe possibility of recurrence because of its key features.Indeed, shock wave therapy increases bioavailability of thesupplement to the tendon tissue6, due to the neo-angiogenicproperties of ESWT[32,33]. To confirm the positive effect of theassociation of Tendisulfur Forte and ESWT, our study showedthat patients in the Tendisulfur Forte group reduced their useof NSAIDs during the 2 months of treatment when comparedto the control group. Moreover, we observed a greaterdecrease of pain in the Tendisulfur Forte group and an improvement of tendon healing after 30 days of treatment.We report no side-ffects in all patients treated with nutraceutical supplement.

The present study reveals that mean age of the study

population group were 47.20±10.06 years in ABI group and 46.20±8.79 years in steroid group. In a study conducted by Jindal et al[24], the mean age of study group were 37.32±7.52 years in ABI group and 39.04±6.67 years in steroid group. Lateral epicondylitis is most commonly seen in working population because this condition is basically an overuse syndrome.

In present study, housewives constituted 50% and manual labourers constituted 16.66% of total patients. In a study conducted by Gani N et al[14], 71 % of total females were housewives and 77% of total males were manual labourers. This could be explained by the repeated microtrauma to extensor carpi radialisbrevis due to overuse of this muscle in activities involving repetitive manual works.

The mean duration of symptoms in ESWT and nutraceutical supplementation group was 8.38±2.35 months where as in ESWT only group it was 7.72±2.11 months. Bostan B et al[34] also found in their study that mean duration of the symptoms was 8.4 months. The subjects selected for this study were resistant cases who had already been tried with conservative management and have not improved symptoms for at least six months.

The ESWT and nutraceutical supplementation group consisted of 8 females and 7 males whereas steroid group consisted of 10 females and 5 males. It was found that females were more commonly affected than males as in previous studies. This higher incidence in females may be explained by the type of household activities where repeated supination and pronation is required.

Majority of patients in both the groups had right sided involvement which was their dominant side. In the study conducted by Jindal et al[24], who also compared autologousblood injection and steroid injection in patient suffering from chronic lateral epicondylitis, they found similar findings about the laterality of this condition. Majority of their patients had right sided dominant hand involvement. These findings explain the theory of overuse injury as the pathogenesis of lateral epicondylitis.

In the present study , there was significant improvement in the mean of VAS score in both the groups at 2 weeks, 3 months and 6 months follow up ($p<0.05$).

In ESWT and nutraceutical supplementation group, the mean VAS score improved from 6.24±0.72 to 4.45±1.04 at 2 weeks and further improved to 3.18±1.18 and 1.49±0.51 at 3 months and 6 months follow up respectively($p<0.05$).

Arik HO et al[28] also found that there was significant improvement of VAS score in both the ABI and steroid groups at 15, 30, 90 and 180 days follow-up but ABI group showed more significant improvement of VAS score at 90 and 180 days follow-up compared to the steroid group. The finding was also in concordance with the present study.

There was improvement of PRTEE scores in both ESWT and nutraceutical supplementation and ESWT only groups at 2 weeks and 6 months follow-up. The control group showed more significant improvement in PRTEE score compared to ESWT and nutraceutical supplementation group ($p<0.05$) at the end of 2 weeks follow up, even though both the groups had significant reduction in the score. However ESWT and nutraceutical supplementation group showed more significant improvement in PRTEE score when compared to the steroid group at the end of 6 month follow-up ($p<0.01$).

There was significant improvement of echo-texture grading in ESWT and nutraceutical supplementation group compared to ESWT only group in 3 months and 6 months followup. In a study conducted by Suresh SPS et al[29], they found that hypo-echoic change score decreased from 6.45 points (at baseline) to 3.85 points at 10 months follow-up and this decrease was found to be statistically significant ($p=0.001$). Neo-vascularity score decreased from pre-procedure mean score of 6.10 points to post procedure mean of 3.60 points, at 10 months where the mean decrease score was found to be statistically significant ($p=0.001$).In the present study we could not find any significant improvement in terms of neo-vascularity scores. This probably would be because of our short term follow up till only 6 months and probably long term follow up could have shown changes in terms of nevascularityscore .

There was significant reduction of tendon size in both the groups but size reduction was more in ESWT and nutraceutical supplementation group when compared to the group receiving ESWT only at 6 months follow-up. In ESWT and nutraceutical supplementation group baseline meantendon size was 4.65±1.02 mm which reduced to 3.78±0.75 mm and 3.27±0.62mm at 3 months and 6 months follow-up respectively. On the other hand ESWT only group baseline tendon size was 4.61±0.26 mm which reduced to 3.44±0.50 mm and 3.65±0.51 mm at 3 months and 6 months follow-up respectively. In a study conducted by Gautam VK et al[30], they also found similar reduction in tendon size in ESWT and nutraceutical supplementation group when compared to that of ESWT only group.

Patients who received the ESWT and nutraceutical supplementation and ESWT only did not have any serious adverse effects during or after procedure.

Additionally, there is no consensus about frequency, number of ESWT and nutraceutical supplementation in chronic resistant lateral epicondylitis. However the present study showed significant pain and function improvement. Hence the results of this study may provide insights into effect of ESWT and nutraceutical supplementation in chronic tendinopathies. It may also contribute to identify as one approach for ESWT and nutraceutical supplementation in resistant tennis elbow.

Long term follow up may require for studying the long term effect of ESWT and nutraceutical supplementation.

CONCLUSION

The present study was done to find out the efficacy of ESWT and nutraceutical supplementation in chronic lateral epicondylitis to improve pain and function. The study showed that ESWT and nutraceutical supplementation is significantly more effective in reducing pain and disability in resistant lateral epicondylitis at 6 months as compared to ESWT only. This study also confirmed that there is significant improvement of ultrasound parameters in ESWT and nutraceutical supplementation group compare to ESWT only group and may be considered as a novel alternative for surgery in resistant cases.

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