Comparison of Ozone and Extracorporeal Shockwave Therapy in the Treatment of Chronic Lateral Epicondylitis

Kronik Lateral Epikondilit Tedavisinde Ozon ve Ekstrakorporeal Şok Dalgası Tedavisinin Karşılaştırılması

ABSTRACT

Objective: The aim of the current retrospective study was to compare the effects of ozone injections and Extracorporeal Shockwave Therapy in the alleviation of pain associated with chronic lateral epicondylitis.

Method: A Retrospective Cohort Study was performed, and data was collected from the documented medical records of 89 patients with unilateral chronic lateral epicondylitis. Patients who received local injections of ozone (n=49) and Extracorporeal Shockwave Therapy (n=40) were evaluated. Pain assessment was made by means of Verhaar scores before and after the first injection and the at 1st, 3rd, 6th, and 9th months after treatment. The two groups were compared with respect to baseline demographics including age, gender, dominant and affected sides and Verhaar scores.

Results: Evaluation of pain scores after the treatment showed significant differences between the two groups. Assessment of pain at the 3rd and 9th months after treatment demonstrated that the ozone group had statistically significantly better scores at rest (p<0.001), on compression (p<0.001) and during activity (p<0.001).

Conclusion: Our results demonstrated that ozone injection may be superior over Extracorporeal Shockwave Therapy which is an effective therapeutic option for long-term pain relief in patients with chronic lateral epicondylitis who are refractory to conservative treatment.

Keywords: elbow pain, ESWT, ozone, lateral epicondylitis

ÖZ

Amaç: Çalışmanın amacı, kronik lateral epikondilit (KLE) ile ilişkili ağrıın azaltılmasında ozon enjeksiyonu ile ESWT’nin etkilerini karşılaştırmaktır.

Yöntem: Çalışmamız tek taraflı KLE’li 89 hastanın dökümente edilmiş kayıtları üzerinden bir retrospektif Kohort çalışmasıdır. Lokal olarak ozon uygulanan hastalar ile (n=49) ve ESWT (n=40) uygulanan hastalar değerlendirildi. İlk enjeksiyon öncesi ve sonrasında Verhaar skorları ile tedavi sonrası 1., 3., 6. ve 9. aylarda ağrı değerlendirme yapıldı. İki grubun temel demografik özellikleri (yaş, cinsiyet, basınç taraf, etkilenen taraf) ve Verhaar skorları karşılaştırıldı.

Bulgular: Tedavi sonrası ağrı skorlarının değerlendirilmesi iki grup arasında istatistiksel olarak anlamlı farklılık olduğu görüldü. Tedaviden sonraki 3. ve 9. ayladaki ağrıın değerlendirilmesinde, ozon grubunun istirahatte (p<0,001), kompresyonda (p<0,001) ve aktifte sırasında daha iyi skorlara sahip olduğunu istatistiksel olarak anlamlı bulundu (p<0,001).

Sonuç: Elde ettığimiz sonuçlar, ozon enjeksiyonunun, uzun süreli ağrı hafiflemesinde, konservatif tedaviye yanıt vermeyen KLE hastaları için etkili bir terapötik seçeneğin olan ESWT’den üstün olabileceğini göstermiştir.

Anahtar kelimeler: dirsek ağrısı, ESWT, ozon, lateral epikondilit
INTRODUCTION

Different treatment modalities for lateral epicondyli-
tis have been found to have different degrees of succes-
s[1,2]. Treatment strategies generally include anti-
inflammatory agents, reduction of physical activ-
ity, splints, physical therapy sessions and local corti-
osteroids [3,5]. The most common methods of con-
servative therapy for primary treatment of lateral 
epicondylitis are ozone and extracorporeal shock-
wave therapy (ESWT) and ozone [6-8].

In the literature, studies comparing these two stud-
ies are limited. For this reason, we aimed to conduct 
a retrospective study to evaluate both treatment 
modalities.

Lateral epicondylitis is defined as an inflammatory 
process [9]. We thought that ozone would be benefi-
cial in the treatment of lateral epicondylitis because 
it stimulates the production of free radical scaveng-
ers and enzymes that activate cell wall protectors
and thus show anti-inflammatory action [10].

Although ozone therapy is an invasive procedure in 
local applications, the complication rate is minimal 
[11].

ESWT is a treatment modality that can be preferred 
in patients who are not suitable for surgery as it is 
non-invasive and has minimal complications [12,13].
We compared the efficacy of these two treatment 
modalities that could be applied for similar indica-
tions.

In the literature, studies comparing these two stud-
ies are limited. For this reason, we aimed to conduct 
a retrospective study to evaluate both treatment 
modalities.

The aim of our study was to compare ozone therapy 
to ESWT and to determine whether ozone therapy 
has a place in the treatment of chronic lateral epi-
condylitis (CLE).

MATERIAL and METHODS

Study design

This retrospective study was performed on data 
extracted from the medical files of patients treated 
in the Orthopedics, Hand Surgery and Sports 
Medicine units of two separate hospitals between 
2014 and 2017.

Our series was comprised of 89 cases (61 women, 28 
men) diagnosed with unilateral CLE. Of the 89 
patients included in the study 40 (44.1%) were 
treated with ESWT, while 49 (55.9%) received an 
ozone injection. These patients did not benefit from 
conservative treatment involving restriction of activ-
ity, cold compression and non-steroidal anti-inflam-
matory drugs (NSAIDs) in the preceding three 
months.

Lateral epicondylitis was diagnosed if there was pain 
with palpation of the lateral epicondyle; or painful 
dorsal flexion of the wrist or passive extension of 
forearm extensory muscle and pain with the force 
exerted against the third finger extansory motion, 
during the examination. We did not use imaging 
methods.

Exclusion criteria consisted of any patient with previ-
ous elbow surgery, entrapment of the ulnar nerve, 
systemic or metabolic disease, previous injections 
for CLE, arthritis, effusion of the elbow, any previous 
fractures of the forearm or upper arm, infection or 
trauma involving the lateral epicondylar region, 
bone tumor involving distal humerus and any patient 
with inflammatory or rheumatologic disease. All 
patients had a positive chair test and a positive Mill’s 
test [14].

Outcome measures

The characteristics of each group including the gen-
der, age, dominant and affected sides were recorded. 
Pain at rest, on compression and during activity was 
examined before and after the injection of ozone or 
ESWT at the 3rd, 6th and 9th months. Results were
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categorized as excellent, good, fair, or poor according to modified VERHAAR criteria (pain relief, patient satisfaction, grip strength, the presence of provoked pain on resisted wrist extension). According to the criteria of Verhaar et al., therapeutic outcomes was defined as; ‘excellent’ (no pain, patient content with the treatment result, no subjective loss of grip strength and no pain exacerbated by resisted dorsiflexion of the wrist), ‘good’ (symptoms considerably decreased, patient satisfied with the treatment outcome, occasional mild pain of the lateral epicondyle after heavy activities, no or slight subjective loss of grip power, and no pain aggravated by resisted dorsiflexion of the wrist), ‘fair’ (discomfort on the lateral epicondyle after strenuous activities but more tolerable than before treatment, patient satisfied or moderately satisfied with the outcome of treatment, slight or moderate subjective loss of grip strength, and slight or moderate pain provoked by resisted dorsiflexion of the wrist), or ‘poor’ (no decrease in pain of the lateral epicondyle, patient disappointed with the result of treatment, serious subjective loss of grip strength and severe pain exacerbated by resisted dorsiflexion of the wrist) [15]. Treatment was considered successful when the patient had an excellent or a good score.

ESWT and ozone injection groups were compared in terms of baseline descriptive data and pain scores at different time intervals.

ESWT procedure
ESWT application was performed with the patient sitting with the elbow at 90 degrees and the forearm in the neutral position. The head of the ESWT device was placed at 90 degrees tangential position over the painful area. Protective earmuffs were used by both the patient and the operator to avoid the discomfort of the loud noise of the device. The application area was cleansed with iodine solution and gel was used to enhance the conduction. Local anesthesia was not used with direct application over the painful area [12,16,17]. ESWT (ElettronicaRoland 2, Pagani, Italy) was performed by the same operator as a two-stage procedure. In the first one, energy density was 0,348 mj/cm² (27 kV), frequency 5 Hz, 300 pulses. In the second stage 0,372 mj/cm² (28 kV), 3,5 Hz and 1200 pulses. ESWT was applied 6 times with 3-day intervals. Ice was applied to the area of treatment. Patients were told to apply ice 20 minutes a day, use of NSAIDs were restricted with no limitation of physical activity, exercises were given to strengthen the muscles and pain on movement was evaluated.

Injection technique
Injections were performed at the attachment site of the common extensor tendon on the lateral epicondyle. No additional medications were given, and no restriction of activity was recommended. We used the trigger points for the ozone injection sites with the patient in a supine position on the examination table with his/her elbow in 90° flexion and neutral rotation position. The production of ozone (O₃) from O₂ was made at a concentration of 5 µg/mL. After sterile preparation, ozone was injected subcutaneously using a 30-gauge needle. The patients were treated for a total of eight sessions at three-day intervals with subcutaneous doses of 5-20 µg (according to patient tolerability). The injection procedure of ozone was performed in accordance with the relevant literature [18].

Verhaar clinical evaluation scoring system tests were used for each patient. The verhaar scores of the patients at 3,6 and 9 months after the end of treatment were obtained from the patient files. Patients did not use any surgical or any alternative treatment after the treatment.

Statistical analysis
IBM Statistical Package for Social Sciences Statistics 22 software (SPSS Inc., Chicago, IL, USA) was used to analyze our data. Normality of distribution for variables were tested via Kolmogorov-Smirnov test. Non-parametric tests were utilized for variables without normal distribution. Comparison of two
groups for variables with abnormal distribution were performed with Analysis of variance (ANOVA). Quantitative data was expressed as mean, standard deviation, median, interquartile range as well as minimum and maximum values. Confidence interval was 95% and p value less than 0.05 was considered as statistically significant.

RESULTS

Evaluation of pain scores between the groups, pain scores at rest, on compression and during activity, demonstrated significant differences. Analysis of pain at the 3rd and 9th month after treatment demonstrated that the ozone group had significantly better scores at rest, on compression, and during activity. The mean duration of pain due to CLE was 24.5±12.5 months (range: 12 to 48). The right side was dominant in most cases (83, 93.3%) and CLE was more commonly detected on the dominant (right) side (60, 67.4%). Of the 89 patients, 40 (44.1%) were treated with ESWT, while 49 (55.9%) received ozone injections (Table 1).

Mean ages of the patients in ESWT (n=40) and ozone (n=49) injection groups were similar (46.8±9.5 versus 45.1±8.1; p=0.45). Similarly, the duration of pain and gender distribution were similar in both groups. In both groups, the right side was more likely to be dominant and was more commonly affected by CLE (Table 1).

Table 1. An overview of baseline descriptive and clinical information of our series.

| Variable               | ESWT   | Ozone injection |
|------------------------|--------|-----------------|
| Gender                 |        |                 |
| Women                  | 28 (70%) | 33 (67.3%)    |
| Men                    | 12 (30%) | 16 (32.7%)    |
| Age (years)            | 46.8±9.5  | 45.7±7.05    |
| Dominant side (R/L)    | 37/3    | 46/3           |
| Affected side (R/L)    | 34/6    | 26/23          |
| Duration of pain (months) | 25.6±12.6 | 23.5±12.5 |

Abbreviations: R: right; L: left

Figure 1. Comparison of venhaar score averages of patients in ESWT group “bt: before treatment, at: after treatment, 3th: 3th month, 6th: 6th month, 9th: 9th month”

Figure 2. Comparison of venhaar score averages of patients in ozone group “bt: before treatment, at: after treatment, 3th: 3th month, 6th: 6th month, 9th: 9th month”

There was no difference between the ESWT and ozone groups with respect to the pain scores at rest, on compression and during activity prior to treatment (p>0.05 for all).

Evaluation of pain scores after the treatment showed significant differences between the two groups as for pain scores at rest, on compression, and during activity. Analysis of pain at the 3rd and 9th months after treatment demonstrated that the ozone group had significantly better scores at rest, on compression and during activity (p<0.001). Ozone therapy was superior to ESWT in all except the 6th- month-evaluation (Figure 1, 2).

Table 2-6 demonstrates the comparative scores of pain at rest, on compression and during activity at different time intervals in ESWT and ozone injection groups.
Table 2. Modified Verhaar score (before treatment).

| Time interval | Condition during evaluation of pain | Modified Verhaar score | Treatment group |
|---------------|------------------------------------|------------------------|-----------------|
|               | At rest                            | Excellent 0 0 0 0      | ESWT n, (%)     |
|               | Good                               | 4 (10) 0 4 (8.2)       | Ozone n, (%)    |
|               | Fair                               | 36 (90) 45 (91.8)      |                 |
|               | Poor                               |                        |                 |
|               | On compression                     | Excellent 0 0 0 0      | ESWT n, (%)     |
|               | Good                               | 5 (12.5) 5 (10.2)      | Ozone n, (%)    |
|               | Fair                               | 35 (87.5) 44 (89.8)    |                 |
|               | Poor                               |                        |                 |
|               | During activity                    | Excellent 0 0 0 0      | ESWT n, (%)     |
|               | Good                               | 3 (7.5) 0 0            | Ozone n, (%)    |
|               | Fair                               | 6 (15) 6 (12.2)        |                 |
|               | Poor                               | 31 (77.5) 43 (87.8)    |                 |

Table 3. Modified Verhaar score (Early after treatment).

| Time interval | Condition during evaluation of pain | Modified Verhaar score | Treatment group |
|---------------|------------------------------------|------------------------|-----------------|
|               | At rest                            | Excellent 1 (2.5) 4 (10) 11 (27.5) 24 (60) | ESWT n, (%)     |
|               | Good                               | 25 (51) 14 (28.6) 4 (8.2) 5 (10.2)    | Ozone n, (%)    |
|               | Fair                               | 15 (37.5) 20 (50) 6 (12.2) 5 (10.2)   |                 |
|               | Poor                               |                        |                 |
|               | On compression                     | Excellent 1 (2.5) 4 (10) 15 (37.5) 20 (50) | ESWT n, (%)     |
|               | Good                               | 25 (51) 13 (26.5) 6 (12.2) 5 (10.2)   | Ozone n, (%)    |
|               | Fair                               |                        |                 |
|               | Poor                               |                        |                 |
|               | During activity                    | Excellent 1 (2.5) 4 (10) 19 (47.5) 16 (40) | ESWT n, (%)     |
|               | Good                               | 25 (51) 13 (26.5) 6 (12.2) 5 (10.2)   | Ozone n, (%)    |
|               | Fair                               |                        |                 |
|               | Poor                               |                        |                 |

Table 4. Modified Verhaar score (3rd month after treatment).

| Time interval | Condition during evaluation of pain | Modified Verhaar score | Treatment group |
|---------------|------------------------------------|------------------------|-----------------|
|               | At rest                            | Excellent 0 0 0 0      | ESWT n, (%)     |
|               | Good                               | 7 (17.5) 12 (24.5) 7 (14.3) | Ozone n, (%)    |
|               | Fair                               | 21 (52.5) 11 (22.4) 7 (14.3) |                 |
|               | Poor                               | 12 (30)               |                 |
|               | On compression                     | Excellent 0 0 0 0      | ESWT n, (%)     |
|               | Good                               | 7 (17.5) 13 (26.5) 11 (22.4) | Ozone n, (%)    |
|               | Fair                               | 21 (52.5) 12 (24.4) 7 (14.3) |                 |
|               | Poor                               | 12 (30)               |                 |
|               | During activity                    | Excellent 0 0 0 0      | ESWT n, (%)     |
|               | Good                               | 12 (30) 13 (26.5) 11 (22.4) | Ozone n, (%)    |
|               | Fair                               | 15 (37.5) 13 (22.4) 7 (14.3) |                 |
|               | Poor                               | 13 (32.5) 11 (22.4) 7 (14.3) |                 |

Table 5. Modified Verhaar score (6th month after treatment).

| Time interval | Condition during evaluation of pain | Modified Verhaar score | Treatment group |
|---------------|------------------------------------|------------------------|-----------------|
|               | At rest                            | Excellent 3 (7.5) 17 (42.5) 16 (40) 6 (15) | ESWT n, (%)     |
|               | Good                               | 18 (36.7) 16 (40) 7 (14.3) 6 (15)   | Ozone n, (%)    |
|               | Fair                               | 12 (30) 11 (22.4) 7 (14.3) 6 (15)   |                 |
|               | Poor                               |                        |                 |
|               | On compression                     | Excellent 1 (2.5) 4 (10) 15 (37.5) 6 (15) | ESWT n, (%)     |
|               | Good                               | 18 (36.7) 16 (40) 7 (14.3) 6 (15)   | Ozone n, (%)    |
|               | Fair                               | 12 (30) 11 (22.4) 7 (14.3) 6 (15)   |                 |
|               | Poor                               |                        |                 |
|               | During activity                    | Excellent 1 (2.5) 4 (10) 18 (45) 6 (15) | ESWT n, (%)     |
|               | Good                               | 16 (32.7) 13 (26.5) 9 (18.4) 11 (22.4) | Ozone n, (%)    |
|               | Fair                               |                        |                 |
|               | Poor                               |                        |                 |

Table 6. Modified Verhaar score (9th month after treatment).

| Time interval | Condition during evaluation of pain | Modified Verhaar score | Treatment group |
|---------------|------------------------------------|------------------------|-----------------|
|               | At rest                            | Excellent 3 (7.5) 4 (10) 18 (45) 15 (37.5) | ESWT n, (%)     |
|               | Good                               | 19 (38.8) 10 (20.4) 6 (12.2) 14 (28.6) | Ozone n, (%)    |
|               | Fair                               | 16 (32.7) 10 (20.4) 8 (16.3) 14 (28.6) |                 |
|               | Poor                               |                        |                 |
|               | On compression                     | Excellent 3 (7.5) 4 (10) 14 (35) 15 (50) | ESWT n, (%)     |
|               | Good                               | 16 (32.7) 10 (20.4) 8 (16.3) 15 (30.6) | Ozone n, (%)    |
|               | Fair                               | 9 (18.4) 16 (32.7) 9 (18.4) 15 (30.6) |                 |
|               | Poor                               |                        |                 |
|               | During activity                    | Excellent 3 (7.5) 3 (7.5) 9 (18.4) 15 (30.6) | ESWT n, (%)     |
|               | Good                               | 16 (32.7) 9 (18.4) 9 (18.4) 15 (30.6) | Ozone n, (%)    |
|               | Fair                               |                        |                 |
|               | Poor                               |                        |                 |
Ozone and ESWT groups showed statistically significant (paired-samples T test) pain relief in all groups before, during, and after treatment at the 3rd, 6th, and 9th months.

There was a statistically significant difference between the two treatment groups (ESWT and Ozone), the ozone group was found to be more successful in pain management than the ESWT group at the third and ninth month after treatment. In addition, there was no difference between the ozone and ESWT groups according to the VERHAAR scoring performed at 6 months after the treatment.

**DISCUSSION**

Lateral epicondylitis is a frequent cause of elbow pain which leads to a disruption in the daily life and interrupts work life. There is not a consensus on its treatment. We discuss how the two techniques could be used as alternative treatment options.

As CLE is a common cause of debilitating pain leading to interference with daily activities, the search to find an effective method of pain relief when conservative treatment fails still continues. Conventional conservative treatment for CLE includes among others activity restriction, oral analgesics, bracing, and corticosteroid injections [19].

The objective of the present study was to compare the pain killing effects of ESWT and ozone injections in CLE patients [20,21]. Physical therapy and other conservative treatment measures have also not been able to provide sufficient pain relief. Yang et al. reported pain relief and overall functional improvement with ESWT treatment combined with physical therapy versus physical therapy alone. This could mean that ESWT has an additive effect to physical therapy as well as being an effective form of treatment on its own. It has been found that this favorable effect can last for at least 6 months. Similar effects of ESWT were noted in several previous studies [22-25].

ESWT is proposed to promote tissue healing and hyper stimulation of nerves leading to repair as well as analgesia [26,27].

Another study by Capan et al. found no difference between sham and ESWT treatment for lateral epicondylitis [28]. Some studies found ESWT to be superior to placebo whereas other studies found it to be ineffective [9]. Minimal adverse effects of ESWT were reported making this a safe form of treatment. In our study there was significant improvement in pain at rest, on compression and during activity at the third, 6th and 9th months after treatment with ESWT leading us to believe that this is an effective form of treatment with few side effects as well as having the advantage of being a noninvasive procedure. It is also interesting to note that at the 6th month both ESWT and ozone treatment were found to have similar affectivity on pain which might make ESWT advantageous to ozone in the short-term treatment as it is an noninvasive treatment.

Treatment with ozone on the other hand was found to be more effective compared to ESWT at the post-treatment 3rd and 9th months leading us to believe this may be a more effective treatment especially in the long term. Thus, patients treated with ozone would have longer follow up before needing further treatment. Ozone injections are considered as safe and effective treatment for orthopedic pain [18,29,30] although there are limited studies on its efficacy in CLE.

Provided that correct dosages have been used, ozone can be used as a powerful tool eliciting useful biological cascades, acting as an antioxidant and possibly reversing chronic oxidative stress due to degenerative processes such as those found in degenerative conditions such as CLE. Indeed, the ozone therapy might be able to restore homeostasis and have a healing effect on the tendon itself thus leading to its long-term effectiveness [31].

Promotion of lymphocytes and fibroblasts could lead
to elimination of irritant substances that are causing pain via irritation of ganglia and nerve tissue [27]. Moreover, anti-inflammatory and painkilling actions of ozone may modify the microenvironment leading to improvement of oxygen supply to the tissues [26].

In our study we found that both ESWT and Ozone therapy had alleviating effects on pain caused by CLE. Ozone therapy led to a significantly greater pain relief at the 3rd and the 9th months possibly due to its immunomodulatory, analgesic and anti-inflammatory effects. Although ESWT is also believed to have effects on the tissues itself with beneficial effects on degeneration, ozone seems to work at a more molecular level and has a wider mechanism of action compared to ESWT leading us to believe that this is a superior treatment method for CLE.

Limitations of our study were small sample size, its retrospective design and lack of a control group. Further studies with a longer follow-up period, larger study group and a control group may provide more accurate and reliable data.

To conclude, in our study, we found both ESWT and ozone therapy to be beneficial in pain relief while ozone therapy being the superior treatment method with regards to long-term pain relief.

Ethics Committee Approval: Canakkale Onsekiz Mart University Clinical Research Ethics Committee (No: 10-15, 08.05.3019).

Conflict of Interest: The authors declare that there is no conflict of interest regarding the publication of this article.

Funding: None

Informed Consent: All participants and their legal representatives provided written informed consent and assent.

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