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Clinical Trial

Effect of neural therapy versus extracorporeal shock wave therapy for the treatment of lateral epicondylitis: A randomized-controlled trial

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ABSTRACT

Introduction: Lateral epicondylitis is a common disease of the elbow joint. The main goal of therapy is to reduce pain and increase function. This study aimed to evaluate the effectiveness of neural therapy (NT) versus extracorporeal shock wave therapy (ESWT) in the treatment of lateral epicondylitis.

Methods: Between August 2018 and November 2018, 76 patients with lateral epicondylitis (26 males, 50 females; mean age: 44, 8 ± 9,5 years; range, 29–65 years) were randomly allocated to either NT or ESWT one session weekly for a total of three weeks. The subjective pain severity was evaluated using the Visual Analog Scale (VAS) and Duruoz Hand Index (DHI) was used to assess the functional disability before and after treatment and at 12 weeks.

Results: When the before and after treatment and 12 weeks variances of values were compared between ESWT and NT groups, there were no significant differences in the VAS and DHI scores between the groups($p > 0.05$) (VAS score at 12 weeks (effect size = 0, 18, 95% confidence interval (CI): -0,358 − 1,619) or DHI score (effect size = 0, 13, 95 % CI: -7,627 − 4,390). However, within the groups, there were significant differences in VAS and DHI scores between before treatment and after treatment($P < 0.05$), and between before treatment and at 12 weeks follow up ($P < 0.05$). No adverse events occured in this study.

Conclusion: The results of this study show that both ESWT and NT have similar effects in reducing pain and hand function in patients with lateral epicondylitis. However neither of two treatment modalities showed superiority.

1. Background

Lateral epicondylitis, which involves the lateral face of the origin of the extensor musculature of the wrist, is a tendinopathy characterized by pain and tenderness, leading to functional disability. It is common due to repeated movements and forceful activities during activities of daily living . It affects about 1–3% of general population [1–3]. It is mostly seen in adults aged 40–50 years and may affect both males and females, although several studies have reported that females are more affected than males [4]. The dominant arm is at the highest risk for the disease.

Lateral epicondylitis is a degenerative and inflammatory process which involves the tendons of the extensor carpi radialis brevis, extensor carpi radialis longus, and extensor digitorum communis [3]. Tendon ruptures can be seen in advanced disease. Treatment includes conservative, medical, and surgical modalities including wrist splints for resting, exercise, physical therapy agents, non-steroidal anti-inflammatory drugs, extracorporeal shock wave therapy (ESWT), local corticosteroid injections, prolotherapy, platelet-rich plasma therapy, and tenotomy [5,6]. In the treatment of lateral epicondylitis, complementary and alternative treatment modalities such as acupuncture, neural therapy, manual therapy, and massage are used. Despite a number of studies investigating the efficacy and safety of these modalities, the results are still controversial and there is no consensus regarding the optimal treatment . When conservative treatment methods fail due to their high cost or lack of availability, an increasing number of patients seek complementary therapy approaches [7,8].

Neural therapy (NT) is a diagnostic and therapeutic method used for illnesses. It is used in the treatment of acute and chronic musculoskeletal diseases, inflammatory diseases, and functional conditions [9,10]. It specifically involves the use of local anesthetic injections into the scar tissues, tendons and ligament insertions, peripheral nerves, autonomic ganglia, and trigger points for the treatment of chronic and painful conditions [11]. It was originally developed by two German physicians practicing in 1920s, namely Ferdinand and Walter Huneke. Their therapy has been widely used in Germany and many other European countries since then. It uses a distinct technique than other injection therapy techniques. First, local injection (quaddel) is applied into the

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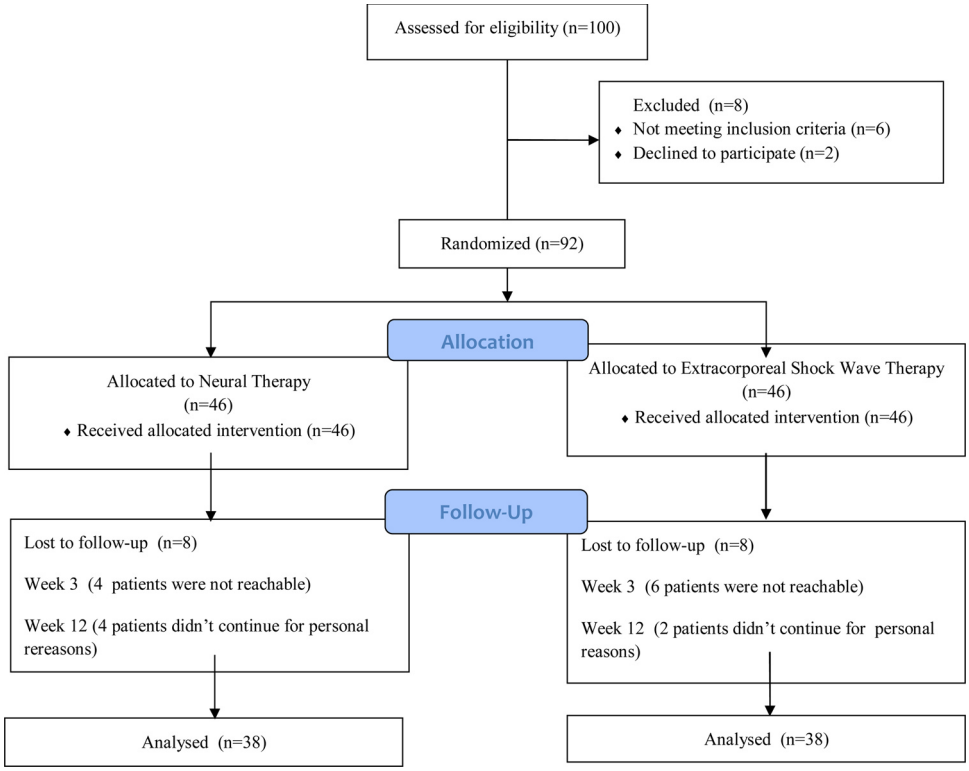

Fig. 1. Flow diagram of the study.

affected area. Second, segmental application is done around the surrounding neuroanatomical segment of the affected area. Third, ganglionic and interference field injections are used, when necessary [12].

Local intradermal injection used in NT is called a quaddel injection. Neural therapy works by injecting the local anesthetics into the skin, ganglia, and interference fields to regulate neurovegetative system and restore the disrupted functional structure [10].

Local anesthetics may alter the cell membrane potential, thanks to their effects on sodium ion channels in the inducible cells, and they also exert neuroprotective effects on the central nervous system. In addition, they have antimicrobial, anti-inflammatory, and vasodilator effects. The aim of the treatment is to stimulate afferent and efferent pathways of the vegetative (autonomous) nervous system (VSS) and to prevent conduction of painful stimuli. It is an effective treatment method by regulating perfusion of the impaired tissues or organs [11].

Extracorporeal shock wave therapy is another effective technique which uses high-pressure acoustic waves to reach the target area. A sudden rise from ambient pressure to maximal pressure at the wave front forms compression and tension strong pressure waves, leading to compression and tension. In recent years, radial ESWT has been increasingly used due to its ease of use and satisfactory results [13,14].

Several methods have been used in the treatment of lateral epicondylitis; however, there is no curative method with 100 % success. On the other hand, it is of utmost importance to identify optimal and cost-effective treatment options with satisfactory outcomes in the settings with limited financial and healthcare resources.

To the best of our knowledge, there is no study comparing NT with ESWT in patients with lateral epicondylitis. In the present study, we, for the first time, aimed to evaluate the effectiveness of NT versus ESWT in the treatment of lateral epicondylitis.

2. Methods

2.1. Trial design

This study was a prospective, randomized, single blind, controlled clinical trial. The study protocol was approved by the institutional Ethics Committee of Umraniye Training and Research Hospital (B.10.1.TKH.4.34.H.GP.0.01/121). The study was conducted in accordance with the principles of the Declaration of Helsinki. Participants aged 29–64 were recruited by the departments of outpatient clinic of Training and Research Hospital between August 2018 and November 2018. Written informed consent was obtained from each patient.

2.2. Participants inclusion criteria and recruitment

This prospective study included 92 patients who were admitted to our Physical Therapy and Rehabilitation outpatient clinic with pain from lateral part of the elbow and diagnosed with lateral epicondylitis by a physician. Inclusion criteria were as follows: pain and tenderness on palpation localized to the lateral epicondyle; wrist or elbow pain with restriction of extension and end of range of movements; and pain worsening with gripping and supination. Exclusion criteria were as follows: bilateral lateral epicondylitis; previous physiotherapy or injection treatment within the past six months before study participation; neurological deficits and presence of radicular pain; prior surgeries and fractures; pregnancy, coagulation disorders, malignancies, inflammatory disease; and previous ESWT or NT sessions.

2.3. Baseline assessment

Potentially qualified patients were eliminated by the research staff through physical examination and clinical tests. Patients were informed of the aims and nature of the study both verbally and via an information sheet. Data including patient demographics, level of education, occupation, and clinical characteristics of patients were recorded. All

patients underwent physical examination and movement functions, muscle ability, and trigger points. The study flow chart is shown in Fig. 1.

2.4. Randomization

The patients were randomly allocated to either the NT group or the ESWT group at a ratio of 1:1 using sequentially numbered, opaque, and sealed envelopes. The researcher who collected data, before and after the treatment period and at the control session 12 weeks later was not consented to attend to the intervention period and were blinded to the group allocation.

2.5. Interventions

2.5.1. Neural therapy

All measurements before (at baseline) and after treatment (at 3 weeks) and 12 weeks were evaluated by a single researcher. NT was applied by a physician who was trained and certificated with a four-year experience with the use of NT once weekly for a total of three weeks. 2% lidocaine hydrochloride (HCL) was diluted in normal saline and used as 0.5%. The quaddel injection was applied with 0.5 mL lidocaine HCL as intracutaneous injection. A total of 16 mL of local anesthetic (5 mg/mL lidocaine HCL) was injected in each session. All local quaddel injections were applied intradermally. Local quaddel injections were done intradermally to 6 points around the most painful and sensitive area covering the elbow completely. Segmental quaddel injections were applied from C4 to T8 for each spinous process and 0.5–2 cm laterally on the affected side (a total of 26 injection areas) [9,10]. Schedule of treatment is shown in Fig. 2.

Neural therapy-related complications such as bleeding, hematoma, or organ injuries can be seen with ganglionic and interference field injections, rather than quaddel injections. Therefore, we did not prefer ganglionic and interference field injections in our study. Detailed injection points for NT are shown in the Figs. 3 and 4.

2.5.2. Extracorporeal shock wave therapy

In the ESWT group, the Modus ESWT device (Serial no.800–1520; Inceler Medical Ltd., Ankara, Turkey) was used. The patients were treated in three sessions at one-week intervals with 2000 impulses per session at a pressure of 1.9 bars and a frequency of 10 Hz [14].

Shock waves can be focal or radial. The focal shock waves have a deeper tissue penetration (10 cm) and power (00,08 to 0,28 mJ/mm^2). However, these waves cannot be used for the treatment of musculoskeletal system disorders due to their high energy levels and technical difficulties. The radial shock waves have limited tissue penetration (3 cm) and power (00,08 to 0,28 mJ/mm^2) [15]. Owing to the low energy levels and user-friendly nature without a need for sedation or for monitoring via a radiographic or echographic device, radial ESWT has been shown to be more effective and beneficial in the treatment of musculoskeletal system disorders [16].

1. Session
   a) Local application: quaddel injection applied to six points around the patients most painful and sensitive area
   b) C4-T8 segmental quaddel injections
2. Session
   a) Local application: quaddel injection applied to six points around the patients most painful and sensitive area
   b) C4-T8 segmental quaddel injections
3. Session
   a) Local application: quaddel injection applied to six points around the patients most painful and sensitive area
   c) C4-T8 segmental quaddel injections

Figure 3

Fig. 2. Neural therapy program.

Fig. 3. Detailed injection points for neural therapy in the treatment of lateral epicondylitis. Local quaddel injections were done intradermally to 6 points around the most painful and sensitive area covering the elbow completely.

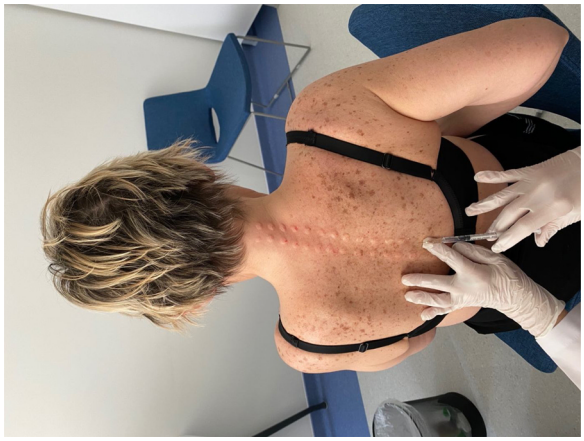

Fig. 4. Segmental quaddel injections were applied from C4 to T8 for each spinous process and 0.5 to 2 cm laterally on the affected side in the treatment of lateral epicondylitis.

The application was done using a 15-mm head. During application, ultrasound gel was used between the apparatus head and skin as a contact medium. The application was performed in the sitting position with 45° shoulder abduction and elbow flexion with forearm wrist and hand support. The ESWT was applied to the lateral epicondyle and the most sensitive surrounding point. Before and during the application, no local anesthetic or analgesic was used.

The ESWT is associated with mild side effects such as erythema, small hematomas, and throbbing pain.

Adverse effects were evaluated by clinical examination and by a patient questionnaire directly after the ESWT and NT procedure and at every follow-up visit. Adverse event for ESWT; Subcutaneous hematoma, Petechiae, Skin irritation, Skin redness and Ecchymosis at treatment site, Increased pain, Bleeding, Swelling of treated arm, Migraine, Syncope, Nausea/Vomiting, Feeling Unwell/Dizziness. Advers events for NT; hematoma, bleeding, organ injuries, Syncope, Nausea/Vomiting, Feeling Unwell/Dizziness.

Sociodemographic characteristics of all patients including age, sex, body mass index (BMI), disease duration, and dominant hand were recorded. The subjective pain severity was evaluated using the Visual Analog Scale (VAS) and Duruoz Hand Index (DHI) was used to assess the functional disability.

2.6. Outcomes

Outcomes are the change of VAS and DHI scores from baseline to scores at follow up 12 weeks. Primary outcome measure included changes in pain using the VAS. The VAS (1−10 cm) was used to evaluate the pain severity of the patients and each patient was asked to rate their subjective pain (at time of measure) (the most severe pain within the previous week). 0 indicates no pain, while 10 indicates most severe pain. The length of the response is measured in units (cm) [17].

The primary outcome measure was pain, while secondary outcome measure was functional recovery. The hand function was evaluated using the DHI consisting of 18 items on kitchen work, dressing, hygienic practices, office work, and other activities: 0 = no difficulty, 1 = a little difficulty, 2 = some difficulty, 3 = much difficulty, 4 = nearly impossible to do, and 5 = impossible Each item is scored and the patients answered the questions based on their experience during the last week. A higher score (range 0–90) indicates worse disability or handicap [18].

No post-treatment complications were seen in any of the patients.

2.7. Statistical analysis

We used G* Power version 3.1.2 (Heinrich Heine-Universität Düsseldorf, Düsseldorf, Germany) to calculate the sample size. Power analysis effect size was found to be 0.375. Power analysis revealed that 38 patients needed for each group for 80% statistical power. We used data from a pilot study [19] in which NT affected VAS scores (standard deviation [SD] = 8.11) which corresponded to an estimated effect size of 0.375.

Statistical analysis was performed using the IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation (SD), and number and frequency. The Shapiro-Wilk test was used to test normality of the data distribution. The Student's test was used compare two groups with normal distribution for quantitative data, while the Mann-Whitney *U*test was used to compare two groups with abnormal distribution. The intra-group comparison of normally distributed quantitative data was made using the paired sampletest, while the Wilcoxon signed-rank test was used to compare abnormally distributed data. The chi-square test, Fisher's exact test, Fisher-Freeman-Halton test, and Yates' continuity correction were used to analyze qualitative data. A Cohen's d calculation between group difference measurements was used to determine the effect sizes. A p value of < 0.05 was considered statistically significant. The results are within the 95% confidence interval, significance was evaluated at the level of $p < 0.05$.

3. Results

One hundred patients were referred to the study. Of these, 8 were excluded (6 did not meet the inclusion criteria and 2 declined to participate). Therefore, 92 patients were included and randomized into the study. In total, 46 patients (50.0%) were randomized to treatment with ESWT, 46 (50.0%) to NT. Sixteen patients dropped out after finishing the treatment, with a drop out rate of 17.3% (16/92): six patients did not come to the follow up visit for personal reasons, ten who patients were not able to be reached. A total of 76% patients completed NT (38 %) or ESWT (38 %). In the ESWT group, 25 were females and 13 were males. In the NT group, 25 were females and 13 were males. The mean BMI was 27.7 ± 5.3 kg/m^2. The right hand was the dominant hand in 93.3% of the patients and the right arm was affected in 73.3%. There was no statistically significant difference in the age, gender, BMI, marital status, education level, smoking history, employment status, dominant hand used, arms affected and duration of disease between the two groups ($p > 0.05$). In the Table 1, affected arm/ dominant hand odds ratio 4.2. Number of outpatient visits in the ESWT treatment group was significantly lower than the NT treatment group (p: 0.002; $p < 0.05$). Demographic and clinical characteristics of the patients are shown in Table 1.

Table 2 reports the comparison of position or activities when the patient was experiencing pain (i.e., resting, sleeping pain, repeated elbow movements, or heavy lifting) in both groups. There was no statistically significant difference in the position or activities when the patients were experiencing pain between the groups before and after treatment and at 12 weeks ($p > 0.05$).

Within ESWT groups, there were significant differences in VAS scores before treatment and after treatment($P < 0.05$), and between values before treatment and at 12 weeks follow up ($P < 0.05$). However, there was no significant differences in VAS scores between after treatment and at 12 weeks($p > 0.05$). Within ESWT groups, there were significant differences in DHI scores between before treatment and after treatment($P < 0.05$), and between values before treatment and at 12 weeks follow up($P < 0.05$) and between after treatment and at 12 weeks follow up values ($P < 0.05$). Within the ESWT group, there was a statistically significant decrease in the DHI scores after treatment and at 12 weeks, compared to baseline (p_1:0.000; p_2:0.000; $p < 0.05$ respectively). Within ESWT group, there was a statistically significant decrease in the VAS scores after treatment and at 12 weeks, compared to baseline ($p = 0.000$; $p < 0.05$, respectively).

Within NT groups, there were significant differences in VAS scores between before treatment and after treatment($P < 0.05$), and between before treatment and with values at 12 weeks follow up ($P < 0.05$) and between values after treatment and at 12 weeks follow up ($P < 0.05$).Within NT groups, there were significant differences in DHI scores between before treatment and after treatment($P < 0.05$), and values between before treatment and at 12 weeks follow up($P < 0.05$) and values between after treatment and at 12 weeks follow up ($P < 0.05$). Within NT group, there was a statistically significant decrease in the VAS scores after treatment and at 12 weeks, compared to baseline ($p = 0.000$; $p < 0.05$, respectively).Within the NT group, there was a statistically significant decrease in the DHI scores after treatment and at 12 weeks, compared to baseline (p_1:0.007; p_2:0.000; $p < 0.05$ respectively).

When the before and after treatment and 12 weeks variances in values were compared between ESWT and NT groups, there were no significant differences in the VAS and DHI scores between the groups ($p > 0.05$)(VAS score at 12 weeks (effect size = 0, 18, 95 % confidence interval (CI): -0,358−1,619) or DHI score (effect size = 0, 13, 95 % CI: -7,627−4,390).

Both treatments significantly decreased the level of pain (VAS) (NT, from 7,71 ± 1,73 to 4,07 ± 1,96 and ESWT, from 7,94 ± 1,73 to 4,59 ± 2,77 ; $p < 0.05$) at the end of the study. In Table 3, significance was evaluated at $p < 0.05$, levels for all values. Both treatments significantly improvement the level of DHI (NT, from 30,02 ± 18,67 to 17,10 ± 12,03 and ESWT, from 26,86 ± 16,06–15,48 ± 14,02; $p < 0.05$) (Table 4).

A Cohen's d calculation between the group difference in measurements was used to determine the effect sizes. There was a clinically weak difference between this study groups.

No relevant adverse events occurred during or after treatment, except for slight pain. In the ESWT group, one patient reported a short and bearable pain during the one session of therapy. In the NT group, there was no adverse event reported either during or after treatment.

4. Discussion

Although several treatment modalities for lateral epicondylitis have been established, it is still controversial which option is the most effective. There are a number of studies using NT and ESWT alone in the treatment of lateral epicondylitis; however, no head-to-head study comparing both treatment modalities is available in the literature. The present study, therefore, is the first to evaluate the effectiveness of NT and ESWT in the treatment of lateral epicondylitis. The age of the

Table 1
Demographic and clinical characteristics of patients.

		ESWT (n = 38) Min-Max (Mean ± SD)	NT (n = 38) Min-Max (Mean ± SD)	Total Min-Max (Mean ± SD)	
Age(year)		30 – 61 (45,8 ± 7,60)	21 – 65 (43,8 ± 11,1)	21 – 65 (44,8 ± 9,5)	[1]0,934
BMI (kg/m^2)		18,7 – 39,5 (28,0 ± 4,6)	20,7 – 39,5 (27,4 ± 6,0)	18,7 – 51,9 (27,7 ± 5,3)	[1]0,636
Disease duration (month) (median)		1 – 12 (3,83 ± 3,61 (3))	1 – 12 (3,0 ± 2,57 (2))	1 – 12 (3,41 ± 3,14 (3))	[2]0,251
Outpatient visit n (median)		1 – 4 (1,37 ± 0,79 (1))	1 – 3 (1,57 ± 0,64 (2))	1 – 4 (1,48 ± 0,72 (1))	[2]0,002*
Gender,n (%)	**Female**	25 (%65,8)	25 (%65,8)	50 (%65,8)	[3]0,563
	Male	13 (%34,2)	13 (%34,2)	26 (%34,2)	
Marital status,n (%)	**Married**	35 (%92,1)	30 (%78,9)	65 (%85,5)	[4]0,086
	Single	3 (%7,9)	8 (%21,1)	11 (%14,4)	
Education level, n(%)	**Primary**	20 (%52,6)	16 (%42,1)	36 (%48,0)	[5]0,290
	High	11 (%28,9)	10 (%26,3)	21 (%28,0)	
	University	7 (%18,4)	12 (%31,6)	18 (%24,0)	
Employment status, n(%)	**Employed**	17 (%44,7)	21 (%55,3)	38 (%50,7)	[3]0,492
	Non-employed	21 (%55,3)	17 (%44,7)	37 (%49,3)	
Smoking, n(%)	**Yes**	11 (%28,9)	11 (%28,9)	21 (%28,0)	[3]1,000
	No	27 (%71,1)	27 (%71,1)	54 (%72,0)	
Dominant hand,n (%)	**Right**	36 (%94,7)	34 (%89,5)	70 (%92,1)	[4]0,358
	Left	2 (%5,3)	4 (%10,5)	5 (%7,9)	
Affected arm, n (%)	**Right**	28 (%73,7)	28 (%73,7)	55 (%73,6)	[3]1,000
	Left	10 (%26,3)	10 (%26,3)	20 (%26,3)	

Affected arm/dominant hand odds ratio 4,2.
[1]*Student t*-test [2]*Mann-Whitney U* test[3]*Yates' continuity correction*[4]*Fisher's exact test* [5]*Chi-square Test*$p < 0.05$.
ESWT, extracorporeal shock wave therapy; NT, neural therapy; SD, standard deviation; BMI, body mass index.

Table 2
Comparison of position or activities when the patients were experiencing pain.

The most severe pain		ESWT (n = 38) n (%)	NT (n = 38) n (%)	Total p n (%)	
Pre-treatment	Resting	4 (%10,5)	2 (%5,3)	6 (%8,0)	[1]0,557
	Sleeping	7 (%18,5)	12 (%31,6)	19 (%25,3)	
	Repeated elbow movements	19 (%50)	18 (%47,4)	37 (%49,3)	
	Heavy lifting	8 (%21)	6 (%15,8)	14 (%18,4)	
Post-treatment	Resting	6 (%15,8)	2 (%5,3)	8 (%10,5)	[1]0,200
	Sleeping	6 (%15,8)	12 (31,6)	18 (%23,7)	
	Repeated elbow movements	15 (%39,5)	17 (44,7)	32(%42,1)	
	Heavy lifting	11 (%28,9)	7 (%18,4)	18 (%23,7)	
12th Week	Resting	7 (%18,4)	2 (%5,3)	9 (%11,9)	[2]0,255
	Sleeping	6 (%15,7)	10 (%26,3)	16 (%21,1)	
	Repeated elbow movements	17 (%44,7)	16 (%42,1)	33 (%43,4)	
	Heavy lifting	8 (%21,05)	10 (%26,3)	18 (%23,6)	

[1]Fisher-Freeman-Halton test.[2]Chi-square test. ESWT, extracorporeal shock wave therapy; NT, neural therapy.

Table 3
Comparison of visual analog scale scores between the two intervention groups.

VAS	Treatment Group		Total			
	ESWT (n = 38) Min-Max (Mean ± SD) (median)	NT (n = 38) Min-Max (Mean ± SD) (median)	Min-Max (Mean ± SD) (median)	*P*	95 %CI	Effect size (d) **
Pre-treatment	4 – 10 (7,94 ± 1,73 (8))	5 – 10 (7,71 ± 1,73 (8))	4 – 10 (7,85 ± 1,69 (8))	0,559	**−0,56 − 1,03**	
Post-treatment	0 – 10 (5,00 ± 2,59 (5))	2 – 10 (4,42 ± 1,94 (6))	0 – 10 (5,6 ± 2,7 (5))	0,276	**−8,78 − 2,90**	0.18
12th Week	0 – 10 (4,59 ± 2,77 (5))	1 – 10 (4,07 ± 1,96 (3))	0 – 10 (4,30 ± 2,70 (4))	0,355	**−7,62 − 4,39**	
Pre-/Post-treatment Week 12, *p2*	0.000*	0.000*				
Pre-/Post-treatment Week 12, *p2*	0.000*	0.000*				

[1]*Mann Whitney U Test*[2]*Wilcoxon Sign Test*$p < 0.05$ **Cohen's d.
SD, standard deviation; VAS, Visual Analog Scale; ESWT, Extracorporeal shock wave therapy; NT, neural therapy;CI, confidence interval.

Table 4
Comparison of Duruoz Hand Index scale scores between the two intervention groups.

DHI			Total			
	ESWT (n = 38) Min-Max (Mean ± SD)	NT (n = 38) Min-Max (Mean ± SD)	Min-Max (Mean ± SD)	P1	95 %CI	Effect size (d) **
Pre-treatment	1–69 (26,86 ± 16,06)	5–69 (30,02 ± 18,67)	1–69 (28,1 ± 17)	0,429	**−11,08–4,76**	
Post-treatment	1–49 (16,75 ± 13,13)	1–47 (19,28 ± 12,27)	1–49 (21,13 ± 14,18)	0,320	**−8,78–2,90**	0.13
12th week	0–49 (15,48 ± 14,02)	0–45 (17,10 ± 12,03)	0–49 (16,02 ± 13,35)	0,593	**−7,62–4,39**	
Pre-/Post-treatment, *p2*	0.000*	0.000*				
Pre-/Post-treatment 12thweek, *p2*	0.000*	0.000*				

[1]*Student's t*-test, [2]*Paired samples t-test,* $*p < 0.05$,**Cohens'd; SD, standard deviation; DHI, Duruoz Hand Index; ESWT, extracorporeal shock wave therapy; NT, neural therapy; CI, confidence interval.

patients and the rate of dominant hand and affected arm are consistent with the literature [20].

Lateral epicondylitis is the leading cause of elbow pain in patients without any trauma history. Repeated movements and forceful activities requiring extension of the wrist lead to exceeding the force, flexibility and endurance threshold resulting in tissue injury. As repetitive tissue injury persists, degeneration-related pain, strength loss and functional disability progress. It has been shown that microcirculation decreases and anaerobic metabolism increases in the extensor carpi radialis brevis in patients with lateral epicondylitis [21]. Autonomic reflex responses are produced due to these local changes and hyperactivity of the sympathetic nervous system occurs, leading to a vicious cycle consisting of neurogenic inflammation and pain. According to Ricker [22], mechanical, thermal, electromagnetic, chemical, physical, toxic, and microbial stimuli alter frequency and amplitudes of the afferent sympathetic neurons. Previous or existing local irritation including inflammatory, chemical processes, injuries, and previous surgeries in any part of the body may create an interference field (irritation zone). External and internal factors result in impaired neurovegetative nervous system, leading to pain and development of other diseases [9,23,24]. In chronic states, altered conduction of the membrane potentials of the nerve fibers is associated with autonomous nervous system changes which can affect sensory and motor fibers in the adjacent ganglia [25].

Abnormal peripheral signals inhibit gate-control mechanism of the spinal cord, leading to an electrical chaos. Abnormal signals advance to the cortex, resulting in central and autonomous nervous system impairment with turmoil in the peripheral nervous system. This turmoil potentiates the impairment in the spinal cord, and a vicious cycle occurred [9,25]. Initially, the primary lesion which produces abnormal signals to the autonomous nervous system is diagnosed in NT, which is known as the interference field or irritation zone. This zone may be a scar or an undiagnosed tooth abscess. Even if fully recovered, such zones may occur in the affected organ [25].

Pain cycle consists of nociceptor activity, sympathetic activity, reduced blood flow into the tissue, neurogenic inflammation, and increased muscle tone. This cycle can be broken by local, segmental, and supra-segmental NT injections. Certain percentages of lidocaine or procaine are used in NT applications. Local anesthetics have been shown to increase the capillary penetration and induce vasodilation owing to their antimicrobial, anti-inflammatory, and sympatholytic effects [10].

In a study involving patients with lateral epicondylitis, the patients were randomized to manual therapy + NT or manual therapy alone or NT alone and combined treatment yielded more favorable outcomes with a less number of sessions [26]. In addition, there are several studies showing that NT is effective in painful musculoskeletal conditions [11,27,28]. Weinschenk et al. [27] applied NT through local anesthetic injection to the pharynx and reported a lower number of trigger points in the trapezius muscle. Similarly, in a randomized-controlled study, Ural et al. [19] showed that NT was an effective and safe modality in the treatment of lateral epicondylitis. However, there are several studies showing the effectiveness of corticosteroid injection in the treatment of lateral epicondylitis. Mardan et al. [29] found that local corticosteroid injection was more effective than NT in their study. In our study, results suggest that NT provided improvement in pain relief through arm functions in patients with lateral epicondylitis and there was no significant difference between groups in treatment of lateral epicondylitis.

In the present study, we used lidocaine, as it is cost-effective and available in abundance. The half-life of lidocaine is short (~2 h) and it produces transient block which requires a repeated injection. However, it is associated with allergic reactions and bleeding [9]. In our study, none of the patients experienced any treatment-related complications. Therefore, we conclude that NT is an effective, safe, cheap, and cost-effective treatment modality in lateral epicondylitis.

Furthermore, a controversy still exists on the optimal impulse of ESWT in the treatment of lateral epicondylitis. Some authors demonstrated its effectiveness, although some others showed no superiority over placebo [14,30]. Aydın et al. reported that comparing the efficacy of ESWT to wrist extensor splint application in the treatment of lateral epicondylitis produced similar improvement in pain and functions, however, there was no statistically significant difference between the two groups. The authors noted limitations of the study were the small patient population [16]. In our study results suggest that both ESWT and NT supply similar improvement in pain relief through arm functions in patients with lateral epicondylitis. However, we found no statistically significant difference between the groups. Similarly, In our study included a relatively small number of subjects, may be leading to insufficient power to detect treatment effects.

Extracorporeal shock wave therapy was firstly applied in a patient to disintegrate kidney stones [31]. It increases the collagen synthesis in the injured tissue and enhances vascularity with increased tensile strength. Although the mechanism of action of ESWT in soft tissues is not fully understood, it has been proposed that it releases angiogenesis-related growth factors by shock waves and enhances vascularity, accelerating oxygenation [32]. In several studies, ESWT was found to relieve pain and to increase gripping strength and function in patients with lateral epicondylitis [33–35]. Similarly, Gunduz et al. [36] reported similar outcomes with ESWT. In our study, there were statistically significant improvements in the VAS and DHI scores in the ESWT group, consistent with the literature. In contrast, in another study involving 1006 patients, Buchbinder et al. [37] Reported that ESWT yielded no or a mild improvement in pain and elbow function. Similarly, in a randomized, placebo-controlled study including 56 patients, Capan et al. [38] demonstrated that ESWT and placebo produced similar improvement in pain and functions.

Both Neural therapy and ESWT therapy were generally well tolerated. During treatment, both groups were advised to refrain from repeated elbow movements and heavy lifting. These suggestions may

have created awareness in the treatment of patients and contributed to the improvement of epicondylitis. We also think that the placebo effect and the Hawthorne effect may also play a role. The lack of difference between groups may be due to this reasons.

5. Limitations

There are some limitations to this study. The number of subjects in the study is small which could have decreased the power of the study. As there was no control group, we could not determine the effect of two therapeutic methods. The lack of blinding, qualitative data/feedback from patients, non treatment group or routine care group, and long-term outcomes are the other limitations of the study. Furthermore, ganglionic (due to possible complicated side effects) and interference field injections (to provide the standardization of treatment protocol) were unable to be used. Therefore, further large-scale, prospective, long-term outcomes, placebo-controlled studies are needed to confirm these findings.

6. Conclusion

The results of this study show that ESWT and NT have similar beneficial effects in patients with lateral epicondylitis. There was a statistically significant improvement in both groups. However, possibly due to small sample size, the results were not statistically significant. ESWT and NT methods may be an option in the treatment of lateral epicondylitis. Future studies are necessary to decide whether the mechanism of the observed effect of ESWT or NT is due to physiological effects, the Hawthorne effect, intensity of provider contact, or placebo effects. A large-scale randomized clinical trial with a control group and a longer-term follow-up is needed.

Author's contributions

Sevgi Gümüş Atalay (SGA): Wrote protocol, drafted manuscript, data collection and analysis, interpretation, critically revised the manuscript.

Ömer Gezginaslan (OG): Data collection and analysis, figures drawing and table design and interpretation

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Declaration of Competing Interest

The authors declare no conflicts of interest with respect to the authorship and/or publication of this article.

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