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Evaluation of Neural Therapy Effects in Patients with Lateral Epicondylitis: A Randomized Controlled Trial

Lateral Epikondiliti olan Hastalarda Nöral Terapi Etkinliğinin Değerlendirilmesi: Randomize Kontrollü Çalışma

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Abstract
Objectives: The purpose of the study is to explore neural therapy (NT) and the effect of it on pain and the functional status of patients with lateral epicondylitis (LE) and to determine whether clinical changes and demographic characteristics have any correlation.
Materials and Methods: Forty-two patients with LE were randomly allocated into two groups; NT & control. The control group was given rest, non-steroidal anti-inflammatory drugs, stretching exercises and a wrist splint. The patients in the NT group received 8 sessions of NT. The visual analog scale (VAS), pain pressure threshold (via algometry) and Duruöz hand index (DHI) scores were noted before and at the end of the treatment in both groups.
Results: All parameters improved in both groups. However, improvement of VAS, algometry and DHI scores were more obvious in the NT group. The clinical change and demographic features of the groups showed no correlation.
Conclusion: NT is a safe and effective treatment method for treatment of patients with LE.
Key words: Neural therapy, lateral epicondylitis, local anesthetics, rehabilitation

Öz
Amaç: Bu çalışmanın amacı lateral epikondilitli (LE) hastalarda nöral terapinin ağrı ve fonksiyonel durum üzerine etkisinin değerlendirilmesidir. Ayrıca, hastaların klinik bulgularında meydana gelen değişiklikler ile demografik özelliklerinin korelasyonunun değerlendirilmesi planlanmıştır.
Materyal ve Metot: LE tanısı olan toplam 42 hasta randomize olarak 2 gruba ayrıldı (Nöral terapi & kontrol) Kontrol grubundaki hastalara istirahat, non-steroidal anti-inflamatuar ilaç, germe egzersizleri ve el bileği splinti verildi. Nöral terapi (NT) grubundaki hastalara 8 seans NT uygulaması yapıldı. Her iki grupta, tedavi öncesinde ve tedavi bitiminde hastaların görsel ağrı skalası (GAS), basınç ağrı eşiği (algometre ile) ve Duruöz el indeksi (DEI) skorları kaydedildi.
Bulgular: Tüm skorlar her iki grupta düzelme gösterdi. Fakat, GAS, algometre ve DEI skorları NT grubunda daha belirgin olarak düzeldi. Her iki grupta klinik değişiklikler ile demografik özellikler arasında korelasyon saptanmadı.
Sonuç: Nöral terapi lateral epikondilitli hastaların tedavisinde etkili ve güvenli bir tedavi yöntemidir.
Anahtar kelimeler: Nöral terapi, lateral epikondilit, lokal anestezik, rehabilitasyon

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Introduction

Lateral epicondylitis (LE), also known as 'tennis elbow', is a painful disorder of the elbow region. The common extensor tendon of the wrist originates from the lateral epicondyle and its' injury due to overuse, is the most common reason of this disorder. LE is called tennis elbow because tennis players are prone to LE due to the strain on the elbow. However, other occupations including highly recurrent movements of the elbow may lead to this disorder. Mostly subjects aged 40 years and older are affected. According to some studies, this syndrome equally affects men and women, [1] while other studies report that women are affected more than men.[1-3] Resting, bracing, non-steroidal anti-inflammatory drugs, injections (corticosteroid, platelet-rich plasma and botulinum toxin), physical therapy, extracorporeal shock wave therapy, and surgical procedures may be used for treatment of LE. [4-8]

Neural therapy (NT) is a treatment technique, which uses the injection of local anesthetics for diagnosis and treatment. Functional disorders, inflammatory diseases, acute or chronic painful musculoskeletal disorders may be treated with this treatment modality. Local intradermal injections, known as a quaddel, spinal segmental quaddel, ganglion injections, and interference field (irritation zone) injections were used in this treatment technique.[9,10] Intradermal injections are called quaddel. Quaddel is applied to the area of pain locally or around the spinal segment. While injecting quaddel in the spinal segment, injections are applied directly and lateral (about 2 cm) to the spinous process. Ganglion injections include the sympathetic ganglions (generally stellat, superior cervical, lumbar 1 and 2) and the parasympathetic ganglions (generally sphenopalatine, ciliare and oticum). Ganglion injections are performed to regulate the vegetative state of the nervous system, when other segmental therapies were ineffective. However, ganglion injections are deep and for this reason there are many more adverse effects (i.e. hematoma, organ injury) than quaddel injections. [9,10] Interference field is described as any disturbed area of the body being asymptomatic leading to another disorder by remote effect. Scar tissue (due to surgery, burn and vaccine) and chronic inflammation of the organs (especially teeth, sinuses and pharynx) may be an interference zone. [9,10] Negative effects of this irritation zone may be eliminated by injections of local anesthetics. [9,10]

In NT, the purpose is not to provide local anesthesia, except for diagnosis. The organization of the vegetative (autonomic) nervous system, tissue perfusion and prevention of positive feedback actions (vicious circle) in the pain cycle are targeted via needle stimulation and local anesthetics (i.e.; vasodilatation, anti-inflammation). The regulatory mechanisms of the nervous system are used mainly on segmental reflector processes and the interference field described as the zone that initiates and/or maintains pain and inflammation, regardless of the related segment.[11-13] The effect of NT was previously reported in various painful musculoskeletal disorders.[9,10] The authors claimed that NT is more effective than traditional treatment methods (including rest, bracing, non-steroidal anti-inflammatory drugs) in these patients. However, the effect of NT in patients with LE has not been studied, yet. Thus, in this study we purposed to evaluate the effect of NT on pain and hand functions in patients with LE.

Materials and Methods

Forty-two chronic LE patients were included in this randomized, controlled, prospective study. LE is diagnosed with clinical examination (tenderness on lateral epicondyle and pain in resistant wrist extension). Presence of bilateral LE, radicular pain, previous surgery or trauma of elbow, peripheral nerve disease of upper limb (median, radial, ulnar) were stated as exclusion criteria. The local ethic committee approved the study protocol and an informed consent form was signed by all participants. This study was conducted in accordance with the declaration of Helsinki.

Subjects (N=42) were randomly grouped into the NT group or control group. Patients were numbered and distributed into two groups using a computer program (Research Randomizer, www.randomizer.org., USA). Subjects were randomly allocated following simple randomization procedures (computerized random numbers) to 1 of 2 treatment groups. Patients in the control group were given rest, non-steroidal anti-inflammatory drugs (diclofenac 150 mg/day, for 10 days), wrist static splint (for 4 weeks) and stretching exercises (for extensor and flexor muscles of the wrist, 10 times per set, three sets per day, for 4 weeks). In the NT group, rest was offered to the patients who were treated with the NT. NT was administrated to each patient by the same experienced physician. A total of 16 ml of local anesthetic (5 mg/ml [%0.5] Lidocaine HCl) was injected in each session. Local quaddel injections and C4-T8 segmental quaddel injections were performed in each session. Quaddel injections were done intradermally. Six points around the patient's sensitive area were chosen for local quaddel injections. Intradermal segmental injections were performed from C4 to T8 for each spinous process and 0.5-2 cm laterally on the affected side (a total 26 injection areas). Approximately, 0.5 ml of local anesthetics was administered per injection site (a total dose of 40 ml). NT was applied two days a week, for 4 weeks (a total of 8 sessions).

Demographic characteristics (age, sex, body mass index, disease duration) of patients were recorded. Severity of pain and functional status of the affected limb were

measured in each patient before and after the treatment. Visual analog scale (VAS) was used to evaluate the severity of pain (0-10 cm). Also, to assess the pressure pain threshold, an algometry (Baseline, USA) with 1 cm^2 surface was used. Initially the painful area was localized with palpation, afterwards a force was applied using algometry until the subjects felt pain or discomfort. The peak exhibiting force in algometry was noted. Three measurements were performed and the mean of these measurements were taken. The functional status of the hand was assessed by using Duruoz hand

index (DHI). DHI includes 18 questions evaluating activities requiring force, rotational movements, ability, precision and flexibility of the first three fingers. [14] Each question is answered using a scale between 0 to 5 and the total score ranges between 0 and 90 where high scores indicate poor functional status.

Statistical analysis was performed using SPSS (SPSS Inc., Chicago, Illinois, USA) version 21.0 for windows, and data was expressed as mean ± standard deviation. Normal distribution of the values (according to the values of Skewness and

Kurtosis) was showed. Independent sample-t test or chi square test was used to compare demographic and clinical measurements between two groups. Clinical changes in each group were evaluated by the paired sample t test. The Pearson test was used to assess the correlation between clinical and demographic characteristics. Statistical significance was accepted as $p<0.05$.

Results

All patients completed the study. Demographic features were given in Table-1. Age, sex, body mass index and disease duration were similar in both groups. The mean age was 44.80±10.45 in NT as the mean age was 50.04±8.36 (p=0.081). NT group included 14 male and 7 female subjects; control group included 11 male and 7 female subjects (p=0.346). The BMI scores were 23.76±2.71 & 26.38±5.91 (NT & control) (p=0.075). Duration of the disease is 27.85±17.43 in NT group as it is 28.47±13.54 in control group (p=0.898).

Table 1. Demographic features of patients

	NT Group (N=21)	***Control Group (N=21)***	***P***
Age (years)	44.80±10.45	50.04±8.36	0.081
M/F	14/7	11/10	0.346
Body Mass Index (kg/m²)	23.76±2.71	26.38±5.91	0.075
Duration of LE (months)	27.85±17.43	28.47±13.54	0.898

Data are given as mean ± standard deviation (min-max) or n. LE; lateral epicondylitis, M, male, F; female.

Clinical characteristics were given in Table-2. The VAS, DHI and pressure pain threshold scores were improved in both groups. In the NT group, pre-treatment VAS score was 8.38±0.74, while post-treatment VAS score was 0.61±0.49 ($p<0.001$); pre-treatment pressure pain threshold score was 2.45±1.75, while post-treatment pressure pain threshold score was 7.35±2.89 ($p<0.001$); pre-treatment DHI score was 63.42±5.52, while post-treatment DHI score was 10.76±5.35 ($p<0.001$). In the control group, pre-treatment VAS score was 7.28±0.56, while post-treatment VAS score was 3.95±0.66 ($p<0.001$); pre-treatment pressure pain threshold score was 2.90±1.77, while post-treatment pressure pain threshold score was 4.59±1.39 (p=0.007); pre-treatment DHI score was 60.47±4.97, while post-treatment DHI score was 34.14±7.18 ($p<0.001$). Percentage changes of VAS (92.77±5.84 % & 45.74±8.11 %) ($p<0.001$), DHI (354.33±260.69 % & 113.17±123.46 %) ($p<0.001$) and pressure pain threshold (83.24±7.93 % & 43.65±10.30) ($p<0.001$) were higher in the NT group compared to the control group (Table-3). Demographic characteristics and changes of clinical measurements did not show significant correlation in both groups.

Discussion

The purpose of this study was to explore whether NT had any effect on pain and functional status in patients with LE. The findings of this study showed that although pain and functionality were improved in both groups, this improvement was more

obvious in the NT group than in the control group. According to our results, it may be said that NT is an effective treatment method for LE.

Wrist flexors and extensors work together during handgrip movements. Loading of extensor and flexor muscles are altered according to the postural situation.[14] Extensor muscle activity was the greatest when the forearm was pronated and the wrist extended, while flexor activity was the greatest during supination and when the wrist was flexion.[15] During easy and low-level grip movements, forearm extensor activity was larger than flexor activity and this condition may be responsible for the development of LE in the workplace.[15] In LE patients, decreased microcirculation and increased anaerobic metabolism in the extensor carpi radialis brevis muscle were reported.[16]

Table 2. Clinical characteristic of patients

	NT Group (N=21)			**Control Group (N=21)**		
	Before	After	p	Before	After	p
VAS	8.38±0.74 (7-10)	0.61±0.49 (0-1)	**<0.001**	7.28±0.56 (6-8)	3.95±0.66 (3-5)	**<0.001**
Algometry	2.45±1.75 (1-7)	7.35±2.89 (1-10)	**<0.001**	2.90±1.77 (1-7)	4.59±1.39 (3-8)	**0.007**
Duruöz hand index	63.42±5.52 (57-80)	10.76±5.35 (3-22)	**<0.001**	60.47±4.97 (53-70)	34.14±7.18 (20-50)	**<0.001**

Data are given as mean ± standard deviation (min-max), VAS; visual analog scale

Table 3. Percent changes of clinical characteristics

	NT Group (N=21)	***Control Group (N=21)***	***P***
VAS	92.77±5.84	45.74±8.11	**<0.001**
Algometry	354.33±260.69	113.17±123.46	**<0.001**
Duruöz hand index(mm)	83.24±7.93	43.65±10.30	**<0.001**

Data are given as mean ± standard deviation, VAS; visual analog scale

Autonomic reflex responses are accompanied with these local changes. Decreased microcirculation, hyperalgesia in the localized area and increased muscle tonus occur due to hyper-activation of the sympathetic nervous system.[17,18] Sympathetic hyperactivity may be responsible for the vicious circle of pain in painful disorders. [18] Additionally, sympathetic irritation leads to neurogenic inflammation. Peripheral sensitization may develop due to neurogenic inflammation. [9,19,20] Furthermore, Ricker showed in an animal model that the sympathetic nervous system has a memory for pain and pathological mechanisms.[21] This pathological cycle maybe restricted with NT applications including local, segmental and supra-segmental injections.[9,18] The vicious circle of pain (nociceptor activity – sympathetic excitation – decreased blood flow – neurogenic inflammation – increased muscle tonus) may be broken through these

local anesthetic applications.[9] Moreover, the pathological memory in the sympathetic nervous system can be removed thanks to this technique.[9,18] Previous studies have demonstrated that NT is an effective treatment modality for painful musculoskeletal disorders.[11,12] Mardani et al. reported that local anesthetic injection (only local application) was not as

effective as corticosteroid injection in patients with LE.[22] NT is not only a local injection, but also includes segmental and supra-segmental injections and the effect of NT in other painful musculoskeletal disorders have been shown in previous studies. [11,12] According to the authors, the effects of NT in patients with LE were shown for the first time in this study, and according to our results, NT is an effective treatment modality for LE.

We used lidocaine for the application of NT in this study. It is easily available and a cheap drug. The elimination half-life of lidocaine is 2 hours, and it reversibly blocks neuronal transmissions. In addition to this effect, repeated injection of lidocaine can decrease neurogenic inflammation.[13] Furthermore, lidocaine has vasodilator effects on blood vessels.[13] The aim of NT is not to provide local anesthesia, but to regulate therapy by targeting injured tissues and increasing microcirculation. Therefore, lidocaine is used in NT for its vasodilator and anti-inflammatory effects.

Allergic reactions, pain and bleeding may be seen due to NT.[9] However, no adverse reaction was observed in our patients. Accordingly, it may be concluded that NT is a safe treatment method when performed by an experienced physician.

The lack of long term follow-up of the patients and evaluation of NT's sham effects are major limitations of our study. Another limitation of our study is the lack of a real

control group. In this study, we aimed to compare effects of NT with combined treatment methods (nonsteroidal anti-inflammatory drugs, splint, and exercises) in LE patients. Furthermore, ganglion (due to complicated side effects) and interference field injections (to provide the standardization of treatment protocol) were not performed. Therefore, in some patients, less efficacy of NT may be attributed to the lack of injections of the ganglion and interference field. Nevertheless, our results are considerable and noteworthy.

NT applications can be applied by all physicians educated in this field. NT is not only used for musculoskeletal disorders, but also used for dysfunctions of all organs.

Because of these features, NT applications are considered in preventive medicine. In our country, orders of preventive medicine are made by family physicians. For this reason, NT has begun to be used increasingly by family physicians in our country.

However, we think that education of NT should be generalized among family physicians.

To summarize, in the light of our findings; NT improves pain and functional status in patients with LE. Also, NT is an easy applicable, safe and cost-effective treatment technique for painful musculoskeletal disorders. Our results need to be confirmed by

future studies that include placebo-controlled and long-term follow-up studies.

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