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ORIGINAL ARTICLE

A randomized-controlled clinical trial comparing the effects of steroid phonophoresis and therapeutic ultrasound in carpal tunnel syndrome

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ABSTRACT

Objectives: In this study, we aimed to compare the efficacy of ultrasonography (US) and steroid phonophoresis (PH) treatments in patients with idiopathic carpal tunnel syndrome (CTS).

Patients and methods: Between January 2013 and May 2015, a total of 46 hands of 27 patients (5 males, 22 females; mean age: 47.3+13.7 years; range, 23 to 67 years) with idiopathic mild/moderate CTS without tenor atrophy or spontaneous activity in abductor pollicis brevis were included. The patients were randomly divided into three groups. The first group was ultrasound (US) group, the second group was PH group, and the third group was placebo US group. Continuous US with a frequency of 1 MHz, an intensity of 1.0 W/cm^2 was used in the US and the PH groups. The PH group received 0.1% dexamethasone. Placebo group received a frequency of 0 MHz, an intensity of 0 W/cm^2 US. Treatments were administered for five days a week, a total of 10 sessions. All patients also wore night splints during treatment. The Visual Analog Scale (VAS), Boston Carpal Tunnel Questionnaire consisting of two parts, namely the Symptom Severity Scale and Functional Status Scale), grip strength, and electroneurophysiological evaluations were compared before the treatment, after the treatment, and three months later.

Results: All clinical parameters improved in all groups after treatment and at three months, except for the grip strength. Recovery in the sensory nerve conduction velocity between palm and wrist was seen in US group at three months after the treatment; however, recovery in the sensory nerve distal latency between the second finger and palm was seen in PH and placebo groups after treatment and at three months after the treatment.

Conclusion: The results of this study suggest that splinting therapy combined with steroid PH, placebo or continuous US is effective for both clinical and electroneurophysiological improvement; however, electroneurophysiological improvement is limited.

Keywords: Carpal tunnel syndrome, steroid phonophoresis, ultrasound.

Carpal tunnel syndrome (CTS) is the most frequent peripheral entrapment neuropathy. It is caused by compression of the median nerve under the transverse carpal ligament at the wrist level.[1] Carpal tunnel syndrome has been attributed to a variety of factors, including endocrinological illnesses, rheumatic diseases, amyloidosis, tumoral formations, traumatic situations, anatomical variances, and infections. It is more prevalent among employees with repetitive wrist movements (e.g., computer keyboard writing, using vibrating tools and working on an assembly operation). Psychological factors can also lead to CTS.[2] The most prevalent cause of CTS is idiopathic CTS, for which no etiological component has been found.[3]

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Therapeutic ultrasound (US), one of the physical therapy techniques used to treat CTS conservatively,[4-7] is a deep warmer that is often employed in the treatment of musculoskeletal problems.[8] On the other hand, phonophoresis is a technique that utilizes US to improve the penetration of topical medications such as local anesthetics, non-steroidal anti-inflammatory drugs, and steroids.[9,10] The most commonly used conservative treatment option is wrist splinting in CTS.[11,12] Splinting of the wrist at the neutral position enables reduction of pressure on the median nerve, while maximizing the volume of the carpal tunnel.[1]

Splint, US, and steroid phonophoresis treatments, which are extensively utilized in the treatment of CTS, have been found to be successful in clinical recovery; however, inconsistent findings regarding electroneurophysiological parameters have been reported.[4-7,9-13] However, no study evaluating the effects of US, stereo phonophoresis, and placebo US in addition to the usage of night splints has been reported in the literature.

In this study, we aimed to compare the efficiency of US and steroid phonophoresis treatments in patients with idiopathic CTS in terms of clinical and electroneurophysiological improvement.

PATIENTS AND METHODS

Study design and study population

This single-center, single-blind, randomized, placebo-controlled clinical study was conducted at Eskişehir Osmangazi University (ESOGU), Faculty of Medicine, Department of Physical Medicine and Rehabilitation between January 2013 and May 2015. Patients with predisposing etiological factors for CTS (diabetes mellitus, acute trauma, rheumatological diseases, pregnancy, hypothyroidism, hyperthyroidism, etc.), cervical radiculopathy or polyneuropathy, reinnervation or fibrillation potentials in the abductor pollicis brevis muscle on electroneuromyography, those who received physical or medical treatment for CTS and who received steroid injections in the previous three months, had median nerve trauma and CTS surgery, severe thenar atrophy and anesthesia, medical problems for whom steroid therapy was contraindicated (steroid allergy, hypertension, etc.) and US therapy was contraindicated (bleeding disorders, acute inflamed joint, acute infection, cancer and precancerous lesions, arteriovenous circulation disorder, etc.) were excluded from the study. Patients who applied to the physical medicine and rehabilitation clinic were screened. At the beginning of the study, all patients had extensive upper extremity examinations, provocative tests for CTS, and electroneuromyographic assessments. All patients had complete blood count, erythrocyte sedimentation rate, comprehensive urine analysis, C-reactive protein (CRP), rheumatoid factor (RF), regular blood biochemistry (fasting blood glucose, uric acid, blood urea nitrogen, creatinine, liver function tests, and electrolytes), and thyroid function tests. As a result of the evaluations, 48 patients (80 hands) with idiopathic mild or moderate CTS were eligible for the study. Twelve (20 hands) patients who did not meet the inclusion criteria and nine patients (14 hands) who refused to participate in the study were excluded from the study. Finally, a total of 46 hands of 27 patients (5 males, 22 females; mean age: 47.3+13.7 years; range, 23 to 67 years) with idiopathic mild/moderate CTS without tenor atrophy or spontaneous activity in abductor pollicis brevis were included. The study flowchart is shown in Figure 1.

Randomization

The patients were randomly divided into three groups using the closed envelope method, numbered from 1 to 3. The first and second groups consisted of 15 hands, while the third group consisted of 16 hands diagnosed with CTS. Each group consisted of nine patients. The patients were asked to choose closed envelopes with steroid phonophoresis, therapeutic US, and placebo. The selected envelope was opened by the physician and the written protocol was applied by the same physician without being told to the patient.

Treatment protocol

Therapies were made by a single physiotherapist. The patients in Group 1 (15 hands, nine patients) underwent continuous US therapy at a frequency of 1 MHz and a power

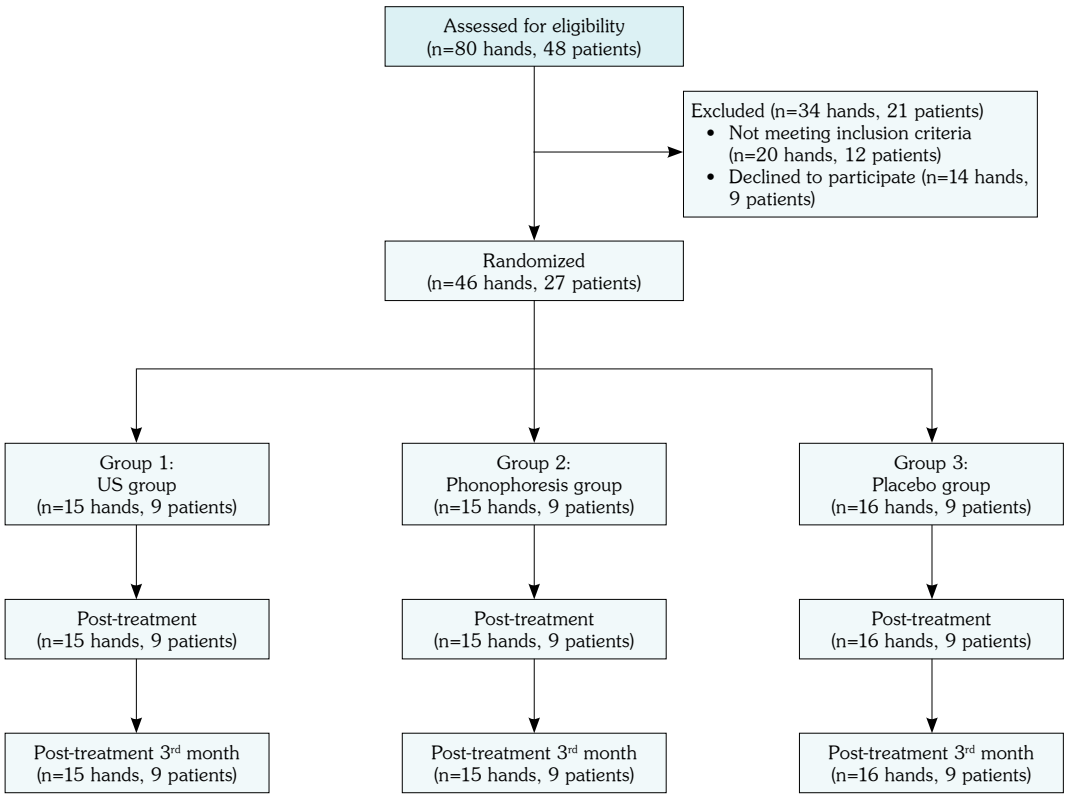

Figure 1. Study flowchart.

density of 1 W/cm^2 for two weeks, five days a week, for 5 min, using a 5 cm diameter applicator (Sonopuls 434 Enraf Nonius, Delft, Netherlands). The patients were positioned in a sitting posture and treated with US utilizing a circular stroke technique and aquasonic gel as a transmission agent. The patients in Group 2 (15 hands, nine patients) were treated with phonophoresis using 0.1% dexamethasone pomade (Maxidex®: ALCON Couvreur n.v. Rijksweg 14 2870 Puurs, Belgium) as a transmitting agent in continuous mode using the same US equipment and technique for 5 min, five days a week, for two weeks. The third patient group comprised of patients (16 hands, nine patients) diagnosed with CTS, received placebo US therapy for 5 min, five days a week for two weeks, using the same equipment and technique.

Splinting

All patients were given a night rest splint on the neutral position of the wrist and patients were instructed to wear the splint for two weeks.

Clinical evaluation

Visual Analog Scale (VAS)

The patients were asked to rate their pain on a scale of 0 to 10, with 0 representing no pain and 10 being the most severe pain they had ever encountered.

Boston carpal tunnel questionnaire (BCTQ)

The questionnaire comprises two parts: symptom severity scale and functional status scale.

Symptom severity scale (SSS)

The patients were asked to choose one of five possible responses to each question on the 11-item questionnaire, with a score ranging from 1 to 5. The mean score was calculated by dividing the total score by the number of questions, with higher scores indicating more symptom severity.[14]

Functional status scale (FSS)

The patients were asked to choose one of five possible responses to each question on the

11 item questionnaire, with a score ranging from 1 to 5. The mean score was calculated by dividing the total score by the number of questions, with higher values indicating impaired hand functioning. The mean score for symptom severity and functional ability were determined separately.[12]

Grip strength

Baseline hydraulic hand dynamometer was used to assess grip strength. Three measurements were made for each patient, and their average was taken.

Electroneurophysiological evaluation

Electroneurophysiological examinations were performed at ESOGU, Department of Neurology, by the same neurologist who was blind to the groups using the MEB-9200K model ENMG instrument manufactured by NIHON-KOHDEN. Medelec Sapphire 4 ME (Medelec, Old Woking, UK) electromyography device.[15] The skin temperature of patients during the ENMG assessment was 32°. All nerve conduction investigations used the orthodromic technique. Motor and sensory conduction investigations were performed across the skin utilizing a superficial stimulator and recording electrodes. The median nerve motor conduction velocity, median nerve motor distal latency, median nerve sensory conduction velocity between the second finger and palm, median nerve sensory distal latency between the second finger and palm, median nerve sensory conduction velocity between the palm and wrist, median nerve sensory conduction velocity between the palm and wrist speed, and median nerve sensory distal latency between the palm and wrist were all evaluated.

In sensory conduction investigations of the median nerve, stimulation of the palm and second finger was used to record from the wrist. Between the stimulator electrode on the second finger and the recording electrode on the wrist, a 14-cm distance was maintained. In the median motor conduction study, electrodes were inserted on the abductor pollicis brevis muscle and stimulation from the wrist and elbow areas was used to record. The recording electrode was placed on the abductor pollicis brevis muscle and the stimulator electrode was placed on the wrist. The distance between the recording electrode and the stimulator electrode was 8 cm. Carpal tunnel syndrome was defined as cases with a sensory conduction velocity less than 44 m/s in the second finger-wrist segment or a median nerve motor distal delay more than 4.2 ms.[15]

Follow-up

Evaluations were recorded on the baseline and post-treatment and at three months after treatment.

Statistical analysis

The study power and sample size calculation were performed using the G*Power version 3.1.9.2 software (Heinrich Heine Universität Düsseldorf, Düsseldorf, Germany). One-way analysis of variance (ANOVA) was performed by taking into account 80% power and 5% type 1 error rate, using statistical information from a pilot study.[16] Accordingly, at least 15 wrists were required for each group.

Statistical analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Continuous quantitative data were expressed in mean ± standard deviation (SD) or median (25^{th} to 75^{th} percentiles), while qualitative data were expressed in n and frequency. The one-way ANOVA and the one-way repeated measures ANOVA were used to analyze normally distributed data including dependent and independent variables, while the Kruskal-Wallis test was used to determine significance. The Friedman one-way ANOVA of ranks on variables that did not exhibit normal distribution, and the repeated measures ANOVA on ranks was applied. A p value of <0.05 was considered statistically significant.

RESULTS

There was no statistically significant difference in the demographic characteristics among the groups ($p>0.05$) (Table 1).

All three groups improved ($p<0.001$) on the VAS, the Boston Symptom Severity (BSS) scale, and the Boston Functional Status (BFS) scale. This improvement was observed immediately after treatment ($p<0.05$) and three months later ($p<0.05$) (Table 2).

Table 1. Demographics features of patient groups

	US (n=15)	Phonophoresis (n=15)	Placebo (n=16)	
	Mean±SD	Mean±SD	Mean±SD	*p*
Age (year)	55.0±11.6	44.9±15.0	42.1±12.0	0.106[a]
Length (cm)	163.4±8.0	163.3±6.9	159.4±4.4	0.362[a]
Weight (kg)	74.4±8.4	73.4±10.1	66.0±9.1	0.127[a]
BMI (kg/m^2)	27.9±2.9	27.8±5.4	25.9±3.0	0.492[a]
Duration of symptom (month)	24.1±15.4	21.9±13.0	14.3±12.0	0.114[a]

US: Ultrasound; SD: Standard deviation; [a] One-way analysis of variance; n= Number of hands diagnosed with CTS.

In all three groups, an improvement was observed, when the grip strength was assessed (p=0.012, p=0.003, p=0.01, respectively). This improvement was significant after treatment for all groups (p<0.05). Group 2 and Group 3 continued to improve at the third month after treatment. However, there was no improvement in the US group at three months (p>0.05) (Table 2).

There was no change in the in the median nerve motor conduction velocity in the US and phonophoresis groups (p=0.933 and p=0.08, respectively). In the placebo US group, a

Table 2. Comparison of repeatedly measured in and inter-group values of clinical parameters

		US (n=15)	Phonophoresis (n=15)	Placebo (n=16)	
	Groups	Mean±SD	Mean±SD	Mean±SD	*p*[1]
VAS	Pre-treatment	5.9±1.4	6.8±2.1	5.2±1.9	0.059[b]
	Post-treatment	3.5±1.8	3.9±2.5	2.6±2.0	0.225[b]
	3rd month	4.1±2.0	3.2±2.5	2.9±1.8	0.159[b]
	P	<0.001[d]	<0.001[c]	<0.001[c]	
SSS	Pre-treatment	2.4±0.6	2.4±0.6	2.5±0.9	0.934[b]
	Post-treatment	1.5±0.4	1.6±0.5	1.8±0.9	0.915[b]
	3rd month	1.7±0.6	1.7±0.4	1.6±0.5	0.670[b]
	P	<0.001[d]	<0.001[c]	<0.001[d]	
	Pairwise comparation p<0.05	1-2, 1-3	1-2, 1-3	1-2, 1-3	
FSS	Pre-treatment	2.3±0.5	2.1±0.5	2.2±0.9	0.418[b]
	Post-treatment	1.6±0.4	1.7±0.4	1.784±0.8	0.738[b]
	3rd month	1.8±0.6	1.7±0.4	1.81±0.8	0.971[b]
	P	<0.001[c]	<0.001[c]	<0.001[d]	
	Pairwise comparation p<0.05	1-2, 1-3	1-2, 1-3	1-2, 1-3	
Grip strength	Pre-treatment	25.1±9.5	19.0±9.5	23.2±8.1	0.174[a]
	Post-treatment	27.5±10.5	21.4±8.3	25.8±8.4	0.180[a]
	3rd month	26.4±12.1	21.9±7.4	25.3±8.2	0.349[a]
	P	0.012[d]	0.003[d]	0.01[c]	
	Pairwise comparation p<0.05	1-2	1-2, 1-3	1-2, 1-3	

US: Ultrasound; SD: Standard deviation; VAS: Visual Analog Scale; SSS: Symptom severity scale; FSS: Functional status scale; [a] One-Way Analysis of Variance; [b] Kruskal-Wallis one-way analysis of variance on ranks; [c] One-Way repeated measures analysis of variance; [d] Friedman repeated measures analysis of variance on ranks.

Table 3. Comparison of repeatedly measured and inter-group values of electroneurophysiological parameters

		US (n=15)	Phonophoresis (n=15)	Placebo (n=16)	
	Group	Mean±SD	Mean±SD	Mean±SD	p^1
mMNCV	Pre-treatment	54.7±5.5	54.6±5.2	55.2±6.8	0.949[a]
	Post-treatment	54.7±5.4	55.4±5.4	59.6±7.2	0.061[a]
	3rd month	56.2±5.5	57.1±3.9	56.7±6.6	0.899[a]
	P	0.933[d]	0.08[c]	0.047[d]	
	Pairwise comparation p<0.05	NS	NS	NS	
mMDL	Pre-treatment	4.5±1.3	4.3±1.1	4.6±1.8	0.434[b]
	Post-treatment	4.4±1.1	4.1±1.3	4.7±2.0	0.458[b]
	3rd month	4.4±1.3	4.1±1.1	4.4±1.6	0.321[b]
	P	0.633[d]	0.155[d]	0.087[d]	
	Pairwise comparation p<0.05	NS	NS	NS	
mSNCV (2nd finger-palm)	Pre-treatment	28.2±11.8	35.3±8.6	28.1±14.8	0.179[b]
	Post-treatment	27.2±14.6	34.7±7.3	29.7±15.7	0.283[b]
	3rd month	32.3±13.0	33.3±9.9	27.1±17.1	0.240[b]
	P	0.880[d]	0.459[c]	0.210[d]	
	Pairwise comparation p<0.05	NS	NS	NS	
mSDL (2nd finger-palm)	Pre-treatment	3.8±0.9	3.6±1.0	3.8±1.1	0.683[b]
	Post-treatment	3.9±1.0	3.4±0.9	3.6±1.1	0.269[b]
	3rd month	3.6±0.7	3.3±0.7	3.5±1.2	0.364[b]
	P	0.678[d]	0.011[d]	<0.001[c]	
	Pairwise comparation p<0.05	NS	1-2, 1-3	1-2,1-3	
mSNCV (palm-wrist)	Pre-treatment	23.6±10.4	22.7±14.9	22.6±12.3	0.858[b]
	Post-treatment	25.0±11.8	30.0±10.2	24.4±13.4	0.318[b]
	3rd month	27.2±3.7	26.18±12.0	23.8±14.6	0.515[b]
	P	0.361[d]	0.185[d]	0.092[d]	
	Pairwise comparation p<0.05	NS	NS	NS	
mSDL (palm-wrist)	Pre-treatment	3.1±0.8	2.4±1.3	2.7±1.1	0.242[a]
	Post-treatment	2.9±0.8	2.2±0.7	2.6±1.1	0.148[a]
	3rd month	2.7±0.5	2.4±0.9	2.6±1.2	0.307[b]
	P	0.003[c]	0.239[d]	0.199[d]	
	Pairwise comparation p<0.05	1-3	NS	NS	

US: Ultrasound; SD: Standard deviation; mMNCV: Median motor nerve conduction velocity; mMDL: Median motor distal latency; mSNCV: Median sensory nerve conduction velocity; NS: Not significant; [a] One-Way Analysis of Variance; [b] Kruskal-Wallis One-Way Analysis of Variance on Ranks; [c] One-Way Repeated Measures Analysis of Variance; d Friedman Repeated Measures Analysis of Variance on Ranks.

significant improvement in the median motor nerve conduction velocity (mMNCV) value was observed, although this improvement could not be calculated when multiple comparisons were made (Student-Newman-Keuls method).

The sensory distal latency of the medial nerve (second finger-palm) improved in the phonophoresis ($p=0.011$) and placebo ($p<0.001$) groups. After treatment ($p<0.05$) and after three months ($p<0.05$), this improvement was substantial (Table 3).

While the median nerve sensory distal latency (palm-wrist) improved in the US group ($p=0.003$), this improvement occurred three months after treatment ($p<0.05$) (Table 3).

Other electrophysiological measures, US, phonophoresis, and placebo groups did not show a significant difference ($p>0.05$) (Table 3).

There was no statistically significant difference in the pre-treatment, post-treatment, and three-month post-treatment values of any clinical and electroneurophysiological parameters among the groups ($p>0.05$) (Tables 2 and 3).

No important adverse events or side effects related to the interventions were reported in any of the patients throughout the study period.

DISCUSSION

Carpal tunnel syndrome is one of the most common hand disorders. Despite the regular use of some treatment modalities, there is no consensus about the most optimal way of managing CTS.[3] The aim of our the placebo-controlled study was to compare the effects of US and phonophoresis treatments in combination with splinting therapy on various clinical and electrophysiological parameters in patients with CTS. As a result of this study, clinical improvements were seen in all groups treated with US, phonophoresis and placebo US, but a partial improvement was detected in electroneurophysiological parameters.

Ultrasound is a deep heating technique that is often employed in the treatment of musculoskeletal disorders. One mechanism of action postulated is that increased temperature causes vasodilation, which results in an increase in metabolic activity and tissue oxygenation. Additionally, an increase in the permeability and suppleness of connective tissue's cell membranes has been reported.[17,18] Numerous studies have shown that US treatment of varying durations, modes, frequencies, and intensities is successful in resolving CTS clinically; however, inconsistent findings have been reported regarding electroneurophysiological recovery.[4-7]

The efficacy of continuous US in CTS has been evaluated in only a few studies.[19,20] In a previous placebo-controlled trial, clinical and electroneurophysiological improvements were reported using US therapy at different doses 1.5 W/cm^2, 0.8 W/cm^2, and 0 W/cm^2.[19] In another placebo-controlled trial evaluating the effect of US at 0.5 W/cm^2 intensity, improvement in clinical variables was observed after treatment, although there was no difference in electroneurophysiological variables.[20]

There are placebo-controlled trials examining various types and frequencies of US treatment in conjunction with a splint in patients with CTS.[4-7] Armagan et al.[4] examined the effectiveness of ten sessions of continuous US at 1 MHz frequency and 1.0 W/cm^2 intensity, as well as 1.0 W/cm^2 1:4 intermittent US treatment at 1 MHz frequency in combination with night splint treatment, in a placebo-controlled study. While clinical improvement was observed in all three groups, improvements in several electroneurophysiological markers were observed in the continuous and intermittent US groups but were not superior to the placebo group. Similarly, in another study comparing continuous (1.0 W/cm^2 intensity at 1 MHz frequency) and intermittent (1:4 intermittent at 1.0 W/cm^2 at 1 MHz frequency) US in addition to night splint to placebo-controlled groups, all groups improved on the VAS, BSS, and BFSscale scores, while only the US groups improved on the coarse grip.[6] All groups demonstrated an improvement in electroneurophysiology. In another study, improvements in VAS and BSS scale assessments were observed following treatment in both groups using continuous US (1.5 W/cm^2 at 3 MHz frequency) and placebo US in addition to night splint treatment. Nevertheless, no improvement in electroneurophysiology was observed.[5]

In this study, 10 sessions of continuous US at a frequency of 1 MHz and a power density of 1 W/cm^2 were used in conjunction with a night rest splint, and it was observed that all clinical parameters improved following treatment, with the exception of grip strength, which remained stable at the three-month mark. At the third month following treatment, there was an improvement in the sensory distal latency between the palms and wrists, one of the electroneurophysiological measures.

As a result, when studies comparing the duration, mode, frequency, and intensity of US were conducted, as well as when studies comparing the agent used and the conservative treatments combined in CTS were conducted, positive results in terms of clinical parameters were obtained, but contradictory results in terms of electroneurophysiological parameters, consistent with the literature.

Phonophoresis is a technique that utilizes US to increase the penetration of topical medications such as local anesthetics, non-steroidal anti-inflammatory drugs, and steroids. High-frequency sound waves have both thermal and non-thermal qualities that increase the diffusion of topically applied medicines. The kinetic energy of the drug molecules in the cell membrane increases upon US heating. The transition points, hair follicles and sweat glands, dilate and blood circulation rises in that location. These physiological changes enable drug molecules to diffuse from the stratum corneum and the capillary network in the dermis to accumulate.[9,21,22]

There are a few placebo-controlled trials examining the efficacy of steroid phonophoresis in CTS.[13,16,23] Similar to our study, Doğan Akçam et al.[13] evaluated the effect of US (1.0 W/cm^2) and steroid phonophoresis (0.1% dexamethasone at 1.0 W/cm^2) at the same dosage and frequency as placebo-controlled groups, while also administering tendon and nerve gliding exercises to all treatment groups. As a consequence, clinical parameters improved significantly in all three groups, but electroneurophysiological parameters improved significantly in the steroid phonophoresis and placebo US groups.

In our study, we used 0.1% dexamethasone phonophoresis at a frequency of 1 MHz and a power density of 1 W/cm^2, and we observed an improvement in all clinical parameters and the second finger-palm median nerve sensory distal delay after treatment and at the three-month mark.

In our study, a night rest splint was used by all of the patients with CTS. Splinting is the most popular and widely used treatment in CTS treatment. The influence of wrist splint therapy has been indicated in several studies.[11,12,24,25] Permoselli et al.[11] reported that splinting therapy improved clinical and electroneurophysiological parameters in CTS patients. In this placebo-controlled trial in which clinical and electroneurophysiological effects of US and steroid phonophoresis combined with splinting were evaluated, all treatment options were shown to be effective in clinical recovery. However, electroneurophysiological evaluations showed limited improvement in all treatment groups.

Contradictory findings have been reported regarding the effects of splint, US, and steroid phonophoresis on electroneurophysiological recovery in CTS.[4-6,11-13] Although the effectiveness of these therapies on nerve regeneration has not been shown, US has been demonstrated to be effective in a limited number of experimental studies.[26-28] Again, it is believed that steroids' anti-inflammatory and tissue stimulating effects.[27-29] and splint therapy may be beneficial for nerve repair in CTS due to their pressure reducing effect on carpal tunnel.[30]

Clinical improvement was observed in all of the splint combination US and 0.1% dexamethasone phonophoresis groups, as well as the placebo US group, in our study; however, electroneurophysiological assessments used to demonstrate the effect of nerve repair showed only modest improvements. It is difficult to determine whether the observed improvement in electroneurophysiology is due to the splint's pressure-reducing effect in the carpal tunnel or to the anti-inflammatory and nerve regeneration effects of US and steroid phonophoresis.

Our study has several limitations. It includes a limited number of patients, blinding of the treating physician was not possible, and the concentration of the steroid administered in the phonophoresis group could not be determined in

the tissue. Additionally, due to ethical constraints, no control group without splint treatment could be developed.

There is currently no agreement about treatment strategies for CTS. The merit of this study was that it compared the effectiveness of splint, US, and steroid phonophoresis in a randomized, placebo-controlled fashion. We believe that our terms would add to the body of knowledge on the standardization of conservative treatment techniques.

In conclusion, our study results suggest that splinting therapy combined with steroid phonophoresis, placebo or continuous ultrasound is effective for both clinical and electroneurophysiological improvement; however, electroneurophysiological improvement is limited. We believe that further well-designed, evidence-based, placebo-controlled, randomized studies involving a large number of patients are necessary to assess the effect of conservative treatment options in CTS.

Ethics Committee Approval: The study protocol was approved by the ESOGU, Faculty of Medicine, Clinical Research Ethics Committee (no: 80558721/92). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Concept, design, writing, materials, data collection and/or processing: B.O, O.A.; Supervision: B.O.; Analysis and/or interpretation: S.O, B.O.; Literature review: B.O, O.A, F.B.; Critical reviews: B.O, O.A, F.B, M.O, F.B.; References: B.O, O.A, F.B, M.O.

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