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ORIGINAL ARTICLE

Evaluation of the efficacy of low-level laser therapy in the treatment of ulnar neuropathy at the elbow in terms of symptoms and clinical and electrophysiological findings: a randomized, prospective, double-blind clinical trial

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Abstract

Ulnar neuropathy at the elbow (UNE) is the second most common entrapment neuropathy and presents with symptoms such as pain, paresthesia, and weakness in the elbow. Provocative tests and electrophysiological examinations are helpful in the diagnosis of UNE. Low-level laser therapy is one of the conservative treatments of UNE however, limited results were reported on the effectiveness of low-level laser therapy (LLLT) in the treatment of UNE. In our study, we aimed to the efficacy of LLLT in reducing symptoms and providing clinical and electrophysiological improvement in patients with UNE. This study with a randomized-sham controlled, and double-blind design included 68 patients aged 18–60 years who were diagnosed with UNE. LLLT was applied to the first group, and sham laser was applied to the second group. The VAS pain, paresthesia, and weakness scores, grip strength, and provocative test positivity were evaluated in clinical examination. The QuickDASH questionnaire was administered to assess functional status. Electrophysiologically, motor distal latency (MDL) differences, sensory distal latency (SDL), motor and sensory nerve conduction velocity (NCV) were examined. Evaluations were performed before treatment and on the 15th day and at the third month after treatment. The LLLT group showed improvement in symptoms, clinical findings, motor NCV, and MDL at both post-treatment evaluations and sensory NCV on the post-treatment 15th day ($p < 0.05$). The comparison of post-treatment changes between the two groups revealed that the LLLT group had greater improvement in VAS day and night pain scores at both post-treatment evaluation times, QuickDASH scores at the third month, and sensory NCV on the 15th day ($p < 0.05$) compared to the SL group. There were no significant differences between the groups in terms of the post-treatment changes in VAS weakness scores, grip strength and electrophysiological findings ($p > 0.05$). It was observed that splinting alone was effective in UNE, but the addition of LLLT, one of the conservative treatment methods, enhanced treatment outcomes.

Keywords Low-level laser therapy · Splint · Ulnar nerve entrapment · Electroneuromyography

Introduction

Ulnar neuropathy at the elbow (UNE) is the second most common entrapment neuropathy of the upper extremity. The ulnar nerve is susceptible to entrapment due to its anatomical location within the elbow. The cubital tunnel and epicondylar groove are the most frequent sites of entrapment [1]. A study investigating the annual incidence of UNE reported it to be 24.7/100,000, with a higher prevalence observed in men [2].

UNE occurs most often as a result of chronic mechanical compression or stretching. The repetitive flexion-extension of the elbow increases the pressure in both the cubital tunnel and other potential entrapment sites, causing tension in the ulnar nerve and increasing intraneural pressure [3]. Other causes of entrapment include compressive masses, cubitus valgus deformity, and fibrous bands [4]. Having a low body mass index (BMI), smoking, and having systemic diseases, such as diabetes, thyroid diseases, and rheumatoid arthritis, all contribute to an increased risk of UNE.

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A detailed anamnesis and a comprehensive physical examination are the basic first steps in making an accurate diagnosis of UNE. In the presence of suspicion, especially electrophysiological examinations play an important role in diagnosis through the assessment of both the location of nerve compression and the severity of the disease [5].

Patients with UNE often complain of paresthesia symptoms, such as numbness and tingling in the fifth finger and the ulnar half of the fourth finger. Due to the ulnar innervation of the majority of intrinsic hand muscles, weakening in these muscles leads to reduced grip strength [4]. Patients may report experiencing pain and sensitivity at the level of the elbow [6].

Both conservative and surgical methods are available for the treatment of UNE. In most patients, especially in cases of mild and moderate entrapments, conservative methods are preferred over surgery as the initial treatment. These methods include activity modification, splinting, exercise, physical therapy agents, and injections. Low-level laser therapy (LLLT), one of the physical therapy modalities, creates photochemical reactions and biostimulation in the cells, interstitial tissue, vascular structure, and immune system. This mechanism, also known as photobiomodulation, involves the absorption of photons. This absorption triggers the activation of transcription factors through cytochrome c oxidase, ion channels, and signaling molecules. Consequently, this process promotes increased expression of genes associated with protein synthesis, cell migration, proliferation, and antioxidant enzymes [7].

LLLT exerts an anti-inflammatory effect by inhibiting the cyclooxygenase-2 enzyme and reducing the level of prostaglandin E2, while its analgesic effect occurs through the inhibition of a nociceptive pathway in peripheral nerves, which decreases pain [8, 9].

Studies have demonstrated that LLLT increases nerve regeneration and nerve conduction, reduces the effects of nerve compression, and may stimulate nerve healing due to its biophysical effect [10, 11]. Several studies have evaluated the efficacy of low-level laser therapy (LLLT) in carpal tunnel syndrome (CTS). Chang et al. conducted a placebo-controlled study and found that patients with CTS who received LLLT experienced a reduction in pain scores, an increase in grip strength, and improvements in functional scores by the second week [12]. Double-blind randomized controlled trials by Lazovic et al. demonstrated the superiority of LLLT over placebo and its short-term effectiveness [13]. Similarly, Fusakul et al. reported significant improvements in clinical and electrophysiological assessments and an increase in grip strength in the LLLT group [14].

In the treatment of ulnar nerve entrapment (UNE), Ozkan et al. conducted a randomized, single-blind study investigating the efficacy of ultrasound and low-level laser therapy (LLLT). Both treatment groups showed significant improvements in clinical and electrophysiological parameters within the first month [15]. However, the absence of a placebo group limited the study's ability to conclusively demonstrate the efficacy of LLLT. To our knowledge, there are no studies evaluating the efficacy of LLLT in UNE, the second most common entrapment neuropathy of the upper extremity. Therefore, our prospective, double-blind, randomized clinical trial aimed to investigate the efficacy of LLLT on symptoms and clinical and electrophysiological parameters in patients with UNE.

Material and method

Study design and participants

The study was designed as a sham-controlled, randomized, and double-blind study. Eighty-three patients diagnosed with UNE were evaluated at the Physical Medicine and Rehabilitation Clinic of the Health Sciences University Antalya Training and Research Hospital between June 2022 and May 2023. These patients were screened for eligibility criteria, and a total of 68 patients, one elbow for each, were included in the sample (Fig. 1). All patients completed the treatment program and the three-month follow-up period. The patients were given detailed information about the study. All patients were informed regarding the importance of refraining from provocative activities (avoiding a bent elbow position for a long time, including while sleeping, and not resting the elbow on hard surfaces). They were also recommended to wear a neoprene splint at night for three weeks, with the elbow maintained in 45° flexion.

Inclusion criteria

Inclusion criteria were accepted as electrophysiologically confirmed entrapped ulnar neuropathy detected between 4 cm below the elbow and 6 cm above the elbow, paresthesia in the fourth and fifth fingers, corresponding to the distribution of the ulnar nerve in the hand, and weakness in the hand during rough grasping movements; an age between 18 and 60 years; the presence of the symptoms, such as elbow pain and night complaints for at least one month; and the provision of written consent.

Exclusion criteria

The exclusion criteria were the presence of thenar, hypothenar, or intrinsic muscle atrophy, diabetes mellitus, and hypothyroidism; electrophysiologically confirmed carpal tunnel syndrome, cervical radiculopathy, brachial

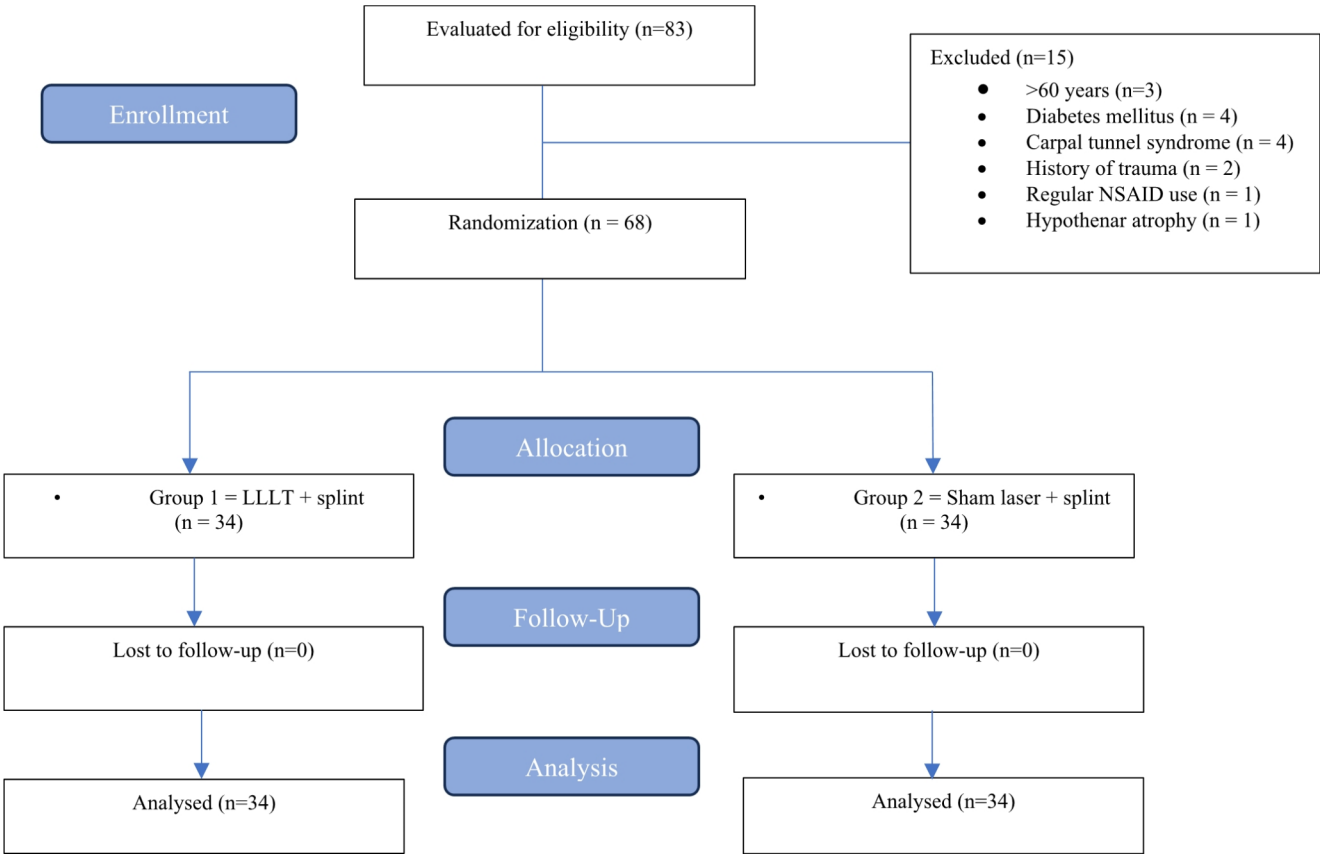


Fig. 1 Patients included in the study

plexopathy, thoracic outlet syndrome, Raynaud's syndrome, ulnar nerve transection, or trauma; malignancy; having received treatment for UNE within the past three months; and the regular use of non-steroidal anti-inflammatory drugs.

Interventions

LLLT group

LLLT group In the first group, i.e., the LLLT group, the Ga-Al-As device (Medical Italia PR999 4 W), available in the Physical Therapy Unit of our clinic, was used. A total of 15 sessions were applied to the patients, five days a week for three weeks. While the elbow was in 45° flexion, laser was continuously applied at 2j/cm^2, 808 nm wavelength, and 5,000 Hz to five separate points, resulting in a total dose of 10j/cm^2. These points were spaced 2 cm apart at a distance of 4 cm below the elbow and 6 cm above the elbow. Each point was treated for 1 min, resulting in a total treatment time of 5 min (Fig. 2.). An expert physiotherapist administered laser therapy.

Sham laser (SL) group

Sham laser (SL) group

The second group, i.e., the SL group, received 0 j/cm^2 laser treatment applied to the same area at 0 nm wavelength for the same duration and for the same number of sessions by the same physiotherapist.

Outcome assessments

The demographic data and clinical findings of all patients were evaluated before treatment. Day and night pain in the elbow and paresthesia and weakness in the ulnar nerve in the hand were questioned using the Visual Analog Scale (VAS). The VAS comprises a 10-cm line on which the patients are asked to express the severity of pain. One end of this line (0 cm) indicates no complaints (best) and the other end (10 cm) indicates very severe complaints (worst). In patients with carpal tunnel syndrome, Doğan et al. It is

Fig. 2 Parameters of LLLT

Parameter (unit)	Value
Diode laser device.	Ga-Al-As (Medical Italia PR999 4W)
Wavelength	808 nm
Frequency	5000 Hz/Continuous output
Energy density.	2 J/cm^2 in each point
Total dose	10 J/cm^2 (five separate point)
Laser prob size	0.5 cm^2
Average power	50 mW
Power density	0.1 W/cm^2
Application mode	Directly and perpendicularly on the skin from 5 points.
Treatment time	60 s at each point (5 min of total treatment time)
Total irradiation sites	5 (These points were spaced 2 cm apart at a distance of 4 cm below the elbow and 6 cm above the elbow.)
Treatment duration	5 days a week for 3 weeks (Total 15 times)

a survey approved in Turkish in terms of validity and reliability [16].

During clinical examinations, hand grip strength and the positivity of provocative tests were evaluated. The QuickDASH questionnaire was used to evaluate functional status. Electrophysiologically, motor distal latency (MDL) changes, motor nerve conduction velocity (NCV), sensory NCV, and sensory distal latency (SDL) were examined in the trapped region.

All groups were evaluated by the same researcher in terms of symptoms, clinical examinations, and electrophysiological findings three times in total: before treatment, on the 15th day after treatment, and at the third month after treatment.

Provocative tests

Tinel's test involves lightly tapping over the ulnar nerve in the medial epicondylar groove. In the elbow flexion (EF) test, the elbow is held in maximum flexion, the forearm in supination, and the wrist in full extension for 60 s. In the ulnar nerve compression (UNC) test, the elbow is kept in 20° flexion and the forearm in supination position. The examiner places the index and middle fingers over the cubital tunnel and applies pressure for 60 s. In all of these tests, if paresthesia or numbness occurs in the ulnar nerve distribution, the result is considered positive [17].

Hand grip strength

As per the recommendation of the American Society of Hand Therapists, the patient was instructed to firmly grip their hand while keeping the shoulder in adduction and neutral rotation, the elbow in 90° flexion, the forearm in mid-rotation, and the wrist in neutral position [18]. The Jamar hand dynamometer (Jamar Hand Dynamometer Hydraulic, 200 LB capacity) was used for the measurements. Three measurements were recorded in kilograms (kg), with one-minute intervals between each measurement, and the averages were recorded.

QuickDASH questionnaire

This questionnaire consists of 11 questions aiming to rapidly evaluate arm-shoulder-hand problems. Using this instrument, the functional evaluation of the patients' upper extremities was performed, and strains during daily living activities were questioned. The best total score is 0, and the worst total score is 100 [19].

Electrophysiological examinations

Electrophysiological examinations were performed using the Nihon Kohden Neuropack S1 MEB-9400 K EMG device available at the Physical Medicine and Rehabilitation EMG Laboratory of the University of Health Sciences Antalya Training and Research Hospital. Median and ulnar NCSs were conducted, and lower trunk lesions with similar symptoms were examined in medial antebrachial cutaneous NCS to exclude thoracic outlet syndrome pathologies. For ulnar nerve short-segment NCS (inching), the forearm was placed in supination and the elbow at 45 degrees of flexion, and six points were marked at 2-cm intervals between the area 4 cm distal to the medial epicondyle and the area 6 cm proximal to the medial epicondyle. Supramaximal stimulation was applied to the ulnar nerve at the marked points

and wrist by recording activity at the abductor digiti minimi muscle. The differences in MDL between the six evaluated points, as well as motor NCV at the elbow were recorded. For the ulnar nerve sensory NCS, the active electrode was placed on the fifth metacarpophalangeal joint, and the reference electrode was placed 2–3 cm distal to the joint. Stimulation was applied from the medial edge of the wrist using the antidromic technique. SDL and sensory NCV were recorded. The main criterion for UNE was accepted to be a delay of > 0.8 m/s between the consecutive points evaluated in MDL or a motor NCV of < 50 m/s in the elbow, with at least one of these parameters being present. In addition, if there was a delay of > 3.1 m/s in SDL and the ulnar sensory NCV was slower than < 43 m/s, each of these criteria was recorded as supportive of the UNE diagnosis [4].

Sample size calculation and randomization

The sample size was determined using the G*power 3.1.9.2 program (power [1-β] = 0.8; α = 0.05; effect size: 0.70) [20]. Accordingly, the required sample size was calculated to be a total of 68 patients: 34 in the LLLT group and 34 in the SL group. The patients were randomized into the two groups using Random Allocation Software.

Blinding

Since light was emitted from the probe in the laser applications used in both groups, the patients were unable to discern which group they had been assigned to, i.e., they were blinded to the groups. All outcome measures were evaluated by another researcher who did not know the group assignments of the patients, ensuring that the study was conducted in a double-blind manner.

Statistical analysis

In this study, statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) v.15.0 for Windows. In the analysis of categorical data, Fisher's exact test was used if the percentage of cells where the expected value was less than 5 was greater than 20%, and the Pearson chi-square test was used otherwise. The assumption of normality was checked with the Shapiro-Wilk test. In the analysis of the difference between the numerical data of the two groups, the independent-samples t-test was used when the data conformed to the normal distribution, and the Mann-Whitney U test was used otherwise. $P < 0.05$ was considered statistically significant. Effect sizes were calculated using Jamovi [21].

Results

No significant difference was found between the LLLT and sham groups in terms of the demographic data, pre-treatment symptoms, and clinical and electrophysiological findings ($p > 0.05$) (Table 1).

There was a significant decrease in VAS day and night pain scores in both groups at the post-treatment 15th day and third month compared to before treatment ($p < 0.05$). While the LLLT group showed a significant improvement in VAS paresthesia, VAS weakness, and grip strength scores at both post-treatment evaluation times compared to the pre-treatment values, the SL group had a significant improvement in these scores only at the post-treatment third month ($p < 0.05$) **(**Table 2**).** In both groups, the QuickDASH scores significantly decreased at both post-treatment evaluation times compared to the pre-treatment evaluation ($p < 0.05$). Concerning the motor NCV values of the affected ulnar nerve, there was a significant improvement at both post-treatment evaluation times for the LLLT group and only on the post-treatment 15th day for the SL group ($p < 0.05$). The differences in MDL between the six evaluated points in the entrapped area of the elbow showed a significant decrease in both groups at both post-treatment evaluation times compared to the pre-treatment period ($p < 0.05$). In addition, compared to the pre-treatment values, the sensory NCV of the ulnar nerve showed a significant increase only on the post-treatment 15th day in the LLLT group ($p < 0.05$), while there was no significant change in the SL group ($p > 0.05$). Lastly, no significant difference was observed in the SDL of the ulnar nerve between the pre-treatment and post-treatment evaluations of either group ($p > 0.05$) (Table 3).

Among the provocative tests performed to evaluate clinical findings, Tinel test positivity was detected in both groups at the post-treatment 15th day and third month compared to the pre-treatment period ($p < 0.05$). In the LLLT group, there was a significant decrease in EF test positivity at both post-treatment evaluations compared to the pre-treatment evaluation ($p < 0.05$), but the SL group showed no significant change ($p > 0.05$). While a significant decrease was observed in UNC test positivity in the LLLT group at both post-treatment evaluation times compared to the pre-treatment period ($p < 0.05$), a significant decrease was detected only at the post-treatment third month in the SL group ($p < 0.05$). When comparing the groups, at the third month post-treatment, all three provocative tests showed a statistically significant decrease in the LLLT group compared to the sham laser group ($p < 0.05$). Additionally, this significant reduction was also observed in the Tinel and UNC tests at the post-treatment 15th day ($p < 0.05$) (Table 4).

Upon analyzing the pre-to-post-treatment change scores between the groups, a statistically significant difference was

Table 1 Demographic and clinical characteristics of the patients in the LLLT and sham laser groups

	LLLT group ($n=34$)			Sham laser group ($n=34$)			
	n	Mean ± SD	(Min-Max)	*n*	Mean ± SD	(Min-Max)	*P*
Age (year)		42.32 ± 11.26	(21–60)		45.71 ± 11.15	(20–60)	0.218[1]
Sex (female/male)	15/19			13/21			0.622[1]
BMI (kg/m²)		26.22 ± 4.56	(17.91–42.97)		27.75 ± 4.18	(22.22–38.51)	0.155[1]
Affected hand (right/left)	19/15			14/20			0.225[3]
Repetitive motion time (hour/day)		4.87 ± 2.49	(1–12)		4.62 ± 1.8	(2–8)	0.698[1]
Duration of complaints (month)		10.29 ± 8.06	(1–24)		8.85 ± 6.21	(1–24)	0.749[2]
VAS pain, day		6.62 ± 1.56	(4–10)		6.21 ± 1.84	(2–10)	0.393[2]
VAS pain, night		7.35 ± 2.14	(2–10)		6.85 ± 2.22	(2–10)	0.310[2]
VAS paresthesia		7.68 ± 1.75	(3–10)		6.76 ± 2.35	(0–10)	0.067[2]
VAS weakness		5 ± 3.64	(0–10)		4.82 ± 2.98	(0–10)	0.686[2]
Tinel test positivity (%)	79			82			0.758[2]
EF test positivity (%)	64			58			0.618[2]
UNC test positivity (%)	73			67			0.595[2]
Grip strength (kg)		27.18 ± 12.85	(10-58.3)		28.28 ± 10.89	(10-49.3)	0.706[2]
QuickDASH		54.67 ± 16.72	(22.5–88.5)		52.98 ± 19.08	(13.5–79.5)	0.873[2]
Motor NCV (m/sec)		42.31 ± 4.73	(29.9–50)		41.7 ± 5.94	(26.5–51)	0.643[2]
MDL difference (msec)		0.94 ± 0.13	(0.8–1.24)		0.96 ± 0.19	(0.8–1.6)	0.971[2]
Sensory NCV (m/sec)		48.44 ± 5.78	(34.6–61.1)		47.1 ± 6.13	(35.5–58.1)	0.512[2]
SDL (msec)		2.39 ± 0.36	(1.68–3.18)		2.52 ± 0.42	(1.72–3.32)	0.148[2]

[1]Independent-samples t-test, [2]Mann-Whitney U test, [3]Pearson chi-square test

LLLT: low-level laser therapy, SD: standard deviation, BMI: body mass index, EF: elbow flexion, UNC: ulnar nerve compression, NCV: nerve conduction velocity, MDL: motor distal latency, SDL: sensory distal latency

Table 2 Post-treatment changes in VAS scores evaluations within the groups

	Pre-treatment (T0)		Post-treatment day 15 (T1)		Post-treatment month 3 (T2)		T0-T1	T0-T2
	Mean ± SD	(Min-Max)	Mean ± SD	(Min-Max)	Mean ± SD	(Min-Max)	*p*	*p*
VAS pain, day								
LLLT group	6.62 ± 1.557	(4–10)	3.26 ± 2.352	(0–9)	2.32 ± 2.815	(0–10)	**0.003**	**< 0.0001**
Sham laser group	6.21 ± 1.839	(2–10)	4.35 ± 2.497	(0–8)	3.71 ± 2.541	(0–9)	**0.033**	**< 0.0001**
VAS pain, night								
LLLT group	7.35 ± 2.145	(2–10)	3.06 ± 2.943	(0–10)	2.38 ± 3.191	(0–10)	**< 0.0001**	**< 0.0001**
Sham laser group	6.85 ± 2.217	(2–10)	4.59 ± 3.036	(0–10)	4.18 ± 3.109	(0–10)	**0.006**	**< 0.0001**
VAS paresthesia								
LLLT group	7.68 ± 1.753	(3–10)	3.82 ± 3.233	(0–10)	2.15 ± 2.819	(0–10)	**< 0.0001**	**< 0.0001**
Sham laser group	6.76 ± 2.349	(0–10)	4.5 ± 2.766	(0–9)	3.97 ± 2.78	(0–9)	0.064	**0.005**
VAS weakness								
LLLT group	5 ± 3.643	(0–10)	2.79 ± 3.236	(0–10)	1.41 ± 2.653	(0–10)	**0.023**	**< 0.0001**
Sham laser group	4.82 ± 2.979	(0–10)	3.26 ± 2.821	(0–10)	2.71 ± 2.898	(0–10)	0.118	**< 0.0001**

observed in favor of the LLLT group for VAS day pain, night pain, and paresthesia scores for both the 15th day and third month ($p < 0.05$). There were no significant differences between the groups in terms of changes in VAS weakness, grip strength, motor NCV, MDL difference, or SDL parameters for either post-treatment evaluation time ($p > 0.05$). While there was no significant difference between the groups in QuickDASH scores for the post-treatment 15th day ($p > 0.05$), a significant difference was detected in favor of the LLLT group for the post-treatment third month ($p > 0.05$). Lastly, there was a significant difference in sensory NCV between the groups in favor of the LLLT group on the post-treatment 15th day ($p < 0.05$), but no significant difference was found at the post-treatment third month ($p > 0.05$) (Table 5).

Discussion

In UNE, the aim of treatment is to relieve symptoms by eliminating or reducing the compression on the nerve [15]. LLLT, one of the physical therapy modalities, is known to

Table 3 Post-treatment changes in grip strength, QuickDASH scores, and electrophysiological evaluations within the groups

	Pre-treatment (T0)		Post-treatment day 15 (T1)		Post-treatment month 3 (T2)		T0-T1	T0-T2
	Mean ± SD	(Min-Max)	Mean ± SD	(Min-Max)	Mean ± SD	(Min-Max)	*p*	*p*
Grip strength (kg)								
LLLT group	27.18 ± 12.85	(10-58.3)	31.52 ± 12.41	(9–65)	34.17 ± 14.65	(10-61.30)	**< 0.0001**	**< 0.0001**
Sham laser group	28.28 ± 10.89	(10-49.3)	30.11 ± 12.17	(11.30–56)	32.26 ± 13.00	(10-59.60)	0.139	**0.004**
QuickDASH								
LLLT group	54.67 ± 16.72	(22.5–88.5)	27.99 ± 18.32	(0–68)	19.59 ± 23.12	(0–75)	**< 0.0001**	**< 0.0001**
Sham laser group	52.98 ± 19.08	(13.5–79.5)	36.15 ± 20.50	(4.5–75)	34.23 ± 22.60	(0–75)	**0.007**	**0.001**
Motor NCV (m/sec)								
LLLT group	42.31 ± 4.73	(29.9–50)	49.14 ± 7.79	(32.90–65.80)	49.57 ± 9.81	(25.60–72.50)	**0.0001**	**0.0001**
Sham laser group	41.70 ± 5.93	(26.50–51)	45.62 ± 6.71	(29.60–55.80)	44.89 ± 8.35	(26.60–58.10)	**0.015**	0.097
MDL difference (msec)								
LLLT group	0.94 ± 0.13	(0.8–1.24)	0.63 ± 0.26	(0.22–1.22)	0.68 ± 0.37	(0.14–1.82)	**< 0.0001**	**0.003**
Sham laser group	0.96 ± 0.19	(0.8–1.6)	0.73 ± 0.28	(0.22–1.32)	0.80 ± 0.40	(0.2–1.94)	**< 0.0001**	**0.046**
Sensory NCV (m/sec)								
LLLT group	48.44 ± 5.78	(34.60–61.10)	51.66 ± 6.71	(34-67.90)	51.41 ± 6.50	(35.50–63.20)	**0.012**	0.091
Sham Laser group	47.1 ± 6.13	(35.50–58.10)	45.84 ± 7.30	(27.40–59)	47.45 ± 9.57	(21.70–59.10)	0.741	0.99
Sensory distal latency (msec)								
LLLT group	2.39 ± 0.36	(1.68–3.18)	2.25 ± 0.37	(1.62–3.2)	2.26 ± 0.32	(1.56–2.82)	> 0.05 0,424	> 0.05 0,160
Sham laser group	2.52 ± 0.42	(1.72–3.32)	2.65 ± 0.58	(2.01–4.74)	2.58 ± 0.73	(1.72–4.84)	> 0.05 0,499	> 0.05 0,297

Friedman test used in all analyses

VAS: Visual Analog Scale, T0-T1: pre-treatment vs. post-treatment day 15, T0-T2: pre-treatment vs. post-treatment month 3, SD: standard deviation, LLLT: low-level laser therapy, NCV: nerve conduction velocity, MDL: motor distal latency, SDL: sensory distal latency

have anti-inflammatory, analgesic, biostimulant, and nerve-regeneration effects [10]. In the current study, we planned to investigate the efficacy of LLLT in the treatment of UNE.

Splinting and activity modification, which are generally the first choice among conservative treatments, were applied to both groups in our study. In the literature, Shah et al. preferred the treatment of fixed rigid splinting at 45 degrees used at night for three months in patients with UNE [22]. In the study conducted by Svernlov et al., a fixed splint at 45 degrees to be worn at night for three months was recommended for patients with cubital tunnel syndrome [23]. In line with literature recommendations, the patients were recommended to wear their splints at night, with the elbow flexed at 45°. The duration of splint use in our study was set at three weeks to enhance patient compliance, as well as considering the short follow-up period.

In the literature, there is no consensus concerning the details of laser application procedures, such as the type of laser used, wavelength, duration, and dosage [15, 24]. In our study, we administered laser therapy to five points at a wavelength of 808 nm, a frequency of 5,000 Hz, and a dose of 2j/cm^2 in continuous mode for 15 sessions. Each point received treatment for 60 s, resulting in a total of 300 s per session.

In a randomized controlled study investigating the efficacy of LLLT in carpal tunnel syndrome, Evcik et al. applied LLLT to one group and SL to another group. The authors showed no significant difference between the two groups in terms of the VAS pain scores evaluated at the third week, but the improvement in pain continued only in the LLLT group through the 12th week [25]. In our study, there was a significant decrease in VAS day and night pain scores in both groups at the post-treatment 15th day and third month compared to the pre-treatment period. Upon analyzing the post-treatment changes in pain between the groups compared to the pre-treatment values, we observed that the LLLT group experienced more pain reduction than the SL group at both post-treatment evaluation times. During laser treatment, the photoreceptors of the mitochondrial membranes in the dorsal root ganglion decrease the mitochondrial membrane potential by absorbing laser wave energies and block pain transmission. This neural blockade can explain the acute effect of photomodulation therapy [26]. The long-term effect of laser therapy can be explained

Table 4 Post-treatment changes in provocative test results within the groups

	Pre-treatment (T0)	Post-treatment day 15 (T1)	Post-treatment month 3 (T2)	T0-T1	T0-T2
	n (%)	**n (%)**	**n (%)**	$p^{\dagger}$	$p^{\dagger}$
Tinel test positivity (%)					
LLLT group	79	35	20	**< 0.0001**	**< 0.0001**
Sham laser group	82	52	50	**< 0.0001**	**< 0.0001**
$p^{\dagger\dagger}$	*0,592*	***0,014***	***< 0,0001***		
EF test positivity (%)					
LLLT group	64	38	32	**0.023**	**0.003**
Sham laser group	58	44	50	0.139	0.282
$p^{\dagger\dagger}$	*0,383*	*0,387*	***0,008***		
UNC test positivity (%)					
LLLT group	73	38	26	**0.004**	**< 0.0001**
Sham laser group	67	52	47	0.195	**0.029**
$p^{\dagger\dagger}$	*0,354*	***0,044***	***0,002***		

$p^{\dagger\dagger}$: Intergroup comparison of provocative tests

†: Cochran's Q test ††: Two proportion z test

T0-T1: pre-treatment vs. post-treatment day 15, T0-T2: pre-treatment vs. post-treatment month 3, LLLT: low-level laser therapy, EF: elbow flexion, UNC: ulnar nerve compression

by the mechanisms of inhibiting nociceptive pathways, changing the pain threshold, and reducing the release of pro-inflammatory neuropeptides [27].

According to our results, there was a decrease in the VAS paresthesia score of the LLLT group at the post-treatment 15th day and third month compared to the pre-treatment period. However, in the SL group, there was only a decrease in the post-treatment third month. The comparative analysis of the post-treatment changes in paresthesia scores between the groups revealed that the LLLT group experienced a greater reduction in paresthesia than the SL group at both post-treatment evaluation times. Yamany et al. stated that laser therapy alleviated pain in cases of diabetic polyneuropathy and might be an effective treatment method for improving neurovascular function. The authors showed that this effect of the laser could lead to improvements in peripheral nerve function by increasing blood flow at the endoneural level and suppressing inflammation [28]. The observed reduction of paresthesia symptoms in our study can be attributed to this mechanism.

We observed a significant improvement in hand grip strength and VAS weakness scores in the LLLT group at both post-treatment evaluations compared to the pre-treatment period, while the SL group showed significant improvement only at the post-treatment third month. There were no significant differences between the two groups in terms of the post-treatment changes in hand grip strength or VAS weakness scores compared to the pre-treatment values. One possible explanation for this finding is that the muscles innervated by the median nerve also have an effect on the grasping movement of the hand, and the weakness of these muscles affects grip strength, which may mask patients' responses to treatment.

In a study investigating the efficacy of laser therapy in improving clinical findings in patients with carpal tunnel syndrome, Jiang et al. reported that the provocative tests Tinel and Phalen became significantly negative at the second- and fifth-week follow-up [29]. In our study, the positivity rates for the Tinel, EF, and UNC tests decreased in the LLLT group at the post-treatment 15th day and third month compared to the pre-treatment values. In the SL group, Tinel test positivity decreased at both post-treatment evaluations, but UNC test positivity decreased only at the third month. We consider that the decrease in Tinel test positivity in both groups could be due to its low sensitivity and specificity. When comparing between groups, significant improvements were observed in the LLLT group in all provocative tests at the third month, and in the Tinel and UNC tests at the post-treatment 15th day compared to the pre-treatment values. The greater reduction in the laser group compared to the SL group indicates a better response to treatment, suggesting that LLLT is more effective in alleviating symptoms. The positive results of provocative tests caused by inflammation and compression in the pre-treatment period became negative following treatment through the anti-inflammatory and nerve regeneration effects of laser therapy, and these improvements were reflected in clinical findings.

In a study comparing the efficacy of laser and corticosteroid treatments in carpal tunnel syndrome, Güloğlu et al. showed a decrease in the QuickDASH scores of both groups at the post-treatment first and sixth months [30]. In our study, the decrease in QuickDASH scores in the LLLT and SL groups at the post-treatment 15th day and third month compared to the pre-treatment period was consistent with the literature. Concerning the intergroup comparison of post-treatment QuickDASH score changes between the groups, the improvement at the third month with reference to the pre-treatment evaluation was found to be more significant in the LLLT group than in the SL group. In our study, laser therapy reduced the patients' complaints and contributed to secondary functional recovery through its biostimulant effects on the nerve tissue and analgesic and anti-inflammatory properties.

Table 5 Intergroup comparison of post-treatment changes in VAS scores, grip strength, QuickDASH scores, and electrophysiological evaluations

	Post-treatment day 15					Post-treatment month 3				
	LLLT group		Sham laser group			LLLT group		Sham laser group		
	Mean ± SD	(Min-Max)	Mean ± SD	(Min-Max)	*p*	Mean ± SD	(Min-Max)	Mean ± SD	(Min-Max)	*p*
VAS pain, day	-3.35 ± 2.78	(-10-0)	-1.85 ± 2.09	(-8-0)	**0.023**	-4.29 ± 2.89	(-10-4)	-2.5 ± 2.31	(-7-2)	**0.003**
VAS pain, night	-4.29 ± 3.05	(-10-0)	-2.26 ± 2.55	(-9-0)	**0.005**	-4.97 ± 3.2	(-10-4)	-2.68 ± 2.8	(-9-2)	**0.002**
VAS paresthesia	-3.85 ± 3.1	(-10-0)	-2.26 ± 3.11	(-10-2)	**0.034**	-5.53 ± 2.82	(-10-2)	-2.79 ± 3.44	(-10-3)	**0.001**
VAS weakness	-2.21 ± 2.75	(-10-0)	-1.56 ± 2.35	(-8-0)	0.26	-3.59 ± 3.47	(-10-2)	-2.12 ± 3.26	(-8-9)	0.159
Grip strength (kg)	4.34 ± 6.3	(-10-22.3	1.84 ± 4	(-4.67-14.3)	0.055	7 ± 8	(-8-21.9)	3.99 ± 5.8	(-6-18.3)	0.213
QuickDASH	-26.67 ± 19.99	(-63.5-0)	-16.82 ± 21.45	(-72.75-27.5)	0.057	-35.07 ± 24.64	(-88.5-22.75)	-18.74 ± 24.17	(-61.5-36.5)	**0.011**
Motor NCV (m/sec)	6.83 ± 8.41	(-11.7-24.1)	3.92 ± 7.3	(-11.1-15.9)	0.132	0.43 ± 9.56	(-17.5-16.4)	-0.73 ± 6.43	(-12.3-17.5)	0.56
MDL difference (msec)	-0.31 ± 0.28	(-0.78-0.2)	-0.23 ± 0.26	(-0.95-0.46)	0.215	-0.26 ± 0.39	(-0.8-1.02)	-0.15 ± 0.4	(-0.88-0.92)	0.229
Sensory NCV (m/sec)	3.22 ± 6.24	(-9.2-24.2)	-1.26 ± 6.33	(-18.6-13.6)	**0.011**	2.97 ± 6.72	(-9-25.4)	0.36 ± 8.77	(-19.3-12.3)	0.56
SDL (msec)	1.87 ± 6.46	(-15.3-16.3)	-1.51 ± 8.02	(-22.4-20)	0.065	-0.13 ± 0.33	(-1.18-0.4)	0.07 ± 0.67	(-1.08-2.28)	0.577

Mann-Whitney U test used in all analyses

LLLT: low-level laser therapy, VAS: Visual Analog Scale, SD: standard deviation, NCV: nerve conduction velocity, MDL: motor distal latency, SDL: sensory distal latency

Özkan et al. evaluated the effects of ultrasound and laser therapy electrophysiologic parameters in UNE and showed that motor latency changes decreased over time in both groups, but there was no significant difference between the groups [15]. Similarly, in our study, a decrease was observed in MDL in the LLLT and SL groups at the post-treatment 15th day and third month compared to the pre-treatment period, but no significant result was observed between the two groups in relation to MDL differences. Sensory latency measurements were not found to be significant in either group. While there was a significant increase in the motor NCV of the ulnar nerve at the affected elbow in the LLLT group at both post-treatment evaluations compared to the pre-treatment period, the only significant increase in the SL group belonged to the post-treatment 15th day. Concerning sensory NCV, there was a significant increase only in the LLLT group at the post-treatment 15th day compared to the pre-treatment values. Although the post-treatment change in motor NCV did not significantly differ between the two groups, the increase in sensory NCV was significantly higher in the LLLT group than in the SL group for the post-treatment 15th day. In trapped neuropathies, demyelination of the nerve and axonal degeneration may develop in advanced cases as a result of long-term ischemia. In vitro studies have demonstrated that photomodulation therapy induces Schwann cell proliferation and the sprouting and growth of neuron cells [31]. It has also been reported that the increase in nerve blood flow at the endoneural level may be the mechanism by which the laser causes improvement in peripheral nerve function [28]. In our study, we found that variations in electrophysiological parameters were influenced by individual differences and environmental conditions, such as temperature, suggesting that the results of the study might be affected. Nevertheless, considering that most patients presenting with a diagnosis of UNE had delayed MDL and slowing down in motor NCV, the improvement in these parameters in the LLLT group indicates the positive effects of laser therapy on nerve function.

The limitations of this study include the absence of patient classification based on electrophysiologic or clinical severity and the insufficient duration of the follow-up period.

Another limitation of our study is the generally low to moderate effect sizes observed in some outcomes. Various factors, including variability within the sample and the relatively small sample size, may have contributed to this. Although we adopted an minimal clinically important difference (MCID) of 1.9 for the VAS pain score based on the study by Randall et al., the actual MCID for our population may differ [32]. This could have affected our ability to detect significant differences. Nevertheless, the results highlight the potential benefits of LLLT in reducing pain and improving clinical outcomes, as evidenced by the greater reduction in VAS pain scores in the LLLT group compared to the sham group. The findings also indicate that the clinical significance of observed improvements should not be overlooked, even if statistical significance was not achieved across all measures.

These limitations underscore the importance of considering larger sample sizes in future studies to increase statistical power and reduce variability.

Conclusion

The results of this study showed that splinting alone could be effective in the treatment of UNE, but the combined use of low-energy laser application, a conservative method, enhanced the efficacy of treatment in terms of alleviating symptoms, improving clinical findings, and producing favorable electrophysiological results. Therefore, we consider that it would be beneficial to incorporate low-energy laser therapy into splinting treatment in cases of UNE.

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Declarations

Ethics approval and consent to participate All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the Clinical Research Ethics Committee of Health Sciences University Antalya Training and Research Hospital (decision number: 18/13, date: September 29, 2022) and the Turkish Medicines and Medical Devices Agency (document number: E-68869993-000-929832, date: October 27, 2022). The study protocol was published in the ClinicalTrials.gov registry (Identifier: NCT06086210). Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare that they have no conflict of interest.

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