Therapeutic and photobiomodulation effects of low-level laser irradiation on Egyptian patients with carpal tunnel syndrome: a placebo-controlled study

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Background/Aim
Carpal tunnel syndrome (CTS) is the most prevalent mononeuropathy, where the median nerve is entrapped in the hand; it affects women more than men and is diagnosed by clinical and electrophysiological examination. Low-level laser therapy (LLLT) was suggested for conservative treatment of CTS. The aim of this study was to evaluate the role of LLLT in the treatment of CTS.

Patients and methods
The study was carried out on 40 female patients with CTS. Patients were recruited from Neurology and Rheumatology clinics at National Research Centre, Egypt. The patients were randomly divided into two groups (20 patients each). The first group was subjected to active LLLT, and the second group was subjected to placebo (sham) LLLT. The patients of the first group were treated with real LLLT by gallium-aluminum-arsenide laser (905 nm) with touch sensor guide light +8 diodes of power output of 100 MW each (800 MW total), and pulsed mode of frequency of 10 000 Hz over two areas, one extends from the proximal palmer crease to the distal wrist crease and the other over the thenar area, for three times per week for 4 weeks (12 sessions). All patients were subjected to clinical and nerve conduction studies evaluations.

Results
LLLT showed significant reduction in erythrocyte sedimentation rate and visual analog scale and significant improvement in functional status scale and symptom severity scale ($P<0.05$) in real laser exposed group when compared with sham laser exposed group. In addition, there was a significant reduction of the sensory ($P<0.05$) and motor latencies ($P<0.05$) and also significant improvement of sensory ($P<0.05$) and motor amplitudes ($P<0.05$), as well as sensory ($P<0.05$) and motor velocities ($P<0.05$) of median nerve conduction studies in real laser exposed group when compared with sham laser exposed group.

Conclusion
This study confirmed the safety and positive effects of LLLT on pain, inflammation, functional capacity, and electro-neurophysiological aspects of median nerve in patients with CTS.

Keywords:
carpal tunnel syndrome, erythrocyte sedimentation rate, laser therapy

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Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy that causes hand discomfort and work disability [1]. CTS is due to compression of the median nerve in the carpal canal causing sensory and motor symptoms (especially in the thumb, index, and middle fingers) worsening at night and often wakening patients [2]. According to the American Academy of Neurology, CTS is recognized as a common disease, affecting 10% of people during lifetime. Workers with tasks involving repetitive hand movements are commonly susceptible to CTS [3]. Polyneuropathies, diabetes, rheumatoid arthritis, hypothyroidism, pregnancy, and other hormonal alterations are risk factors to develop CTS. As the expansion of the structures contained within the canal leads to increased pressure at the carpal tunnel, CTS is diagnosed by physical examination and nerve conduction studies (NCS) for grading of its stage [4].

The main therapeutic approaches in CTS are conservative treatments including anti-inflammatory medications, physical therapy, splinting, and steroid

injections in carpal tunnel [5]. Severe and refractory cases are often referred for surgical decompression [6]. Sometimes, medications showed no more effects than placebo in relieving the symptoms [7]. Although NSAIDs are highly effective in relieving pain, they may cause serious adverse effects such as gastrointestinal ulcer and renal morbidity [8]. The local injection of corticosteroid may ameliorate the symptoms for longer period [7]. It is only indicated if there is no sensibility loss or atrophy of thenar muscle and only effective if the symptoms are intermittent rather than constant [9]. On the contrary, the surgical therapy will be considered if the symptoms are severe and not responding to conservative measures [6].

Low-level laser therapy (LLLT) was suggested to have positive effects on pinch grip strengths in patients with CTS [10]. Laser may decrease pain related to inflammation by decreasing the levels of pain mediators such as tumor necrosis factor-alpha, prostaglandins, beta endorphins, and interleukin 1-beta. It also improves local microcirculation, leading to better healing [1].

Laser therapy can be used in the treatment of CTS, being a noninvasive, painless modality and safe for any patient, especially when corticosteroids are contraindicated, such as diabetic and hypertensive patients [1]. Laser therapy has a good prognosis in the regeneration of peripheral nerves in both neurosensory and neuromotor deficits through local and systemic effects [11]. Moreover, laser improves the recovery and decreases degeneration of the injured peripheral nerve and of the neurons in the corresponding segments of the spinal cord [12].

The aim of the present work is to reveal the effect of LLLT on clinical, inflammatory, and electrophysiological aspects in patients with CTS.

Patients and methods

Study design

A total of 40 female patients with clinical and electrophysiological evidence of early to moderate CTS were included in the present study. Patients were recruited from Neurology and Rheumatology Clinics and received laser sessions at Complementary Medicine Clinics of the Medical Centre of Scientific Excellence of National Research Centre, Egypt, during the duration from March 2019 to Jun 2019. The present study started with 58 patients. Some cases (n=11) did not fulfill the inclusion criteria and were excluded from the study. Other cases (n=7) were irregular in attending laser sessions. These cases were excluded as well so as not to affect the statistical analysis.

Inclusion criteria

Pain/paresthesia in the median nerve distribution, positive clinical provocative test for CTS (Tinel and Phalen), and electrophysiological evidence of median nerve entrapment at wrist were the inclusion criteria.

Exclusion criteria

The following were the exclusion criteria: presence of conditions affecting nerve conduction or abnormal findings in other nerves such as the presence of polyneuropathies, or proximal neuropathies affecting nerve trunks, plexus, or cervical roots diagnosed by physical examinations and comprehensive electrodiagnostic studies; diabetes and other endocrine diseases; renal failure; alcoholism; history of previous acupuncture or steroid injection to a carpal tunnel or physical therapy in last 3 months; previous surgery, trauma, burns, or fractures in the affected limb; and any rheumatologic, neurologic, or orthopedic upper limb diseases.

Participants were randomized for this study in a 1 : 1 allocation ratio using a computer-generated random number table into two groups (A and B), with 20 women each. Group A was subjected to active LLLT and group B was subjected to placebo LLLT.

In group A, patients received the gallium-aluminum-arsenide laser device (Medical-Italia LIS 1050, pesaro, Italy), with MLA 8/800 laser probe 905 nm, with touch sensor guide light +8 diodes of power output of 100 MW each (800 mW total), and pulsed mode frequency of 10 000 Hz. The diameter of each laser beam at the treatment point was 2 cm^2 for 1-min exposure time over two areas: one extends from the proximal palmer crease to the distal wrist crease and the other over the thenar area, giving energy of 6 J per each laser beam (48 J total) for each area, and energy density per each laser beam of 3 J/cm^2 (24 J/cm^2 total) for each area, for three times per week, for 4 weeks (12 sessions). The laser device was calibrated and tested before and after the study and showed a steady effect.

In group B, patients were exposed to placebo LLLT with the same areas and duration while the device was turned off. This study was a prospective, double-blind (for both participants and medical technician), randomized, placebo-controlled trial. Visual analog scale (VAS), functional status scale (FSS), symptom severity scale (SSS), erythrocyte sedimentation rate

(ESR), and electrodiagnostic tests were assessed at baseline and at the end of the study to assess the clinical and electrophysiological responses to laser treatment in CTS.

Ethical consideration

Before the start of the study, informed consents were obtained from all patients in accordance with Helsinki Declaration 1964. This study was approved by the Medical Research Ethics committee of the National Research Centre, Cairo, Egypt, with approval number 17/065.

Methods

Patients were not allowed to take any analgesics during the whole period of the study. They were subjected to history taking, clinical rheumatological and neurological examination, and serum ESR second hour evaluation, according to the method of Westergren [13]. Physical examination included Tinel and Phalen signs [14]. VAS was used to assess pain. Patients were subjected to self-administered SSS and FSS, according to the method of Levine *et al*. [15].

Diagnosis of median nerve entrapment at the level of the wrist was confirmed and graded by electrodiagnostic studies according to the American Association of Neuromuscular and Electrodiagnostic Medicine [16] by performing median nerve motor and sensory conduction studies for all cases [17] by using Deymed TRU-TRACE EMG NCV 4 Channel System machine (AU7-12060002). Electrophysiologic grading is of important value to stage the severity of cases and to specify the efficacy of LLLT according to it.

Statistical analysis

All data are presented as the mean±SD values. The Mann–Whitney test was used for determination the level of significance between the two groups, and the Wilcoxon test was used to compare before and after findings in each group, using statistical programs (Statistical Package for the Social Sciences, version 16; SPSS Inc., Chicago, Illinois, USA). The difference is considered significant at *P* value less than 0.05.

Results

Demographic data are illustrated in Table 1 for the studied groups, which revealed no significant difference between the two studied groups regarding age, weight, height, and BMI.

Table 1 Demographic characteristics of the study patients

Variables	Group A (*n*=20)	Group B (*n*=20)	*P* value*
Age (years)	51.4±8.3	53.6±7.5	0.306
Weight (kg)	76.00±9.2	74.3±9.2	0.573
Height (cm)	157.7±4.6	156.03±4.7	0.628
BMI (kg/m^2)	31.00±4.4	30.6±4.8	0.776

All data are expressed as mean±SD. *All data are nonsignificant at *P* value more than 0.05.

Table 2 Baseline clinical and electrophysiological parameters of patients with carpal tunnel syndrome

	Group A (*n*=20)	Group B (*n*=20)	*P* value*
ESR 2nd h (mm/h)	33.8±16.7	40±12.1	0.211
VAS	8.04±1.6	8.3±1.6	0.244
FSS	24.6±6.0	25.4±7.8	0.869
SSS	35.3±7.9	32.8±10.03	0.391
M_DL (ms)	4.9±0.90	5.5±2.08	0.194
M_AMPLITUDE (mv)	10.05±3.4	8.07±4.09	0.362
M_VELOCITY (m/s)	48.5±5.5	44.6±11.3	0.488
S_DL (ms)	4.5±1.02	5.3±2.2	0.069
S_AMPLITUDE (μV)	23.4±2.8	12.6±2.5	0.028
S_VELOCITY(m/s)	38.1±9.1	29.05±13.6	0.109

All data are expressed as mean±SD. DL, distal latency; ESR, erythrocyte sedimentation rate; FSS, functional status score; M, motor; S, sensory; SSS, symptom severity scale; VAS, visual analog scale. *All data are nonsignificant at *P* value more than 0.05.

As revealed in Table 2, there was no significant difference in basal ESR. Moreover there were no significant differences in basal values of the clinical parameters (VAS, FSS, and SSS). In addition, there were no statistical significant differences in both motor and sensory electrophysiological parameters.

The data recorded in Table 3 illustrate values of the clinical and electrophysiological measurements for group A patients before and after real laser treatment.

After real laser treatment, there was a significant decrease in ESR ($P<0.05$), and also there were significant decreases in the clinical parameters (VAS, FSS, and SSS) ($P<0.05$).

Moreover, there was a significant decrease in the motor distal latency ($P<0.05$), and a significant increase in motor conduction velocity ($P<0.05$), but there was no significant difference in motor amplitude for group A patients before and after real laser treatment.

There was a significant decrease in the sensory distal latency ($P<0.05$), a significant improvement in sensory amplitude ($P<0.05$), and a significant increase in sensory conduction velocity ($P<0.05$) after real laser treatment.

Table 3 Clinical and electrophysiological parameters of group A patients before and after real low-level laser therapy

	Before	After
ESR 2nd h (mm/h)	33.8±16.7	18.6±11.2*
VAS	8.04±1.6	1.8±1.4*
FSS	24.6±6.0	9.3±1.8*
SSS	35.3±7.9	14.9±3.5*
M_DL (ms)	4.9±0.9	4.3±0.7*
M_AMPLITUDE (mv)	10.05±3.4	10.9±2.6*
M_VELOCITY (m/s)	48.5±5.5	51.5±3.1*
S_DL (ms)	4.5±1.02	3.7±0.5*
S_AMPLITUDE (μV)	23.4±2.8	27.4±3.0*
S_VELOCITY(m/s)	38.1±9.1	44.5±7.9*

All data are expressed as mean±SD. DL, distal latency; ESR, erythrocyte sedimentation rate; FSS, functional status score; LLLT, low-level laser therapy; M, motor; S, sensory; SSS, symptom severity scale; VAS, visual analog scale. *Significant differences than before LLLT at *P* value less than 0.05.

Table 4 Clinical and electrophysiological parameters of group B patients before and after sham low-level laser therapy

	Before	After	*P* value*
ESR 2nd h (mm/h)	40.0±12.4	41.0±13.6	0.358
VAS	8.3±1.6	8.1±1.8	0.875
FSS	25.4±7.8	25.4±8.5	0.429
SSS	32.8±10.03	32.7±9.06	0.711
M_DL (ms)	5.5±2.08	5.5±2.1	0.102
M_AMPLITUDE (mv)	8.07±4.09	7.6±4.3	0.433
M_VELOCITY (m/s)	44.6±11.3	42.2±14.9	0.104
S_DL (ms)	5.3±2.2	5.36±2.3	0.269
S_AMPLITUDE (μV)	12.6±2.5	11.07±2.4	0.482
S_VELOCITY (m/s)	29.05±13.6	29.1±14.5	0.767

All data are expressed as mean±SD. DL, distal latency; ESR, erythrocyte sedimentation rate; FSS, functional status score; M, motor; S, sensory; SSS, symptom severity scale; VAS, visual analog scale. *All data are nonsignificant at *P* value more than 0.05.

As shown in Table 4, there were no significant differences in the ESR, the clinical parameters of (VAS, FSS, and SSS), or the electrophysiological parameters in group B before and after sham laser treatment.

The data recorded in Table 5 show a significant decrease in ESR in group A ($P<0.05$), Furthermore, there were significant decreases in the clinical parameters (VAS, FSS, and SSS) ($P<0.05$) in group A compared with group B sham laser group.

There was a significant decrease in motor distal latency ($P<0.05$), significant improvement in the motor amplitude ($P<0.05$), and significant increase in motor conduction velocity ($P<0.05$) for group A compared with group B. There was a significant decrease in the sensory distal latency ($P<0.05$) and significant increases in the sensory amplitude and conduction velocity ($P<0.05$) of median nerve for group A compared with group B.

Table 5 Clinical and electrophysiological parameters of studied groups after 4 weeks of real low-level laser therapy

	Group A after LLLT	Group B after sham LLLT
ESR 2nd h (mm/h)	18.6±11.2	41.0±13.6*
VAS	1.8±1.45	8.1±1.8*
FSS	9.3±1.8	25.4±8.5*
SSS	14.9±3.5	32.7±9.06*
M_DL (ms)	4.3±0.7	5.5±2.1*
M_AMPLITUDE (mv)	10.9±2.6	7.6±4.3*
M_VELOCITY (m/s)	51.5±3.1	42.2±14.9*
S_DL (ms)	3.7±0.5	5.3±2.3*
S_AMPLITUDE (μV)	27.4±3.0	11.07±2.4*
S_VELOCITY (m/s)	44.5±7.9	29.1±14.5*

All data are expressed as mean±SD. DL, distal latency; ESR, erythrocyte sedimentation rate; FSS, functional status score; LLLT, low-level laser therapy; M, motor; S, sensory; SSS, symptom severity scale; VAS, visual analog scale. *Significant differences than group B are at *P* value less than 0.05.

Discussion

In our study, LLLT showed significant improvement of ESR, VAS, FSS, and SSS in patients with CTS, when compared with sham laser exposed group. LLLT ameliorated sensory and motor latency, amplitude, and conduction velocity of median nerve fibers of the real laser therapy patients as compared with the sham group.

LLLT, also known as photobiomodulation, involves the exposure of tissues and cells to infrared or red light (600–1100 nm) [18], leading to stimulation of cellular functions leading to beneficial clinical effects [19], so we used laser of 905 nm. Most of the literature reports that LLLT to be effective should have frequencies generally in range from 0.04 to 50 J/cm^2 [20,21], which is also in agreement to our study, as we used 24 J/cm^2.

In a study investigating the action of LLLT (940 nm) with different energy intensities on bone healing, it was suggested that its biomodulatory effects are dose dependent [22] and also affected by the method of application, so the choice of parameters to use in LLLT experiments seems to be dependent on the experimenter's experience, not from a consensus statement by an authoritative body [20]. This makes comparing different outcomes from various studies really difficult, as different frequencies, wavelengths, and target tissue type are used by different authors [23].

Several trials estimated the value of LLLT in CTS. Many studies detect the effect of laser plus splinting on CTS. For instance, Yagci *et al.* [24] performed a comparison study between splinting plus LLLT and splinting alone in mild or moderate CTS. In another double-blinded randomized controlled study, one group of patients received 15 sessions of a laser treatment at a frequency of 810 nm and dosage of 18 J per session over the carpal tunnel area with neutral wrist splint, whereas the second group received placebo laser therapy with neutral wrist splint [25]. In agreement with our study VAS, SSS, and FSS showed significant improvement in laser group; however, most of the electro-neurophysiological parameters in their study showed no significant differences. The positive results of NCS in our study might be owing to use of different laser parameters at a frequency of 905 nm and more laser dosage of 48 J per session. In many studies, the use of splint would affect the result, as immobilization of the wrist in a neutral position could improve the condition, thus splinting might obscure the power of LLLT; therefore, our patients did not receive any treatment except LLLT, as we designed our study to detect the isolated effect of laser in CTS.

In agreement with our results, several studies revealed that LLLT is effective in treating CTS pain and numbness; in addition, laser improves power of the hand grip and electrophysiological measurements [26,27]. A placebo-controlled study concluded that LLLT exhibited verifiable therapeutic effects for mild cases [28]. In a review published by Naeser [29] evaluating the therapeutic efficacy of laser in CTS, five studies suggested that real laser with high dosages had better effect than sham laser, whereas lower dosages were used in the other two studies and did not observe a better effect than a control condition, so we used high laser dose (24 J/cm^2) in our study to get better clinical and electrophysiologic effects. According to a previous study by Zahra *et al.* [30], it was postulated that combined corticosteroid injection and laser therapy were advantageous in the short-term treatment of mild and moderate CTS. Another practical study performed by Dincer *et al.* [31] comparing the effectiveness of ultrasound, splinting, and LLLT documented that LLLT with splinting exhibited notably the best efficiency in relieving CTS symptoms.

On the contrary, Bakhtiary and Rashidy-Pour [32] found that ultrasound was superior to LLLT concerning VAS, pinch strength, and electroneurophysiologic results. Comparing LLLT for CTS with the standard open carpal tunnel release surgery, through clinical and NCS evaluation LLLT was proven to be an effective and noninvasive treatment modality of early and mild-to-moderate CTS cases. However, the surgical therapy could be preserved for chronic moderate and severe cases [33]. In contrast some studies were not able to reveal the differences between LLLT and placebo treatment of CTS, as they were carried out on heterogeneous subjects using various session numbers and various doses of laser therapy [34]. One placebo-controlled study emphasized that the scale of pain and FSS improved in patients with CTS who underwent LLLT at a power output of 50 mW with 780 nm gallium-aluminum-arsenide laser and dosage of 1.5 J/per point over the median nerve at volar side of the wrist area, but this LLLT group was not statistically different from the placebo group concerning other clinical and electrophysiological measurements [35]. Another randomized placebo-controlled study relative to pain relief and functional capacity postulated that there was no difference between LLLT group and placebo group, whereas LLLT affected positively the strengths of the hand and pinch grip [10], and finally, a study on 50 patients with mild and moderate CTS, who were randomly divided into three groups [group I received LLLT (50 mW and 880 nm with total dose of 6 J/cm^2) and splinting, group II received sham LLLT and splinting, and group III received only splints], revealed no significant changes among the three groups regarding clinical and electrophysiological measurements [36].

In our study, LLLT showed reduction of ESR, whereas sham LLLT showed no improvement. As observed in our study, the high ESR in patients with CTS of value 33.86±16.76, as compared with the reference normal value of 8.75±0.8 indicates the significant role of inflammation in the pathogenesis of this disease. The swelling which results from inflammation causes excess pressure on the median nerve in the wrist area leading to pain in the carpal tunnel. Fibrinogen (acute-phase protein), which is synthesized in response to tissue inflammation, is responsible for the increased ESR. The erythrocytes are responsible for carrying a negative surface charge that impedes their aggregation. Presence of the high-molecular-weight positively charged proteins, like acute-phase proteins, reduced tendency for the erythrocytes to repel each other. This subsequently leads to promotion of erythrocyte aggregation [37]. For this reason, the ESR level increased in the patients with CTS because the aggregated erythrocytes sediment more rapidly in case of inflammation.

Interestingly, it was previously found that the LLLT was effective in reducing the ESR level in patients with arthritis [38]. This may be attributed to LLLT efficiency in reducing level of plasma fibrinogen and hence decreasing the erythrocyte sedimentation process then lowering the ESR level [39]. Low-level laser modulates the inflammatory effects in injured tissue through altering the distribution of inflammatory cells and reduction of edema, hemorrhage, and necrosis [30]. These effects are reflected on the clinical parameters of patients with CTS. LLLT showed significant pain reduction based on severity of the symptoms, assessed by the VAS, and significant improvements in functional capacity based on the FSS, whereas sham LLLT showed no improvements in these parameters.

Low-level laser promotes neural regeneration even after crush injury or transaction [40]. It prevents motor cell degeneration, induces Schwann cell proliferation, and leads to higher neural metabolism, with increasing myelination and axonal regeneration [41].

Nerves irradiated with LLLT (904 nm) show increase in the total number of large axons diameter [42] and enhancement of peripheral nerves regenerative processes [43]. These LLLT effects are reflected on the median NCS of our patients with CTS, as real LLLT caused significant reduction of median sensory and motor latencies among the exposed group, which is consistent with another study [44], whereas Naeser [29] in 2006 reported no significant changes in NCS. There was also significant increment of sensory and motor amplitudes of median nerve after real LLLT among patients with CTS, which was approved by another study [45] and contraindicated by another [46]. Patients with CTS exposed to real laser showed significant increment for sensory and motor conduction velocity results, which is in agreement with some other authors [47,48], whereas others reported no improvement in such parameters [29,49], which may be owing to discrepancy in cases selection, severity, session number, and doses of laser therapy. Therefore, more high-quality studies with the same laser intervention protocol and follow-up time are needed to decrease discrepancy and to confirm the effects of LLLT on CTS. Most of our patients started improvement after the third and fourth session. As LLLT has a cumulative effect (every session has a better effect than the previous one), all cases were evaluated at the end of the treatment protocol duration. Our study of LLLT for CTS confirms favorable short-term effects, whereas some authors reported that the effectiveness of LLLT can be maintained up to 5 weeks, but limited evidence is available for 3–6-month follow-up [1], so we recommend similar studies with longer follow-up periods.

Conclusion

In conclusion, our findings suggested that LLLT parameters used in our study exhibit their beneficial therapeutic efficiency for the CTS treatment through relieving pain and minimizing severity of symptoms in addition to ameliorating electrophysiological parameters of median nerve and score of the functional capacity. It exerts its photobiomodulation therapeutic effect through alleviating the inflammation, swelling, and pressure in the wrist. This subsequently leads to reducing pain in patients with CTS and improving the function of hand. We suggested that further studies should be conducted with long follow-up periods to support the findings that LLLT is a highly effective conservative treatment in treating mild and moderate CTS.

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Conflicts of interest

There are no conflicts of interest.

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