Effect of low level laser therapy in rheumatoid arthritis patients with carpal tunnel syndrome

A placebo controlled study

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Summary

Objective: the aim of the present study was to evaluate the efficacy of low level laser therapy (LLLT) in patients with rheumatoid arthritis (RA) with carpal tunnel syndrome (CTS).

Material and methods: a total of 19 patients with the diagnosis of CTS in 19 hands were included and randomly assigned to two treatment groups; LLLT (Group 1) (10 hands) with dosage 1.5J/ per point and placebo laser therapy group (Group 2) (9 hands). A Galium-Aluminum-Arsenide diode laser device was used as a source of low power laser with a power output of 50 mW and wavelength of 780 nm. All treatments were applied once a day on week days for a total period of 10 days. Clinical assessments were performed at baseline, at the end of the treatment and at month 3. Tinel and Phalen signs were tested in all patients. Patients were evaluated for such clinical parameters as functional status scale (FSS), visual analogue scale (VAS), symptom severity scale (SSS) and grip-strength. However, electrophysiological examination was performed on all hands. Results were given with descriptive statistics and confidence intervals between group means at 3 months adjusted for outcome at baseline and for the difference between unadjusted group proportions.

Results: clinical and electrophysiological parameters were similar at baseline in both groups. Improvements were significantly more pronounced in the LLLT group than placebo group. A comparison between groups showed significant improvements in pain score and functional status scale score. Group mean differences at 3 months adjusted at baseline were found to be statistically significant for pain score and functional status scale score. The 95\% confidence intervals were [-15 - (-5)] and [-5 - (-2)] respectively. There were no statistically significant differences in other clinical and electrophysiological parameters between groups at 3 months.

Conclusions: our study results indicate that LLLT and placebo laser therapy seems to be effective for pain and hand function in CTS. We, therefore, suggest that LLLT may be used as a good alternative treatment method in CTS patients with RA.

Key words: carpal tunnel syndrome; low level laser; rheumatoid arthritis

Introduction

Carpal tunnel syndrome is an entrapment neuropathy caused by compression of the median nerve at the wrist in the carpal canal [1]. Carpal tunnel syndrome is a common disease according to the American Academy of Neurology, and there is 10\% lifetime risk of developing this condition [2]. Although the aetiology of CTS is unknown, occurring more commonly in workers with tasks involving repetitive hand movements (eg, computer keyboard typing, operating machinery, assembly line work). In addition to ergonomic stressors, psychosocial factors may contribute to CTS [3]. The well-known causes of this disease include tenosynovitis associated with Rheumatoid arthritis and other inflammatory disorders (thyroid disease, diabetes mellitus, gout, obesity) acute trauma, pregnancy [4].

Rheumatoid arthritis is a chronic inflammatory disease, which often results in progressive joint destruction [5]. During the course of the disease, patients may develop extra-articular features, such as alveolitis, glomerulonephritis, vasculitis and neuropathy [6].
A number of distinct forms of neuropathy occur in RA: entrapment neuropathy, peripheral neuropathy due to vasculitis, amyloid neuropathy and neuropathy due to drugs or coincidental disease [7]. Nerve compression is a common cause of neurological impairment in RA [8].

Entrapment neuropathies are the result of synovial thickening occurring in a location where the peripheral nerve passes through a confined anatomical space. Carpal tunnel syndrome is an entrapment neuropathy that is strongly associated with RA [7]. Prevalence of CTS in patients with RA has been reported to range between 23–69% [9].

Treatment modalities of CTS include hand splint, non-steroidal anti-inflammatory drugs, physical therapy, electrotherapy, steroid injections, ultrasound, iontophoresis and LLLT [10, 11].

A limited number of controlled studies have so far reported the efficacy of LLLT in relieving symptoms of CTS [11, 12]. However, the efficacy of LLLT has not been investigated in RA patients with CTS to date. Therefore, the present study aims to determine the effects of LLLT or placebo LLLT on electrophysiological and clinical parameters in RA patients with CTS.

Material and methods

The study was performed at the Physical Therapy and Rehabilitation Department of Osmangazi University Hospital. A total of 19 patients with clinical and electrophysiologic evidence of CTS with RA were studied. Three amongst 19 patients have got bilateral CTS. Only dominant hands of patients who have got bilateral CTS were included in the study. All unilateral affected hands were on the dominant side. As a result, our study was performed in a total of 19 patients of CTS (19 hands) with RA.

Exclusion criteria were such underlying metabolic disorders as diabetes mellitus, thyroid disorders, acromegaly, cervical radiculopathy, previous wrist trauma, peripheral neuropathies, anæsthesia, or intractable pain due to CTS, history of steroid injection to a carpal tunnel in last 3 months, history of physical therapy in last 3 months for CTS, and history of physical therapy in last 3 months on joints with RA. Also, patients with either thenar atrophy or spontaneous activity (fibrillation potentials and positive sharp waves) on electrophysiologic examination of the abductor pollicis brevis muscle were excluded from the study.

At baseline, demographic characteristics of patients, disease duration of RA (years), duration of symptoms for CTS (months), C-reactive protein (CRP) (mg/dl) were recorded. In our study, Disease Assessment Score 28 (DAS 28) was used to evaluate the disease activation of RA [13]. Disease Assessment Score 28 was evaluated to include 28-joint counts for swelling and tenderness. According to DAS 28, none of the patients in our study had a high disease activity. Patients were not allowed to take any analgesics during the whole period of the study. However, they went on taking disease-modifying anti-rheumatic drugs (DMARDS) that they were already using before being enrolled into the study.

The patients were randomly divided into two groups. Ten patients (10 hands) in group 1 underwent LLLT and 9 patients (9 hands) in group 2 underwent placebo LLLT. Patients in the first group received the Gallium-Aluminium-Arsenid (Ga-Al-As) laser device (Endolaser 476-Enraf Nonius, Netherlands) was used with a power output of 50 mW and wavelength of 780 nm. The laser was set to deliver a continuous form of energy. The diameter of the laser beam at the treatment point was 1 mm. Patients in the first group received Ga-Al-As laser irradiation to various five points of the skin overlying the median nerve on the volar side at the wrist. A two minute irradiation at each point (a total of 10 minutes) was considered as one irradiation dose. The dose per tender point was 1.5 joule.

The total dose per treatment was 7.5 joule and accumulated dose for ten treatments was 75 joule.

To standardise the total dosage that each subject received, a thin clear plastic template with 1 cm² cm grids was placed over the wrist and palm. The template was placed at an identical location at each session. A total of 5 points across the median nerve trace were irradiated with the laser probe.

The patients in the second group were treated with placebo LLLT, determining points were irradiated for a duration two minute (a total of 10 minutes). The dose per tender point was 0 joule. For the placebo laser application the same laser device seemed to be working but with no laser beams being transferred to the treated area.

The patients in the second group were treated with placebo LLLT. The same laser device seemed to be working but with no laser beams being transferred to the treated area was used for the placebo LLLT application.

All treatments were applied once a day, five days a week for a total duration of 10 days. All patients were treated by the same physician.

A “blinded” physician unaware of the treatment allocation performed the clinical and electrophysiological parameters at baseline, post treatment and at month 3.

Physical examination included Tinel, Phalen signs and grip strength measurement.

Tinel sign: the examiner gently tapped the area over the median nerve of the wrist. The test result was considered positive if this produced tingling in the fingers.

Phalen sign was performed by full flexion of the patient’s wrists for 60 sec. If numbness and tingling were produced or exaggerated in the median nerve distribution of the hand within sixty seconds, the test result considered positive.

Grip strength was measured with dynamometer and mean score of three trials was recorded. Pain was assessed by VAS. Patients responded to the self-administered SSS and the FSS [14].

The Symptom Severity Scale has 11 items in relation to pain, nocturnal symptoms, numbness, tingling and weakness [14].

The Functional Status Scale has 8 items (difficulty in writing, buttoning clothes, opening jars, holding a book, gripping of a telephone handle, household chores, carrying of grocery bags, bathing, and dressing). Each item of these scales has five ordinal response categories ranging from 1 (no symptoms or no difficulty) to 5 (severe symptoms).
Electrophysiological examinations were performed at baseline, at the end of the treatment, and at month 3. By using standard techniques, all electrodagnostic tests were performed by the same physician with a Medelec Sapphire 4ME, electromyography apparatus. All hands were warmed prior to testing by seating the patient for 15 minutes in room at 22–24 °C in which the studies were performed. Median nerve; motor distal latency (DL), motor nerve conduction velocity (NCV), sensory DL, palm-wrist sensory NCV measures were performed on all the patients. Surface stimulation and recording electrodes were used for the sensory and motor nerve conduction tests, employing standard methodology [15]. Compound muscle action potentials of the abductor pollicis brevis muscle were recorded induced from supramaximal electrical stimulation on the median nerve at the wrist 8 cm to the recording electrode. Distal motor latency and motor NCV study from the wrist to APB muscle were done within the distance of 8 cm. Sensory nerve conduction studies, the median sensory fibres were stimulated antidromically at midpalm and wrist with a distance of 7 cm and 14 cm from the recording ring electrode looped around the proximal interphalangeal joint of the third digit. The onset latencies of negative potentials were taken into consideration. For sensory testing, sweep-speed velocity was set at 10 msec, whereas for motor testing sweep-speed was set at 30 msec, and the duration of stimulus was 0.1 msec in both studies. The voltage was increased until action potentials reached maximal amplitude.

The main electrophysiological criteria for diagnosis of CTS were the slowing of sensory nerve conduction velocity of median nerve in palm-wrist segment or absence of sensory nerve action potential of the median nerve along with prolonged terminal motor latency [16]. In our electrophysiology laboratory, if the median nerve motor distal latency was 3.9 ms and above, and if the median nerve sensory latency of 3 ms and above, and if the sensory nerve conduction velocity of median nerve in palm-wrist segment was 35.2 m/sn and below, the subjects were accepted as CTS.

This study was a prospective, double-blind, randomised, placebo-controlled trial. A staff physician not involved in the present study performed the randomisation. Another physician not “blinded” to treatment allocation applied the treatments. This physician was not involved in the outcome measure assessment. Neither the three investigators nor the patients were informed of the treatment separation. The study was approved by the ethics committee Osmangazi University.

Results were given with descriptive statistics and confidence intervals between group means at 3 months adjusted for outcome at baseline and for the difference between unadjusted group proportions. In the analysis, confidence intervals between group means for outcomes at 3 months are calculated for 19 hands. In each case, 95% confidence intervals for the difference between group means having adjusted for the covariate (the outcome at baseline) calculated in ANCOVA analysis were reported. Also in each case, confidence intervals for the difference between unadjusted group proportions are calculated. Statistical analysis was performed by using SPSS 13 for Windows Statistical Software. Results were expressed as mean (SD) (95% CI). A p value of <0.05 was deemed statistically significant.

### Results

Twenty-four RA patients with CTS were evaluated by the present study. Investigations revealed Diabetes mellitus in 3 patients and hypothyroidism in 2 patients. Consequently 5 patients excluded out of 24 patients. As a result, 19 RA patients with carpal tunnel syndrome (18 women, 1 man, and total 19 hands) aged between 33–72 years were included in the trial and all of them completed the study period. Their mean age was 52 years and mean disease duration of RA 5 years, mean duration of symptoms for CTS 30 months.

Table 1 shows the baseline demographic characteristics of the patients. Table 2 shows clinic and electrophysiological parameters at baseline, post treatment, at 3 months of patients in study. Clinical and electrophysiological parameters were similar in both groups at baseline. Improvements were significantly more pronounced in the LLLT group than placebo group. A comparison between groups showed significant improvements in pain score and functional status scale score. Mean differences at 3 months adjusted for outcome at baseline was found as statistically significant. The 95% significant confidence intervals were found as [-15 – (-5)] and [-5 - (-2)] respectively. There were no statistically significant improvements in the other clini-

<table>
<thead>
<tr>
<th>Variables</th>
<th>LLLT group n = 10 (n = affected hand number)</th>
<th>Placebo group n = 9 (n = affected hand number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48 (11)</td>
<td>55 (6)</td>
</tr>
<tr>
<td>RA disease duration (years)</td>
<td>5.2 (3)</td>
<td>5 (2)</td>
</tr>
<tr>
<td>CTS disease duration (months)</td>
<td>32 (12)</td>
<td>29 (14)</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>1.2 (0.4)</td>
<td>1.26 (0.8)</td>
</tr>
<tr>
<td>Morning stiffness (minutes)</td>
<td>51 (15)</td>
<td>50 (15)</td>
</tr>
<tr>
<td>DAS 28</td>
<td>4.3 (0.5)</td>
<td>4.4 (0.6)</td>
</tr>
<tr>
<td>Sex (female/male)</td>
<td>10/0</td>
<td>8/1</td>
</tr>
<tr>
<td>Affected side (right/left)</td>
<td>9/1</td>
<td>8/1</td>
</tr>
</tbody>
</table>

LLL T = Low level laser therapy  
RA = Rheumatoid arthritis  
CTS = Carpal tunnel syndrome  
CRP = C-reactive protein  
DAS 28 = Disease Assessment Score 28
Table 2
Comparison of the clinical parameters and electrophysiological parameters at baseline, post treatment and at 3 months between group 1 (n = 10 hands) and group 2 (n = 9 hands).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Measurement at:</th>
<th>Difference between groups at 3 months [95% confidence interval] *</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline mean (standard deviation)</td>
<td>Post treatment mean (standard deviation)</td>
</tr>
<tr>
<td>Pain-Visual Analogue Scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active laser</td>
<td>56 (14)</td>
<td>29 (6)</td>
</tr>
<tr>
<td>Placebo laser</td>
<td>55 (15)</td>
<td>42 (9)</td>
</tr>
<tr>
<td>Symptom Severity Scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active laser</td>
<td>29 (8)</td>
<td>16 (4)</td>
</tr>
<tr>
<td>Placebo laser</td>
<td>27 (9)</td>
<td>22 (3)</td>
</tr>
<tr>
<td>Functional Status Scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active laser</td>
<td>19 (7)</td>
<td>14 (3)</td>
</tr>
<tr>
<td>Placebo laser</td>
<td>19 (6)</td>
<td>18 (3)</td>
</tr>
<tr>
<td>Grip strength values</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active laser</td>
<td>0.3 (0.1)</td>
<td>0.1 (0.1)</td>
</tr>
<tr>
<td>Placebo laser</td>
<td>0.3 (0.1)</td>
<td>0.3 (0.1)</td>
</tr>
<tr>
<td>Motor DL</td>
<td></td>
<td></td>
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<tr>
<td>Active laser</td>
<td>4 (1)</td>
<td>3.3 (0.6)</td>
</tr>
<tr>
<td>Placebo laser</td>
<td>3.2 (0.5)</td>
<td>3.2 (0.4)</td>
</tr>
<tr>
<td>Motor nerve conduction velocity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active laser</td>
<td>57 (6)</td>
<td>55 (7)</td>
</tr>
<tr>
<td>Placebo laser</td>
<td>56 (4)</td>
<td>55 (4)</td>
</tr>
<tr>
<td>Sensory distal latency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active laser</td>
<td>2.1 (0.7)</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>Placebo laser</td>
<td>2.1 (0.3)</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td>Palm-wrist sensory NCV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active laser</td>
<td>29 (6)</td>
<td>30 (8)</td>
</tr>
<tr>
<td>Placebo laser</td>
<td>28 (3.2)</td>
<td>14 (7)</td>
</tr>
<tr>
<td>Tinel positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active laser</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Placebo laser</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Phalen positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active laser</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Placebo laser</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

* The first eight outcomes represent the confidence intervals for the difference between group means at 3 months adjusted for outcome at baseline; the last two outcomes represent the confidence interval for the difference between unadjusted group proportions at 3 months.

Discussion

In the few previously conducted studies, effects of LLLT on clinical symptoms, pain parameters, hand function and electrophysiological parameters in patients with idiopathic CTS have been evaluated [11, 12, 17, 18, 19]. Existing data in the literature are very scarce. Low level laser therapy has been reported to be effective in the treatment of idiopathic CTS in uncontrolled studies [17, 18]. However, there are two controlled studies which have evaluated the efficacy of LLLT in idiopathic CTS [11, 12]. A controlled trial study by Irvine et al. showed LLLT not to be any more effective than placebo in improving CTS symptoms, pain, hand function and electrophysiological parameters [12]. A recently published controlled study by Naesar et al. found an active treatment to be more effective than placebo in relation to pain and electrophysiological parameters [11].

Clinical results of laser treatments have thus far been controversial. A review that applied a laser therapy to patients has assessed the limited number of studies into laser treatment in CTS and concluded that such a treatment could be a beneficial and cost-effective method [20]. A minimal effec-
tive dosage and an optimal wavelength of an ideal treatment with laser has not been established [21–23]. Still obscure, regarding optimal laser treatment, are the area which should be irradiated, the application time and duration of a course of treatment.

Irvine et al. studied the efficacy of a laser treatment in idiopathic CTS cases in one of their studies in which they applied 860 nm a low-level Ga-Al-As laser at a dosage of 6 J/cm² over the carpal tunnel. Their study groups underwent treatment three times per week for 5 weeks [12]. In a study by Naeser et al., infrared laser (pulsed, 9.4 W, 904 nm) was applied to a minimum of 5 deeper acupuncture points on the upper extremity, the upper trapezius, and cervical paraspinal areas. Each acupuncture point was treated for a minimum of 1 minute, at each of 3 pulse settings with energy densities ranging from 1.81 J/cm² at the highest frequency to 0.04 J/cm² at the lowest frequency. The latter study also used transcutaneous electrical nerve stimulation, but it is not clear whether or not the improvement they observed was due to LLLT [11].

In our study, The Ga-Al-As laser device was used with a power output of 50 mW and wavelength of 780 nm. The diameter of the laser beam at the treatment point was 1mm. The laser was set to deliver a continuous form of energy. All treatments were applied to five points once a day, five days a week, and total duration of 10 days. Patients in the first group received Ga-Al-As laser irradiation to various five points of the skin overlying the median nerve at wrist. A two-minute irradiation at each point (a total of 10 minutes) was considered as one irradiation dose. The dose per tender point was 1.5 joule. The total dose per treatment was 7.5 joule and accumulated dose for ten treatments was 75 joule.

Laser therapy is becoming increasingly popular amongst patients, therapists and medical practitioners, for the treatment of acute and chronic musculoskeletal pain syndromes, including RA [24–29]. However, efficacy of LLLT has not been investigated in RA patients with CTS. The present study aimed to evaluate the effect of a LLLT on clinical, functional and electrophysiological parameters in RA patients with CTS.

Our study results indicated that LLLT was effective on pain and hand functions in RA patients with CTS. Still, we could find no statistical difference for electrophysiological and the other clinical parameters in LLLT and placebo groups. Our study results showed a partial similarity to those of the few controlled studies.

The mechanism of pain reduction by LLLT is yet not fully understood. Different experimental studies suggest that LLLT has anti-inflammatory and analgesic effects [30–32]. Moreover, it has been reported that LLLT therapy has both anti-inflammatory and anti-oedematous effects due to its reductive effect in prostaglandin synthesis [32].

Upon evaluation of hand function, our study determined that LLLT group improved more than placebo group. We attributed the increase in hand function and daily life activities in LLLT group to the improvement in pain and hand functions parameters in RA patients with CTS. However, the limited number of studies showed efficacy on pain, inflammation and hand function of LLLT in patients with RA [24, 27, 29].

The major limitations of the present study are the design and the restricted number of patients, owing in part to the extremely labour intensive treatment protocol. Each subject came to the laboratory 5 times per week for 2 weeks, with each session taking 10 min. and clinical and electrophysiological assessments were performed at baseline, at the end of the treatment and at month 3.

The present study determined that real and placebo laser treatments were both effective on hand functions and pain in RA patients with CTS both in the short and in the long terms. However, a comparison between the patients undergoing real and placebo laser treatments showed that the LLLT group benefited more.

Our study is the first of its kind in that no previous study has investigated efficacy of LLLT in RA patients with CTS thus far. CTS only add to the suffering of RA patients with disorganized hand functions. Based on our study results, we suggest that LLLT could be an alternative treatment for RA patients with CTS for pain relief and improvement of hand function. However, we still think further studies are needed to shed light on the benefit of LLLT in RA with CTS.

References


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