Low-level laser treatment on relieving pain and neurological symptoms in patients with carpal tunnel syndrome

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ABSTRACT

〔Purpose〕This placebo-controlled study was investigated the therapeutic effects of low-level laser treatment (LLLT) to apply on the transverse carpal ligament of carpal tunnel syndrome (CTS).

〔Subjects and Methods〕Idiopathic CTS patients were recruited and were randomly assigned to two groups. The laser group (n = 45) received laser treatment (10 Hz, 60 mW, 9.7 J/cm^2, 830 nm), but the placebo group (n = 42) received sham laser treatment. The visual analog scale (VAS), Boston Questionnaire scale, neurological symptoms and nerve conduction study (NCS) were assessed before, immediately after and 5 week follow-up.

〔Results〕After LLLT, there was statistically significant decrease for VAS in laser group ($p < 0.05$). Especially, the effect of LLLT on pain alleviation in the mild CTS group continued after five weeks. Regarding Boston Questionnaire scale, neurological symptoms and NCS, only mild CTS patients in the laser group had statistically significant improvements after treatment ($p < 0.05$).

〔Conclusions〕LLLT with 830 nm diodes laser on transverse carpal ligament had preferable therapeutic effect for mild CTS patients.

INTRODUCTION

Carpal tunnel syndrome (CTS) is a median nerve lesion due to compression in the carpal tunnel. The median nerve and tendons of the hand pass through the carpal tunnel and the transverse carpal ligament locates on the palm side of the carpal tunnel. The tendons and transverse carpal ligament become inflamed and swollen because of the pressure imposed on the median nerve below it[1)]. The abnormal sensation and weak muscle strength of hands are common clinical symptoms and signs. The diagnosis of CTS is usually based on physical examination and electromyography. These symptoms should be differentiated from the neural paralysis caused by diabetes or other metabolic diseases[2)]. The neurological symptoms are usually caused by high pressure on the median nerve inside the carpal tunnel instead of the neuropathy of median nerve.

Many studies suggested that conservative treatments for the initial onset of CTS were safer than surgeries[3, 4)]. Low-level laser treatment (LLLT) is one of the choices of conservative treatments for CTS[5)]. The effects of LLLT in treating CTS were controversial. Some studies demonstrated that it had better therapeutic effects to treat CTS[5, 6, 7)]. However, one study found that LLLT did not have greater improvements than other conservative treatments[8)]. Recently, some researchers tried to use LLLT to treat CTS and irradiated on the transverse carpal ligament of wrists[9)]. They provided appropriate parameters of LLLT and treatment location, but did not compare the therapeutic effects for different severity of CTS. To go a step further, we tried to imitate the same process of LLLT for mild and

moderate symptoms of CTS. The purpose of our study was to investigate the clinical outcome and neurophysiological results of the mild and moderate CTS.

SUBJECTS AND METHODS

This study was approved by the Institutional Review Board on Human Subjects Research. Volunteers were the patients from the rehabilitation center of a teaching hospital and recruited from the out-patient clinic. In Table 1, the patients with CTS were diagnosed in accordance with the guideline[10]. For all patients, nerve conduction studies (NCS) on the ipsilateral ulnar nerve were normal for both the motor and sensory conduction.

The inclusion criteria in our experiments were the patients with idiopathic CTS who experienced repeated pain more than a year. The exclusion criteria included that patients had medical history of systemic diseases (rheumatoid arthritis, diabetes, and metabolic diseases), received any surgical operation and other treatments such as anti-inflammatory medicine, acupuncture, and physical therapy. In the sample size of our study, the type I error was set 0.05 ($\alpha = 0.05$) and power was set 0.8 ($\beta = 0.2$). The required the number of samples which was calculated the outcomes based on literatures was at least 14 for each group[9]. The 90 patients were randomly assigned to two groups based on the criterion of a double blinding experiment. The laser group received LLLT, and the placebo group received sham laser treatment. The sham laser had the same procedure as the laser treatment, but its power supply was cut off and did not generate energy output in order to avoid any psychological effect.

94 The laser instrument (Painless Light PL-830, Advanced Chips & Products Corp., USA) was adopted
95 in this study. The operation parameters of PL-830 were as follows: wavelength = 830 nm; output
96 frequency = 10 Hz, average power = 60 mW (2 × 30mW); and the treatment dosage = 9.7 J/cm^2,
97 respectively. The two diodes laser that emitted a laser beam (irradiated area = 370mm^2) on the palm
98 side of the wrist (between pisiform and navicular bones). LLLT was executed for 10 minutes, and 5
99 times per week for two weeks.

100 Each patient was assessed before, immediately after the treatment, and in the five weeks follow-ups.
101 Four assessments, such as pain, symptoms, neurological signs, and nerve conduction study, were
102 blinded to one evaluator (test-retest reliability = 0.96). All data after the treatments and in the
103 follow-ups were collected and compared with a baseline before the treatments.

104 (1) Pain assessment: Pain intensity was assessed by a visual analog scale (VAS). The most painful
105 sensation would be scored 10 and painless sensation was scored 0. The patients who participated
106 in the study used their past experience of pain as criterion and scored their pain intensity at
107 present.

108 (2) Symptoms assessment: A self-administered questionnaire, Boston Questionnaire scale, is used to
109 describe the discomfort of CTS[11]. It consists eleven questions to assess the symptom (Table 2).
110 The symptom at night was assessed by items 1, 2, 9, and 10, and the symptom during the day was
111 estimated by items 3～8 and 11. The scale of each item was quantified to range from 1 (mildest)
112 to 5 (most severe), and all scales of individual items were calculated and averaged.

(3) Neurological signs: Two clinical tests for CTS were used.

Phalen's sign test

The patients in this test bend their wrists by back-hand to back-hand against each other for 60 seconds. If there was a pricking or abnormal sensation in the radial side of the thumb, index finger, middle finger and ring finger, then the test result would be positive.

Tinel's sign test

Physician tapped the top of the carpal tunnel of patients' wrists. If the patting caused a pricking or abnormal sensation in the radial side of the thumb, index finger, middle finger and ring finger, then the test result would be positive.

(4) Nerve conduction study

The NCS was performed with a portable electromyograph (Medelec Synergy, Oxford, UK), and the stimulating electrodes were placed at the wrist proximal to the carpal tunnel. Accounting the recommendations[10], a pair of surface recording electrodes was placed on the abductor policis muscle to record compound muscle action potentials. The distal motor latency and sensory peak latency of the median nerve were measured by stimulating the nerve action potential. The room temperature remained at around 26～29 °C. The NCS for the CTS patients were conducted and diagnosed by the same physician, and the treatments were conducted by the same physical therapist. Both were blinded in this study.

All data collected from the patients was analyzed by SPSS13.0, and each statistical parameter in both groups was calculated. Because the distributions of all parameters using the Kolmogorov-Smirnov test were not normal ($p > 0.05$), so non-parametric tests were used in our statistical analysis. Mann-Whitney U Test was used to test the difference between the parameters of the basic data before the treatment. For comparing the differences in VAS, symptom, neurological signs, and NCS values of distal motor latency and sensory peak latency between both groups, the Wilcoxon test was used. Mann-Whitney U Test was also used to analyze the differences of assessments before and after the treatment, and in follow-ups. For categorical variables of Phalen's and Tinel's sign tests, the Fisher exact test was used to compare the score before the treatment with that after the treatment, and the scores in follow-ups. In all of the analyses, a two-tailed test was adopted and the α value was set at 0.05.

RESULTS

In this study, there were 90 patients with CTS, but 3 patients of placebo group dropped out during the experiment. In the laser group ($n = 45$), 27 patients were diagnosed as mild CTS, and 18 patients as moderate CTS. In the placebo group ($n = 42$), 27 patients were diagnosed as mild CTS and 15 patients as moderate CTS. In the baseline of age, duration, VAS, symptom, neurological signs, and NCS, there were no statistically significant differences between two groups before the treatment ($p > 0.05$). The basic data were summarized in Table 3.

For the patients with either mild or moderate CTS, there was an obvious statistical difference ($p < 0.05$) in VAS decrease between the laser group and the placebo group after the treatment. In addition, there was a significantly statistical difference ($p < 0.05$) in pain relief for the mild CTS patients during follow-ups.

According to the statistical results, the decrease of the severity in the Boston Questionnaire scale for the laser group is statistically greater than that for the placebo group, either during the daytime or at night ($p < 0.05$, Fig. 1 and 2). After the treatment, there was a statistically significant decrease in the total symptom scale for the patients with mild CTS in the laser group ($p < 0.05$), but not for the placebo group (Table 4).

In the neurological signs for CTS (i.e., Phalen's sign and Tinel's sign), if those signs occurred after the treatment, the assessment would be marked as a positive one. And if no signs occurred, the assessment would be scored as a negative one. After the statistical analysis, as shown in Table 5, we found that the amount of positive neurological signs in the Phalen's sign and Tinel's sign for the laser group was reduced greater than that for the placebo group after the treatment and in the follow-ups. This difference was statistically significant ($p < 0.05$). The laser group with mild CTS was particularly statistically reduced in Phalen's sign and Tinel's sign. ($p < 0.05$). In the NCS for mild CTS, there was a statistically difference between the laser group and the placebo group after the treatment ($p < 0.05$).

During the whole course of this study, no patient complained about any side effect and dropped out from LLLT.

DISCUSSION

This research was a controlled study that tried to treat CTS via providing contact band irradiation on transverse carpal ligament. After two weeks of LLLT with 830 nm laser, the VAS of the mild CTS patients in the laser group was decreased to 2.32 ± 0.78. The VAS of the moderate CTS patients was decreased to 3.76 ± 1.81. The results of our study were similar to the previous researches[3, 5] and confirmed immediate pain alleviation of LLLT. We also found that LLLT could not maintain this effect for the next five weeks, and thus further research with longer follow-up periods were required. The analgesic effect of LLLT is still controversial, but the clinical effect is confirmed[4, 9]. Many researchers have discovered that LLLT could promote the production of adenosine triphosphate from the mitochondria[5, 7, 9, 12], and enhance the respiration metabolism of the cells[13]. Those metabolisms reduce the wastes from the inflammation including leukotrienes and metabolite which could improve the healing process. Fulop et al. found that the pain alleviation might be caused by serotonin and endorphins[14] which could effectively raise the pain threshold[15]. The CTS patients who had neurological symptoms and pain due to the inflammation and swelling of the wrist often interfered with functional hand activities. In the result of our study, we found that a decrease of symptoms in the Boston Questionnaire scale accompanied a reduction of VAS. Although our study did not provide a direct proof regarding the changes of biochemical reaction in the affected wrist, we believed that LLLT had a positive effect on CTS.

187 The inflammation effect of the CTS wrist often causes neurological signs and median nerve
188 injury. In the electromyography, the mechanism of pain alleviation was better understood and the
189 reduction of pain could also be explained. In the previous research, LLLT was found to enhance the
190 conduction velocity of sural nerve after diode laser irritation on the normal nerve[16].Our research found
191 that after the 830 nm LLLT, the NCS values of distal motor latency and sensory peak latency were
192 reduced. We conjectured that nerve conduction velocity increased due to the repair of nerves. This
193 contention is same as that in the past research[17]. Applied to clinical treatments of CTS, LLLT was
194 more effective than other conservative treatments[18, 19]. It was apparent based on their results as well as
195 ours, especially for the improvement in symptom severity and neurological signs. Elwakil et al.
196 compared LLLT with the standard open carpal tunnel release surgery, and found that LLLT could
197 improve hand weakness and the atrophy of thenar muscles[7]. The velocity of neural conduction also
198 showed statistical significance after the treatment ($p < 0.05$). Some studies found that LLLT performed
199 better than other conservative treatments in reducing neurological signs and nerve conduction
200 velocity[18, 19]. Although the effect on neural tissues generated by LLLT is not clear yet, the NCS of
201 CTS were found to be related to the degree of severity of the symptoms in our research. In our study,
202 irradiation area of LLLT was not the distribution of median nerve. We also found that the NCS of the
203 laser group were statistically less than those of the placebo group after applying LLLT to transverse
204 carpal ligament ($p < 0.05$). Accordingly, this result indicated that using the LLLT with an 830 nm
205 diodes laser on the injured nerve is effective.

206 In an animal research, Gigo-Benato et al. used laser irradiation (wavelength: 808 nm; dosage: 29
207 J / cm^2; duration: 39 seconds) for the end-to-side neurorrhaphy of mouse, and irradiated directly on the
208 exposed axon of median nerve. They found that this approach could enhance the growth and healing
209 of the injured nerve[20]. However, it is difficult to apply to CTS patients. Because of median nerve of
210 human beings is located at the palm side of the wrist, and LLLT should target and reach the nerve in
211 the soft tissue under the skin. Thus, the laser energy might be absorbed by the soft tissue, and
212 insufficient energy reaches the injured nerve. Bakhtiary and Rashidy-Pour tried to use an 830 nm
213 point-like LLLT (1.8 J / point) to irradiate 5 points on the distribution of median nerve[8], and they
214 obtained an unsuccessful result. The reason was that the nerve dispersion is different from each patient,
215 and this method is very hard to provide an appropriate dosage for the injured section of the nerve[21].
216 Naeser et al. also tried to mark the hand and wrist with a square cm grid to treat each marked area with
217 the same dosage, and it resulted in an average dosage on each squares[6]. They found that the patients
218 experienced a pain alleviation of 50 %, but statistical difference was not seen ($p > 0.05$). Naeser et al.
219 asserted the reason for no obvious statistically difference in the assessment might be that the injured
220 nerve did not absorb enough treatment dosages[6]. Hence, the approach of point-like LLLT seemed
221 ineffectively to treat the CTS. Chang et al. thought that the main pathophysiology for CTS is the
222 inflammation and swelling of transverse carpal ligament, and essayed a beam-like diodes laser to
223 irradiate on transverse carpal ligament[9]. An identical 830 nm LLLT (9.7 J/cm^2) on the injured
224 transverse carpal ligament were imitated in our study. We also found that the pain alleviation for the

mild CTS patients was higher than that for the moderate CTS patients, and the reduction of symptoms for the laser group was higher than that for the placebo group after two weeks of LLLT. As mentioned in the previous research, it would take 4 to 5 weeks of LLLT to treat the mild and moderate CTS in order to achieve statistically significant reductions of neurological symptoms ($p < 0.05$)[6]. We considered that 830 nm diodes LLLT (9.7 J / cm^2) is a referable parameter for CTS, and a beam-like laser irradiated on transverse carpal ligament is a practical method. Therefore this kind of treatment is effective, especially for mild CTS.

Traditionally, the preferred priority treatments for CTS were the conservative methods which aim at pain relief and symptom alleviation[3, 4]. The successful treatment approaches include splinting, and corticosteroid injection[22]. The success rate of splinting was 70%, but the rate decreased to a range from 12% to 30% one year later[23]. The success rate of injection at a specified area for pain alleviation ranged from 51 % to 93.5 %, but the rate declined and fell to a range between 6.5 % and 33 % after one year[24]. However, we found that the disappearances of the Phalen's sign and the Tinel's sign reached 40 % and 47 % respectively after LLLT, and 60% and 47 % after five weeks. However, the comparison between LLLT and other conservative treatments was not investigated in this research, and was still needed to study in the future.

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301 Table 1. Diagnostic criteria of CTS

Diagnostic items	Mild CTS	Moderate CTS
Electromyography	The sensory peak latency value of median nerve was above 3.6 ms, and the distal motor latency value was lower than 4.3 ms.	The sensory peak latency value of median nerve was above 3.6 ms, and the distal motor latency value was above 4.3 ms.
Symptoms	The patients also had two or more of the following symptoms: (1)Phalen's sign (2) Tinel's sign (3)wakefulness at night due to the pain (4) wrist pain (5)abnormal sensation in the first three fingers.	The patients also had two or more of the same symptoms.

302

303 Table 2. Boston Questionnaire scale

Items	Scale
1. How severe is the hand or wrist pain that you have at night?	1～5
2. How often did hand or wrist pain wake you up during a typical night in the past 2 weeks?	1～5
3. Do you typically have pain in your hand or wrist during the daytime?	1～5
4. How often do you have hand or wrist pain during the daytime?	1～5
5. How long, on average, does an episode of pain last during the daytime?	1～5
6. Do you have numbness in your hand?	1～5
7. Do you have weakness in your hand and or wrist?	1～5
8. Do you have tingling sensations in your hand?	1～5
9. How severe is the numbness or tingling at night?	1～5
10. How often did hand numbness or tingling wake you up during a typical night in the past two weeks?	1～5
11. Do you have difficulty with the grasping and use of small objects such as keys or pens?	1～5

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307 Table 3. The basic data in two groups

	Laser group		Placebo group	
	Mild CTS	Mod CTS	Mild CTS	Mod CTS
Number of samples	27	18	27	15
L't / R't wrist	3/24	0/18	3/24	0/15
Age (y/o)	46.44 ± 10.12	48.76 ± 14.57	51.10 ± 12.19	44.60 ± 9.60
Duration of re-onset (months)	2.13 ± 0.86	3.02 ± 0.67	2.07 ± 0.30	2.89 ± 0.97
VAS	5.07 ± 0.76	7.91 ± 1.12	5.16 ± 0.79	7.10 ± 0.55
Severity scale	2.68 ± 0.68	2.89 ± 0.90	2.50 ± 0.52	2.49 ± 0.43
SPL (ms)	3.84 ± 0.24	4.05 ± 0.15	3.79 ± 0.11	3.96 ± 0.21
DML (ms)	4.10 ± 0.17	4.34 ± 0.45	4.09 ± 0.09	4.49 ± 0.69

308 All data are expressed as mean ± standard deviation, except for items of samples and L't / R't wrist,

309 which are presented as n.

310 VAS: Visual Analog Scale, SPL: Sensory Peak Latency, ML: Motor Latency.

311

312 Table 4. Mean changes from baseline scores of parameters, and analysis of changes after treatment

313 and five weeks follow-up

	After treatment			Follow-up		
	Laser group	Placebo group	*p* value	Laser group	Placebo group	*p* value
VAS						
Mild CTS	–2.76 ± 1.48	–0.50 ± 0.83	0.001***	–1.01 ± 0.91	0.01 ± 0.71	0.02*
Mod CTS	– 3.17 ± 1.81	–2.01 ± 0.91	0.01**	–1.25 ± 0.78	–0.51 ± 0.86	0.19
Severity scale						
Mild CTS	–0.78 ± 0.31	–0.12 ± 0.25	0.001***	–0.06 ± 0.53	0.31 ± 0.49	0.17
Mod CTS	–0.91 ± 0.32)	–0.29 ± 0.76	0.14	–0.47 ± 0.41	0.31 ± 0.72	0.06
SPL (ms)						
Mild CTS	–0.24 ± 0.12	–0.08 ± 0.13	0.006**	–0.02 ± 0.23	0.01 ± 0.04	0.11
Mod CTS	–0.08 ± 0.05	–0.05 ± 0.04	0.18	–0.14 ± 0.06	–0.04 ± 0.07	0.05
DML (ms)						
Mild CTS	–0.29 ± 0.21	–0.16 ± 0.14	0.002**	0.01 ± 0.11	–0.03 ± 0.25	0.19
Mod CTS	–0.07 ± 0.04	–0.04 ± 0.13	0.92	–0.07 ± 0.03	–0.02 ± 0.06	0.14

314 Data are expressed as mean ± standard deviation.

315 *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

316 Table 5. Number of participants (%) with positive neurological signs

	Phalen's sign test			Tinel's sign test		
	Before treatment	After treatment	Follow-up	Before treatment	After treatment	Follow-up
Laser group						
Mild CTS (n = 27)	27 (100)	12 (44)***	9 (33)***	27 (100)	9 (33)***	9 (33)**
Mod. CTS (n = 18)	18 (100)	15 (83)	9 (50)	18 (100)	15 (83)	15 (83)
Total (n = 45)	45 (100)	27 (60)**	18 (40)***	45 (100)	24 (53)***	24 (53)*
Placebo group						
Mild CTS (n = 27)	24 (89)	24 (89)	21 (78)	24 (89)	21 (78)	18 (67)
Mod. CTS (n = 15)	15 (100)	12 (80)	12 (80)	15 (100)	15 (100)	12 (80)
Total (n = 42)	39 (93)	36 (86)	33 (79)	39 (93)	36 (86)	30 (71)

317 Data are expressed as number of positive cases (percentage).

318 *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

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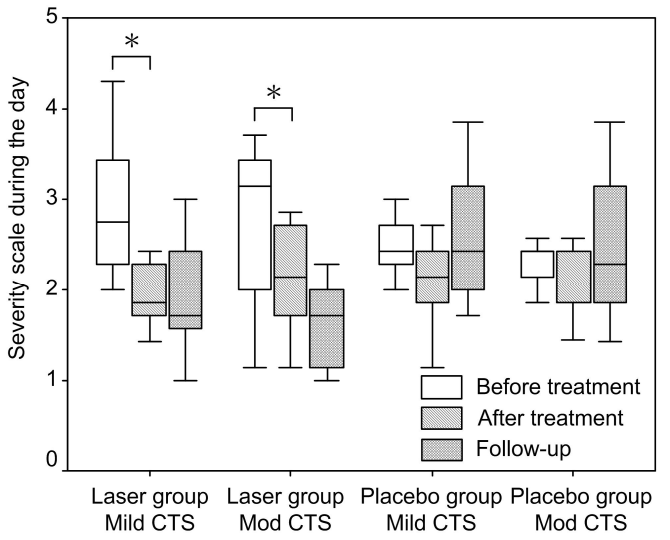
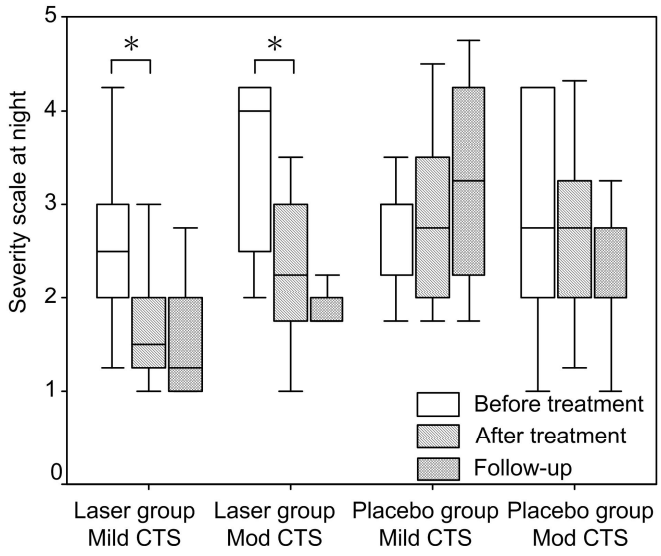


Fig. 1. Changes in the symptom scales during the day in both groups.



*: Significant differences were seen between groups ($p < 0.05$).

Fig. 2 Changes of symptom scales at night in both groups.