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REVIEW ARTICLE

Clinical effectiveness of low-level laser treatment on peripheral somatosensory neuropathy

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Abstract Peripheral sensory neuropathy treatment is one of the common treatment problems and causes morbidity and mortality in people suffering from that. Although treatment depends on the underlying cause of the condition, nevertheless, in some cases, there is no cure for it, and it requires palliative and symptomatic treatment. In laboratory studies, low-level laser has been effective in the nerves protection and restoration. The aim of this article is to investigate the clinical efficacy of low-level laser on improvement of the peripheral somatosensory neuropathy. Search in the articles published up to 30 October 2015 (full text and abstracts) in databases PubMed (Medline), Cochrane library, Physiotherapy Evidence Database was performed. The studies of low-level laser trials on patients with peripheral neuropathy were carried out and evaluated in terms of the exclusion criteria. There are 35 articles among which 10 articles had the intended and required criteria. 1, 3, and 6 articles study the patients with diabetes, neuropathy caused by trauma, and carpal tunnel syndrome, respectively. In six studies, laser led to a reduction in sensory impairment and improvement of the physiological function of the sensory nerves. In these articles, lasers (Diode, GaAlAs, He-Ne) had wavelength range 660–860 nm, radiation power 20–250 mW, energy density 0.45–70 J/cm^2. The intervention sessions range was 6–21 times and patient follow-up was 0–6 months. According to the results of these studies, low-level laser therapy can improve sensory function in patients with peripheral somatosensory neuropathy, although little research have not been done, laser treatment regimens are varied and do not recommend a specific treatment protocol. It seems it requires more research to sum up better, particularly in relation to diabetes.

Keywords Low-level laser · Peripheral · Sensory · Neuropathy

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Introduction

Neuropathy means damage and impairment of neuronal function, and it can involve the central or peripheral nervous system. Peripheral neuropathy is a common therapeutic problem [1]. With the spread of certain diseases and medical interventions, it seems the incidence of this disease in a substantial proportion of the population is inevitable. Carpal tunnel syndrome (CTS) [2], diabetes in about 50% of cases [3], chemotherapy in more than 30% of cases [4], a significant amount of medical and dental surgical interventions [5, 6], and direct effects of trauma in 1.5% cases [7] are of the common causes of peripheral neuropathy.

Neuropathy can be divided based on neural function involved into three groups of sensory, motor, and autonomic. Among the types of neuropathy, the sensory neuropathy is a common type. Pain, paresthesia (tingling, loss of feeling, and numbness) are of common symptoms of peripheral sensory neuropathy [8]. Peripheral neuropathy is significantly based on its severity by reducing quality of life, decreased physical function, and associated increased mortality [9–11].

Although the treatment of this disease is eliminating the underlying cause, however, in some cases, correcting the underlying cause is not possible and it may require relief and symptomatic treatment. Medical treatment options for peripheral neuropathy are limited and include common items such as antiepileptic drugs, antidepressants, analgesics, and opioid. Regardless of side-effects, these factors, based on clinical results, have a variety of efficacy and response to treatment is not the same [12, 13]. Hence, the use of new treatment options is ideal and desired.

Light has cell effects [14] and the emission of its wavelengths of the laser in the tissue is presented today as a means of therapy in some diseases. Low-level laser (LLL), with suitable tissue acceptability has been under clinical trial in different areas and has developing applications. In systematic and meta-analysis review studies, LLL has an effective role in healing wound [15], prevention, and treatment of oral mucositis [16], oral recurrent aphthous ulcers [17], and musculoskeletal pain relief have been shown [18–20].

In laboratory studies, LLL has been effective on improving neurons repair with different intensity of damage, which can suggest a new method of treatment as peripheral neuropathy therapy. In axonal injury, (axonotmesis) LLL leads to improved nerve function [21], the formation of the myelin sheath, increasing the number of neurons and Schwann cells [22]. In severe neural damage (Neurotmesis) that is accompanying with complete or relative disrupt, although results are contradictory, but generally the intervention of LLL is led to neuron regeneration and improvement of neurological function [23–28]. Also in spinal cord injury, LLL has reduced cell death by neuroprotective effect against ischemic conditions [29].

LLL has been under clinical trial for peripheral neuropathy therapy in several studies. The aim of the present study was a review of clinical trials on the effect of the LLL on peripheral somatosensory neuropathy (PSN). The effectiveness of the LLL affected by various factors such as type of laser, its radiation characteristics, pathology type, treatment regimens, and treatment outcomes, in other words, the effects of a type of radiation on different pathology and vice versa can have different results, and it is not necessarily generalizable to each other [18, 20, 30]. The finding of this study can help to better understand the available clinical evidence of LLL therapy to PSN treatment.

Materials and methods

In this review, the full text or abstract articles of clinical trials have been published until 30 October 2015 in connection with the therapeutic effect of LLL on the treatment of PSN in below databases, according to the following keywords and the common terms and expressions in the MeSH, a search was done. Also the articles related to the studies carried out to increase the scope of search in PubMed were investigated.

Database

1. PubMed (Medline)
2. Cochrane library
3. PEDro (Physiotherapy Evidence Database)

Keywords

(Low-Level Laser) AND (Peripheral neuropathy OR Hyperesthesia OR Hypoesthesia or Paresthesia OR Nerve injury OR Nerve trauma OR Neurosensory OR Sensory neuropathy OR Nerve conduction study OR Nerve conduction velocity)

Inclusion criteria

1. LLL clinical trial studies on the treatment of patients with peripheral somatic neuropathy

Exclusion criteria

1. Non-English articles
2. Unavailability of full text articles
3. Studies of case reports
4. Neuropathy associated with central nervous system diseases, radiculopathy such as spinal diseases, rheumatologic disease
5. Lack of control group (placebo or no treatment)
6. Non-random distribution of patients
7. Failure to report exposure conditions of laser such as radiant wavelength, radiant energy, time, and location of radiation

In order to review the standards and quality of studies in the literature, two browsers reviewed and monitored the articles found, and they were evaluated by the above mentioned criteria and their methodology.

In this study, sensory performance assessment criteria included clinical and electrophysiological standard evaluation. Conditions of radiation such as light power, radiation wavelength, energy density, duration, and location of radiation were carefully studied. Also in case of lack of direct report, the variables were added to the findings as possible based on available reports in the articles to complete information using the formula. The time of follow-up of patients, the result of laser irradiation on improving sensory neuropathy, and the complications of laser radiation were investigated.

Results

There were 35 articles based on inclusion criteria (Fig. 1). Two were non-English articles. Three articles due to lack of access to full-text, one research examined the patients with CTS suffering from rheumatoid arthritis, fourteen articles have no placebo group or no treatment, four studies were excluded due to lack of adequate information on radiation conditions or complete methodology for appropriate judgment, and one article due to lack of numerical results report of their findings was

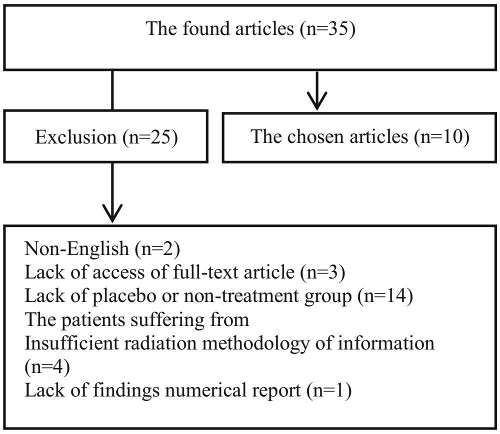

Fig. 1 The results of articles search

excluded. At the end, ten articles were assessed and the information is shown in Fig. 1.

Patients and sample size

Three neuropathy studies caused by trauma (36 patients) include two jaw osteotomy surgical interventions of bilateral sagittal split osteotomy (BSSO), and a study on patients with body peripheral nerves trauma resulting in paresis which the primary reason did not mention were treated by laser (10 patients). Six studies in connection with the treatment of CTS (229 affected hands) and a study of diabetic did laser treatment intervention on patients with polyneuropathy (15 patients).

Laser specifications

Six studies of the diode laser Gallium-Aluminum-Arsenide (GaAIAs), three articles of diode laser without its underlying material type and one article of He-Ne gas laser were used. Radiation wavelength in these studies had a range from 660 to 860 nm. The radiated power range was 20–250 mW (one study did not directly noted radiated power). Energy density had a range from 0.45 to 70 J/cm^2 and generally less than 10 J/cm^2. Radiation dose per session at 9 studies was between 0.9 and 4500 J and in a study total dose was not calculable [31].

The number of therapy sessions and follow-up time

The number of treatment sessions was between 6 and 21 times. Two studies did not follow patients after completion of treatment [32, 33]. In other studies, follow-up period was from 2 to 6 months after the intervention of the laser.

Method of measuring sensory function

In the studies, there were two approaches for laser effect on neuronal sensory function including clinical evaluation and electrophysiological study as shown in Table 1.

LLL and trauma

Gasparini et al. did laser intervention on half mandibular jaw of the patients with jaw deformity correction in BSSO surgery were subjected to sensory impairment in the path of inferior alveolar nerve and other half jaw of patients as the placebo group was considered. Radiation was conducted immediately and 24, 48, 72 h after surgery [including 11 points of oral surgery (660 nm), mandible, preauricular, jugular-digastric, and submandibular lymph nodes (789 nm)] and two other radiations within 48 h after the fourth day [including the surgery area, 4 points of lower lip mucosa, and 11 points in the lower lip and chin (780 nm)]. The results showed that 15, 30, and 60 days after the intervention, laser resulted in improved two points discrimination and accelerating the sense of touch to the normal conditions than the control group [34]. In the same study, Führer-Valdivia et al. conducted laser radiation for eight sessions in patients with sensory disorder of the lower jaw due to BSSO. In their study, intraoral three points of surgery, mental foramen, and mandibular both right and left directions were irradiated in days 1, 2, 3, 5, 10, 14, 21, and 28 after surgery and compared with the control group. In their findings during one and two months after the laser intervention, it had a positive effect on improving the performance of our sense of touch and kept its recovery process up to the end of the sixth month (68, 8% versus $p = 0.001$, 21, 4%). In this study, laser did not show analgesic effect, improvement of the sense of temperature and sense of direction [35].

Rochkind et al. conducted the laser intervention on the patients with at least 6 months after peripheral nerve injury, including axillary, brachial and peroneal, and suffering from muscle weakness and compared with LED illumination control group with the power less than 15 mW as the control group. Laser radiation was conducted on two sites of spine in the segment related to the damaged nerve (each session 2 h) and nerve injury section (each session 3 h) which was continued for 21 consecutive days. At the end of the sixth month of follow-up, the sense of touch and needle in the laser group was better than the beginning of study, but there was a significant difference than the control group; on the other hand, lasers resulted in improved muscle function in ascending during 2, 3, and 6 months of follow-up compared with the control group [36].

LLL and CTS

In six studies related to CTS in general, patients were suffering from slight to moderate disease. In the results of these studies, a conflicting effectiveness of the LLL based on the type of laser and exposure conditions have been reported.

CTS patients suffering from pain and numbness in the fingers were in the study carried out by Lazovic et al. were improved after 20 treatment sessions of LLL over 5 weeks

Table 1 Studies details

Writer	Neuropathy type number/study type	Irradiation point	Laser (nm)	Radiation power (mW)	Energy density (J/cm^2)	Energy per session (J)	Total sessions	Follow-up (month)	Sensory function evaluation	Results
Gasperini et al. 2014 [34]	Trauma 10, DB RCT [a]	Mandible, lip, chin	GaAlAs [m] (660, 789,780)	20,60,70	5, 30, 70	21.6, 50.4	6	2	TPD [b], ST [c]	Effective[n]
Führer-Valdivia et al. 2014 [35]	Trauma 16, RCT	Mandible	GaAlAs, (810 ± 20)	100	32	54*	8	1, 2, and 6	VAS [d], TPD, DD [e], TD [f]	Effective
Rochkind et al. 2007 [36]	Trauma 10, RCT	Spine and injury site	Diode(780)	250	7.5	1800* and 2700*	21	3 and 6	LSUMC[g], NCS[h]	Ineffective
Fusakul et al. 2014 [37]	CTS[l] 56 hands, DB RCT	Wrist	GaAlAs (810)	50	0.45*	18	15	3	SSS[i], VAS, NCS	Ineffective
Lazovic et al. 2014 [38]	CTS 40(61 hands) , DB RCT	Wrist	GaAlAs (780)	30	3.4	10.8*	20	3 weeks	VAS, NCS	Effective
Tascioglu et al. 2012 [32]	CTS 40, DB RCT	Wrist	GaAlAs(830)	50	–	3 and 6	15	NO	VAS, NCS, SSS	Ineffective
Jiang et al. 2011 [39]	CTS 45, DB RCT	Wrist	Diode(830)	60	9.7	36*	10	5 weeks	VAS, BQS[j], NCS	Effective
Chang et al. 2008 [40]	CTS 20 hands, DB RCT	Wrist	Diode(830)	60	9.7	36*	10	2 weeks	VAS,SSS, NCS	Effective on VAS, SSS
Irvine et al. 2004 [31]	CTS 7, DB RCT	Wrist	GaAlAs (860)	60	6	0.9*	15	1	LQ[k], NCS	Ineffective
Yamany and Sayed. 2012 [33]	Diabetic polyneuropathy 15, RCT	Lumbosacral and foot	He–Ne(850)	–	5.7	–	12	NO	VAS, NCS	Effective

[a] Double-blind randomized controlled trial

[b] Two-point discrimination

[c] Sensory Test

[d] Visual analog scale

[e] Direction discrimination

[f] Thermal discrimination

[g] Louisiana State University Medical Center

[h] Nerve conduction study

[i] Symptom severity scale

[j] Boston Questionnaire Scale

[k] Levine CTS Questionnaire

[l] Carpal tunnel syndrome

[m] Galliume-Aluminiume-Arsenide

[n] Laser intervention was reported to have significant difference against the control group

*Dose (J) = mean power *x* treatment time per session (reviewer corrections) and three-week follow-up. 81.6% of the patients in the study with slight pain at the beginning of the study were improved at the end of the treatment. Also the patients in the study continued only gliding training activities and lack splint, physical therapy, steroid, and non-steroid anti-inflammatory medications [38].

Chang et al. observed that a 830 nm laser intervention, although it did not differ at the end of 2 weeks of intervention (5 days a week and 10 min a day) with the control group, except the pain, but in the two-week follow-up, the laser reduced physical symptoms such as pain, sensory disturbances such as paresthesia and function improvement of patients hand. Also LLL will also have an impact on sensory transmission delay in electrophysiological study [40].

The 380 nm laser in the study carried out by Jiang et al. (5 days a week for 2 weeks and 10 min of irradiation) only had a significant effect on mild CTS. Patients of this study with mild disease compared with patients with the moderate disease at the end of the intervention with reduced sensory symptoms and improved their sensory nerve transmission delay. Patients with moderate disease showed a reduced pain, transitionally. After 5 weeks of follow-up, although pain in mild CTS was added compared with the end of the study, but was still lower than the control group. Also at the end of follow-up, sensory transmission delay did not differ from the control group [39].

The 830 nm laser in the study of Tascioglu et al. had no effect on sensory impairment. In this study, patients were divided into the 20-patient three groups of laser intervention 3 and 6 joules and control (5 days a week for 3 weeks, each 5 and 10 min). Although at the end of the laser intervention, it has positive results in reducing pain, severity of sensory disorders, and improvement of muscle strength and sensory nerve conduction velocity with the preferred 3 joules radiation, but it did not make a significant difference with placebo group [32].

Laser intervention (5 weeks, 3 days a week, and 6 min) in the study of Fusakul et al. on CTS patients that used splint like the control group, reduced the severity of sensory symptoms at the end of the study but during three-month follow-up, this decline has no reliability effect and did not make a significant difference compared to control group. In the electrophysiological study, distal motor latency was improved and it has a placebo effect on distal sensory latency, sensory nerve action potential amplitude (64). LLL did not affect the 7 patients with CTS in the study carried out by Irvine et al. (three times a week for 5 weeks) during 4 weeks of follow-up on the severity of symptoms, sensory loss, pain, and electrophysiological findings [31].

LLL and diabetes

Yamany and Sayed divided 30 patients with diabetes at least 6 months after polyneuropathy of their lower extremities and complained of paresthesia and burning pain and the use of analgesic drugs such as NSAIDs, opioids were forbidden for them without changing regime over a month before and up to the end of the study, into two 15-patient random groups. The patients without vascular complications and advanced atherosclerosis were based on the ankle-brachial index. At the beginning of the patients' intervention, in terms of age, sex, duration of diabetes, pain intensity, and duration of the symptoms of neuropathy were similar. Then 850 nm radiation was performed at Lumbosacral and the soles of the feet, each 15 min (3 days a week for 1 month). At the end of the intervention, the pain of the patients in laser group was significantly reduced (−1.6 cm). Also the sural sensory nerve conduction velocity was significantly improved [33].

Discussion

Subjective clinical and electrophysiological findings of the reviewed ten articles reported changing results on LLL efficacy in improving the patient's PSN. Sensory disorder in the course of alveolar nerve of subsequent correction of deformity of mandibular by BSSO method is a common complication, and it can make a permanent neuropathy in terms of the severity of the damage for patients [41]. LLL in the study of Gasperini and Führer-Valdivia [34, 35] can compensate relatively the sensory impairment of jaw in patients under BSSO. On the other hand, this intervention accelerated the recovery process of neurapraxia and axonotmesis. Neuronal trauma of organs in Rochkind et al. [36] patients by laser effect resulted in improved motor neuron electrophysiological parameters and improved muscle function, but it had a placebo effect on sensory function of patients [36]. In three studies out of six studies of CTS patients, a similar effect to sensory function of patients was found [38–40]. In diabetics, the study of Yamany and Sayed shows a decrease in sensory impairment of patients with LLL effect [33].

In vitro studies have been shown that LLL can result in restoring neurons and consequently an increase of nerve function [21, 22] which is consistent with positive findings in these studies.

The exact mechanism of LLL on cell repair has not been known. According to published studies, several mechanisms could be involved in this regard that include gene regulation and cell proliferation [42], improvement of tissue perfusion and creating peripheral vessels and improving microcirculation of the lesion and ischemic region [43], modulating the immune response and the effects of anti- inflammatory such as TNF-α reduction in a radiation dose-dependent [44, 45] reduction of IL1, IL6, and inflammatory cells at the site of injury [45], modulation of oxidative stress that reduces neuronal damage [46, 47]. In laboratory studies, acute and chronic nerve damage has been associated with reduction of the inflammatory mediators TNF-α, IL-1b, HIF-1a (Hypoxia-inducible factor 1-alpha) resulted in reduction of inflammation, pain, and improvement of neurological function [48]. Another study of laser irradiation leads to increase of cell metabolism to produce ATP, which is essential for neuronal function life [49]. LLL also facilitates Schwann cells production, myelin production [22, 26, 27], and the growth of nerve terminal [22, 50]. These mechanisms combined with each other in the pathogenesis of neuropathic patients of this study can be effective and justify positive effects of LLL in these studies. In CTS, the median nerve can be pressured. The resulting pressure not only leads to degeneration of ischemic conditions but it is with the myelin degeneration of nerve and fibrosis around the nerve [51]. All causes related to diabetic neuropathy are not known. The diabetic sensory neuropathy at each part of neural pathway from the environment to brain cortex can be built [52]. In a division of factors related to the impairment in blood supply to the nerve, ischemia, increased oxidative stress, glycosylation of neuron protein components caused by hyperglycemia are of the main causes that lead to impaired neuron metabolism and its function [53].

Challenge of the effectiveness of LLL is to determine a treatment regimen including radiation settings. Based on our review, there is no any specific treatment regimen for laser therapeutic effect in a particular disease. In a meta-analysis study on the laser radiation on control of neck pain, the author suggested that in a wavelength 820–830 nm, energy average of 5.9 ± 3.4 J, and at a wavelength of 904 nm radiation energy 2.2 ± 1.6 J at each point of emission can have positive and optimal results [20]. Bjordal et al. suggested a range of radiation conditions to control pain in some joints based on type of laser in 11 Clinical trial studies [54]. In present study, we cannot suggest a certain setting for the treatment of traumatic neuropathy, CTS, and diabetes, because the various factors including three main groups of type and severity of pathology, patient's conditions, and conditions of laser and radiation can affect the results. For example, diabetics in the study carried out by Yamani suffered from controlled diabetic and it passed about 6 months of neuropathy, and the same radiation conditions may not affect the patients with poorly controlled diabetes. In CTS patients, many patients suffered from slight to moderate disease severity and effects of laser irradiation may lead to good results and depend on disease severity [32]. As well as in radiation conditions of the same 830 nm if Chang and Jiang with 36 J energy density [39, 40] of effective laser, but in the study of Tascioglu, radiations of 3 and 6 J of 830 nm wavelength had a placebo effect on CTS sensory impairment [32]. In conclusion, it can be stated that in accordance with the findings of the 10 articles, the effective regimes can be used in other studies as a model, however, to conclude the effectiveness of the LLL in the patients and to determine the minimum and maximum of optimal dose, there is a need to study more.

In the evaluation of patients sensory function, a variety of methods of subjective measurement were performed for patients so that these findings are based on patient reports and persons may have a different understanding of sensory disorders that can cause confounding effect on conclusion due to lack of a measurement method.

In addition, among other restrictions of the said studies are lack of follow-up or length of short-term follow-up of patients (up to 6 months), which can have positive or negative effect on the results.

In the articles reviewed, only in the study carried by Fusakul, two slight pains and two tingling feelings in the hands of the patients were reported that have been relieved at the end of the study [37]. Therefore, it seems that LLL radiation from a clinical viewpoint may be a non-invasive and safe action.

Finally, according to the reviewed ten articles, LLL can be effective as a complementary therapy in the treatment of peripheral sensory neuropathy such as pain and paresthesia caused by trauma, primary CTS, and diabetic polyneuropathy, even if there is a need to sum up and present an optimal dose. Also LLL potentially can be effective in other PSN and can be used as a complementary tool trial.

Compliance with ethical standards

Conflict of interest All the authors certify that there is no conflict of interest with any financial organization regarding the material used and/or discussed in this research. The research was funded by authors and no grant or third party finances were used.

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