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ORIGINAL ARTICLE

Role of low-level laser therapy in post-herpetic neuralgia: a pilot study

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Abstract

The aim of the present study was to investigate the influence of low-level laser radiation at a wavelength of 650 nm for treating post-herpetic neuralgia, an extremely painful condition which frequently occurs severely in old age and may persist for years with no predictable course. In total, fifteen patients were included in the present study, out of which 8 were females and 7 were males aged between 42 and 82 years. All patients were treated through 16 sessions for 8 weeks, and pain scoring was done on a visual analogue scale and statistical analysis was made for comparison before and after treatments. The final pain score was 0 in 11 patients although their initial pain score was severe in 8 and moderate in 3 patients. In three patients, pain reduced to mild intensity (2–3), and in one, the final pain score was 4 on the visual analogue scale. Patients treated during the present study have not complained for recurrence of pain or any other abnormality even after many months since completion of the therapy. Overall, low-level laser therapy (LLLT) proved itself an excellent therapeutic modality for the relief of pain in post-herpetic neuralgia patients, which may replace pain management medicines in future.

Keywords Low-level laser therapy (LLLT) · Post-herpetic neuralgia (PHN) · Pain relief · Laser diode at 650 nm · Photobiomodulation · Visual analogue scale

Introduction

Post-herpetic neuralgia (PHN) is a painful condition which affects nerve fibres. It is the complication of herpes zoster that affects 50% individuals over the age of 50 years who develop shingles [1]. PHN is a burning, stabbing and extremely severe pain that occurs along a damaged nerve. It results from the inflammation of the sensory dorsal root ganglia of affected skin [1, 2]. Chronic neuropathic pain needs medications on a regular basis that requires balanced efficacy and tolerability in order to prescribe drugs with the least side effects. The first-line trials of anticonvulsants, tricyclic antidepressants and serotonin-norepinephrine reuptake inhibitors, alone or in combinations, can be used. Opioid medications like methadone proved their excellent effects in refractory cases. Some therapies like carbamazepine have been used successfully for long duration for treating trigeminal neuralgia pain; however, these should not be considered to the exclusion of other more recent, less supported therapies like botulinum toxin A, especially in refractory cases [3].

Recently, low-level laser therapy (LLLT) has shown significant effects in reducing pain associated with neuralgia [1, 4–8]. When tissue is stimulated with LLLT, its regeneration initiated which includes new vessel formation, muscle and nerve regeneration, and production of cartilage, collagen and even bone. It has a significant effect in reducing inflammation that causes the abnormal stimulation of the nerves in the case of PHN [1]. In another study, it has been reported that early application of low-level laser therapy reduces the incidence of post-herpetic neuralgia [9]. During the past few decades, the safety and efficiency of LLLT has been evidenced in treating a variety of skin diseases [10–17]. In physiotherapy, it is used to

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treat a wide variety of chronic musculoskeletal aches and pains [18]; dentistry to treat inflamed oral tissues and ulcerations [19–21]; dermatology to treat edema, ulcers, burns, dermatitis and acne; rheumatology to relieve pain, treat chronic inflammations and wound healing [22–27]. The United States Food and Drug Administration (FDA) has approved LLLT as a safe and effective alternative—a drug-free way for managing pain through 510(k) clearance.

This trial was designed to see the efficacy of LLLT in the pain management of well-established and unrelieved post-herpetic neuralgia. Few studies have been reported on the treatment of post-herpetic neuralgia [1, 2, 4–9]: Randolph et al. used laser sources at 660, 830 and 840 nm; Waked et al. and Moore et al. used 830; and D. J. Knapp employed two laser wavelengths at 810 and 980 nm. However, in the present study, continuous wave (CW) laser at 650 nm has been used to investigate the efficacy of LLLT for treating post-herpetic neuralgia because at this wavelength, cheap laser sources are available and they can be used to develop handy devices to treat skin diseases. In addition, most of the studies on the topic have been performed on European skin and the present study is performed on Asian skin (skin type IV) as per the Fitzpatrick scale.

In this study, a hypothesis has been made that LLLT may efficiently treat post-herpetic neuralgia which was based on the cited literature where it has been applied in different situations to reduce pain [1, 2, 4–8, 18, 22, 26]. The present study has been conducted at the dermatology OPD of PAEC General Hospital Islamabad to investigate the role of LLLT for the reduction of pain in patients with PHN. The trial was approved by the ethical committee of the hospital.

Nuts and bolts of LLLT

During LLLT, mitochondria convert oxygen and nutrients through oxidative phosphorylation and electron transport chain into adenosine triphosphate (ATP) that is considered an energy currency for metabolism in cells. In disease, injury or infection, cells get stressed because nitric oxide (NO) inhibits oxygen consumption. This reduces the production of ATP and increases reactive oxygen species (ROS), which leads to oxidative stress, which causes inflammation and cell death via gene transcription factor. In most diseases including neuralgia, oxidative stress may be the cause of pain.

LLLT uses red to NIR light (600 to 1000 nm) to shine the affected parts of body. It displaces NO from cytochrome c oxidase, allowing oxygen back and thereby restoring ATP production. Once normal mitochondrial function is restored, the cell metabolism improves and, as a result, the patient gets better more quickly [28, 29]. The ultimate effect of LLLT is produced by the transcription factor activation which modulates downstream cellular and tissue responses. It has been observed that cellular proliferation, migration, production of cytokines and growth factors have been shown to be stimulated by low-level red and NIR light.

The efficacy of LLLT depends upon the wavelength, dose and laser type: pulsed or CW. According to severity of disease, it is applied in several sessions with intervals ranging from twice a day to twice a week. The selection of laser wavelength therefore plays a vital role in the treatment because it determines the penetration depth inside the tissue, which depends upon the absorption and scattering properties of tissue for that specific wavelength used for treatment. When light is shined on the skin, it interacts with five main chromophores including deoxy-/oxyhaemoglobin, melanin, water and lipids, whose extinction coefficients are displayed in Fig. 1 which is reproduced from literature [1, 30, 31]. It shows that a wavelength which has low absorption in the chromophores should be selected so that it can penetrate deep into the tissue. It is evident that the laser light at 650 nm can penetrate up to 6 mm [32] in the vicinity of blood vessels to enhance ATP production, ultimately reducing the inflammation in the dermal nerves through the low-level laser therapy mechanism for treating post-herpetic neuralgia. However, human skin thickness varies, i.e. it is 0.5 mm on the eyelids; 4 mm or more on the palms of the hands or soles of the feet. In normal skin, it is ~2 mm up to the dermis, and beneath the dermis, there is a layer of hypodermis that contains subcutaneous fats and blood vessels [32], whose thickness varies among individuals. This wavelength of light targets the epidermis, dermis and hypodermis parts of the skin, containing several types of nerve sensors which are detectors of pain, temperature and itchiness. This suggests that the applied laser wavelength in present studies is the appropriate one for treating post-herpetic neuralgia.

Materials and methods

The present study has been carried out on 15 patients suffering from post-herpetic neuralgia. The study was fully explained to the patients and a written consent was obtained from all patients. Patients admitted to the trial were taken from routine check-up and who have been suffering from post-herpetic neuralgia for 1 month to 1 year with little or no response to a wide range of pharmaceutical treatments which included analgesics, and anti-inflammatory drugs like carbamazepine, amitriptyline and gabapentin. The pain was refractory to all forms of drugs. The presenting complaint was pain which was very agonizing for the patients. They actually had multiple neuralgic complaints like tickling, burning, stabbing,

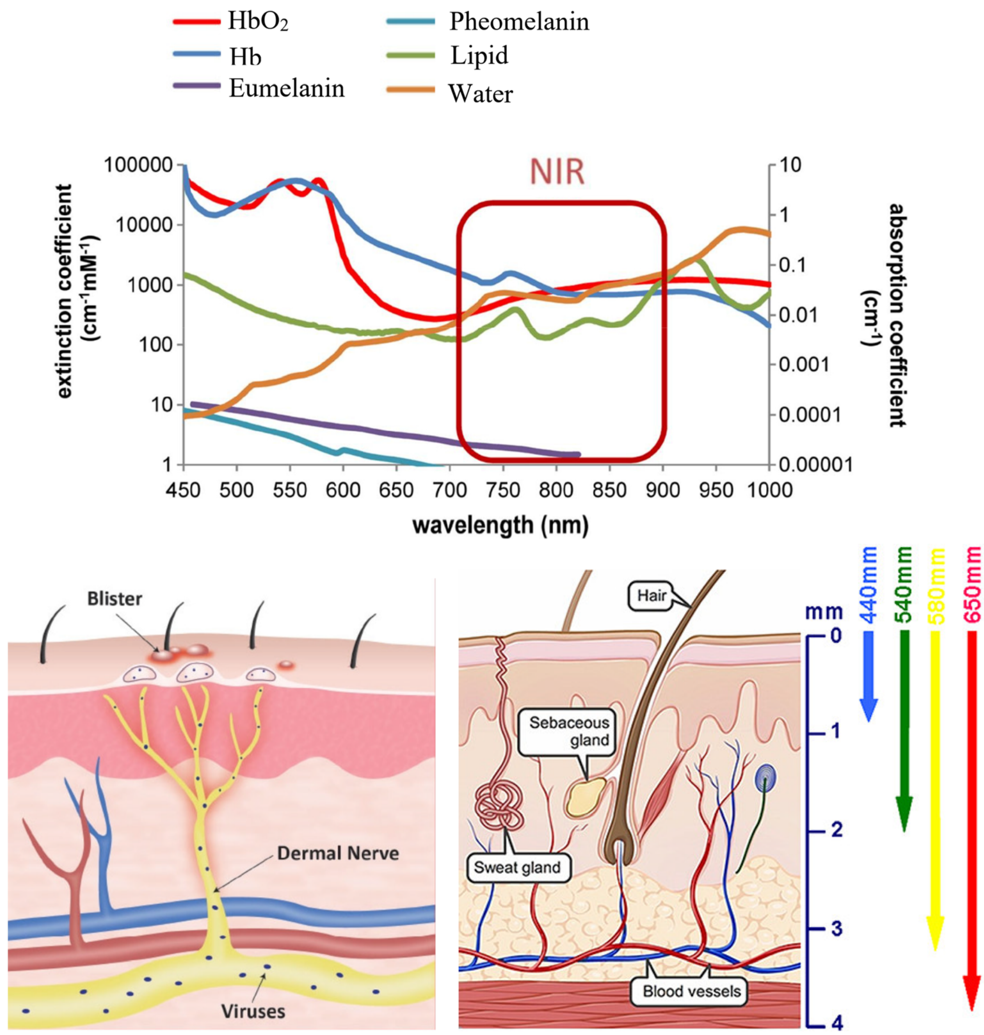

Fig. 1 **a** Wavelength-dependent absorption of light in oxy- and deoxyhaemoglobin, melanin, lipids and water that restrict the inside penetration of light in tissue. A window of absorption of chromophores approximately from 600 to 900 nm is called the near-infrared range. It is reproduced from Aswendt et al. [31]. **b** The mechanism of the development of post-herpetic neuralgia (reproduced from Randolph et al. [1]) showing the visualization of dermal nerve virus attacks that might appear as post-herpetic neuralgia. **c** The depth of light penetration into the skin, at various wavelengths (reproduced from Weijie et al. [30]), showing that laser wavelength at 650 nm can approach the blood vessels to reduce the inflammation in dermal nerves through low-level laser therapy mechanism for treating post-herpetic neuralgia

shooting, cutting pain, feeling of crawling insects and feeling of trickling sweat drops. All the patients included in the study had thoracic involvement of dermatomes. The patients with active herpes, current skin infection at site, with cardiac pacemakers or malignancy were excluded from the study.

The present study was conducted using laser system LLLT-650 (NILOP, Pakistan), which is a fibre-coupled aluminium gallium arsenide (AlGaAs) diode laser that emits red colour at 650 nm in CW mode. It can deliver laser power output from 10 to 2000 mW with steps of 10 mW on the site of interest. It has been employed to illuminate the body parts affected by post-herpetic neuralgia. The fibre probe of the laser system was developed in such a way that uniform laser illumination can be made on skin tissue in different spot areas. The laser system is TEC (thermoelectric cooler) cooled so that the laser wavelength should not be drifted due to the heating of diode p–n junction.

The laser dose (energy density) used in the present study was 3.6 J/cm^2 per tender point on the thorax [8] and it was applied for 1 min. Energy density was calculated by using the formula:

$$\text{Energy density}\left(\frac{\text{J}}{\text{cm}^2}\right)=\frac{\text{Total energy (J) delivered}}{\text{Treatment area}\ (\text{cm}^2)}$$

Where,

$$\text{Total energy (J)}=\text{Laser power}\left(\frac{\text{J}}{\text{s}}\right)\times\text{Treatment time (s)}$$

All the patients were given 16 sessions twice a week for 8 weeks. The pain scores (PS) were obtained by using a visual analogue scale (VAS) before and after applying LLLT. It consists of a straight line with endpoints defining extreme limits such as ‘no pain at all’ and ‘pain as bad as it could be’ [33]. The distance between ‘no pain at all’ and the mark on VAS defines the patient’s pain. VAS is also called Graphic Rating Scale (GRS). VAS used in the present study was graded from 0 to 10 points on a straight line, indicating 0 for ‘no pain at all’ and 10 for ‘pain as bad as it could be’.

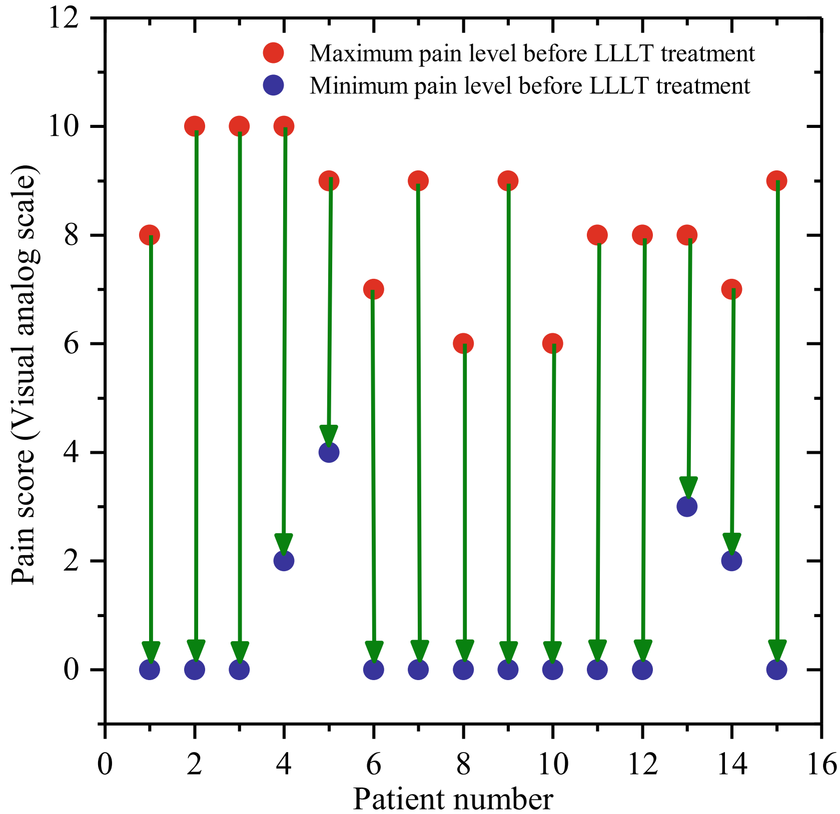

Fig. 2 The treatment effect of LLLT on the post-herpetic neuralgia patients using a diode laser at 650 nm. It is clearly illustrative that pain in 10 patients out of 15 is dropped to 0, whereas in the remaining 5 patients, it is also reduced to a reasonable lower level

In order to evaluate the efficacy of the LLLT treatment, statistical analysis was made by calculating the *p* value of the treatment outcomes by using a self-written routine in MATLAB 2014a (The MathWorks, USA). In statistics, the *p* value is the probability of obtaining the results from a test by assuming that the null hypothesis is correct. It is the level of marginal significance within a statistical hypothesis that represents the probability of the success of treatment. If the *p* value is less than 0.05, there is strong evidence against the null hypothesis upon which an experimental study has been

Table 1 A detailed overview of the post-herpetic neuralgia patients treated with low-level laser therapy (LLLT) using a diode laser at 650 nm

Patient ID	Maximum pain score on visual analogue scale	Final pain score	Remarks
Patient 1	8	0	16 sessions given
Patient 2	10	0	16 sessions given
Patient 3	10	0	16 sessions given
Patient 4	10	2	16 sessions given
Patient 5	9	4	Pain improved but cutaneous sensations persisted for which patient had multiple nerve blocks and ultimately had nerve ablation after 1 year
Patient 6	7	0	16 sessions given
Patient 7	9	0	Developed musculoskeletal pain during therapy but relieved with muscle relaxants and pain killers
Patient 8	6	0	16 sessions given
Patient 9	9	0	16 sessions given
Patient 10	6	0	16 sessions given
Patient 11	8	0	16 sessions given
Patient 12	8	0	16 sessions given
Patient 13	8	3	16 sessions given
Patient 14	7	2	16 sessions given
Patient 15	9	0	16 sessions given

devised. However, if p is greater than or equal to 0.05, then that value strongly supports the null hypothesis and predicts the success of an experimental study. In the present study, p value statistics has been used to test the hypothesis made in the present clinical trial. The outcomes of LLLT shown in Fig. 2 have been used to determine the p value.

Results and discussions

In order to investigate the efficacy of LLLT for treatment of post-herpetic neuralgia, it was applied on 15 patients who were diagnosed for the disease. Among 15 patients, 8 were females and 7 were males and the age range of the patients was between 42 and 82 years (mean 62 years). Using a visual analogue scale, the pain of patients was estimated upon their arrival at the clinic on different days. The patients were then treated through 16 sessions of LLLT by shining a red laser light of 1-cm-diameter spot on the selected points on the complained area of the affected skin. Based on the visual analogue scale, the final outcomes of the treatment of 15 patients after 16 sessions are shown in Fig. 2 which depicts a graphical overview of the treatment outcomes. The improvement in pain was judged by recording the visual analogue scale which has been divided into 10 equal intervals. The final pain score was 0 in 11 patients for whom initial pain score was severe in 8 and moderate in 3 patients. In three other patients (4, 13 and 14), who estimated pain as 10, 8 and 7 on VAS before LLLT treatment and after 16 sessions of treatment, pain was reduced to 2–3 on VAS. All the patients treated with LLLT using a laser diode at 650 nm showed significant improvement in pain except patient 5 for whom pain was improved but whose cutaneous sensations persisted. Actually, he had multiple nerve blocks which were later on ablated after 1 year. Similarly, patient 7 developed musculoskeletal pain during therapy which was relieved with muscle relaxants and painkillers. The rest of the patients remained absolutely fine throughout LLLT treatment sessions on different days and times. In most cases, initially, pain reduced to mild or no pain at the end of the low-level laser therapy session. The other parameters which indicated the improvement in pain management were the reduction of painkiller dosages and other drugs used for post-herpetic neuralgia, and improvement in the quality of life. Patients treated with LLLT during the present study still have not complained for recurrence of pain or any other abnormality even after many months since the completion of therapy.

The details of the treatment of all patients are also depicted in Table 1 for a comprehensive overview. By applying a self-written code in MatLab 2014a on the data in Table 1, p value was calculated to be 0.1, which is much higher than the significance level 0.05, therefore supporting the initial hypothesis that LLLT utilizing a red light (650 nm) can efficiently treat post-herpetic neuralgia.

The present study indicates that LLLT is very effective in terms of pain relief in patients with post-herpetic neuralgia. It has therefore been suggested that neural activity inhibition might be responsible for the therapeutic effect and that laser irradiation selectively inhibited nociceptive signals at the peripheral nerves [3]. However, treatment can be affected by various factors such as the physical condition of the patients, the characteristics of the laser (wavelength, dosage, CW or pulse) and the irradiated areas and the time duration.

Conclusion

The outcomes of the treatment of post-herpetic neuralgia patients with LLLT in the present study were satisfactory because these patients have not complained for recurrence of pain or any other abnormality even after many months since the completion of therapy. It provides a non-invasive, painless and safe method of therapy. Amazingly, patients get treated without any medication; in addition, this helped patients avoid the side effects of medicines. It can therefore be concluded that LLLT is an efficient modality for pain management in PHN patients. LLLT is now a regular practice at our clinic for treating post-herpetic neuralgia and other skin diseases like acne, aphthous ulcers, diabetic ulcers and neuropathic pain.

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Compliance with ethical standards

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

Ethical approval The present clinical trial was approved by the ethical committee of PAEC General Hospital through approval letter No. hosp-1(1)/13.

Informed consent All patients were informed about the study and a written consent was obtained from them.

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