Novel treatment (new drug/intervention; established drug/procedure in new situation)

Closure of non-healing chronic ulcer in Klippel–Trenaunay syndrome using low-level laser therapy

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Summary

A 69-year-old man diagnosed with Klippel–Trenaunay syndrome (KTS) reported to the physiotherapy outpatient clinic with the complaint of a non-healing ulcer over the right medial malleolus, for a 6-month duration, that was non-granulating and had moderate pus discharge with foul odour at initial assessment. There was a decrease in scores of the Pressure Ulcer Scale of Healing, a significant increase in granulation tissue, a decrease in the amount of discharge and foul odour along with complete closure of the chronic wound after irradiation with a light-emitting diode (LED). This is a novel case study analysing the possible effect of a helium–neon laser and LEDs on non-healing chronic ulcers associated with KTS, where the complete closure of the chronic ulcer that was initially not responsive to standard medical care was observed.

BACKGROUND

Klippel–Trenaunay syndrome (KTS) is characterised by the triad of vascular malformation, venous varicosities and hypertrophy of soft tissue and bone.¹ Varicosities in KTS are different from commonly occurring varicose veins. The distribution of varicosities too is different in KTS, being more extensive, and age-related, usually manifesting during infancy or early childhood. However, clinicians in India commonly encounter lower leg ulcers due to venous disease, pressure and diabetes, but association of ulcers with KTS is rarely observed in a clinical scenario. Surgery is usually considered as the cornerstone in the management of skin ulcerations leading to functional disabilities in this rare genetic disorder.¹ KTS is a complex syndrome and the management of ulcers is still a challenge in a clinical scenario as the recurrence of ulcers is common; moreover, management of recurrent ulcers is expensive and limited to a few therapies, which usually do not have promising results. Among the currently available therapies, the ability to induce complete wound healing is variable; there remains a need for a therapy that can improve or accelerate the healing process in the management of non-healing ulcers.² From acute wound management to augmentation of scar tissue remodelling, the clinician seeks to optimise wound care to promote healing. Over many decades in studies of varying quality, photobiomodulation, using low-level lasers to stimulate wound healing, has been heralded as an efficacious treatment in the management of wounds. This form of treatment has had high appeal owing to its novelty, relative ease and low morbidity profile.²

Low-level laser therapy (LLLT) is an umbrella term and is usually referred to as ‘low-intensity laser’, ‘low-power laser’ or ‘cold laser’. LLLT emits a single, coherent, monochromatic wavelength of light. A study by Maiya *et al*³

found that LLLT promotes photo stimulation, which accelerates the tissue repair process of diabetic wounds. A randomised controlled trial done by Hopkins *et al*⁴ not only outlined LLLT to be an efficacious tool for wound management but also stated enhanced healing as measured by photography and rate of wound contraction. The study by Hopkins *et al*⁴ advocates a clinically important role of LLLT to be an effective modality to facilitate wound contraction for partial-thickness wounds. Light-emitting diodes (LEDs) need to be differentiated from LLLT as beams generated by them are neither monochromatic nor coherent, but they have an advantage of treating a larger area using varying wavelengths in wound healing.² LEDs are postulated to stimulate basic energy processes in the mitochondria (energy compartments) of each cell, particularly when near-infrared light is used to activate the wavelength-sensitive constituents inside the cell (chromophores, cytochrome systems). It has also been established in earlier studies that LEDs accelerate the process of wound healing.⁵

The objective of the present case study was to assess the potential of wound healing induced by a combination of helium–neon (He–Ne) and LED lasers on non-healing ulcers lasting for a 6-month duration in a subject with KTS.

CASE PRESENTATION

A 69-year-old man presented with the chief complaint of a non-healing ulcer over the right medial malleolus, with pain and swelling for a 6-month duration, that was not favourably responding to standard medical care. The subject reported pain over the affected area while walking and was referred to the physiotherapy department for wound management. Despite rigorous medical measures in the form of frequent debridement and dressing for

Figure 1 (A, B) A view of the upper and lower extremities of the subject suffering from Klippel–Trenaunay syndrome.

ulcer, the subject had a recurrent chronic wound on the right medial malleolus with an area measuring 13.68 cm^2 . On initial examination, the subject had a Pressure Ulcer Scale of Healing (PUSH) score of 11 for the non-healing ulcer. The greatest length (head to toe) and the greatest width (side to side) was measured using a centimetre ruler; the wound length was found to be 3.6 cm and the width was found to be 3.8 cm. The ulcer was in stage II, the wound margins were not well defined and the exudates amount was moderate with a foul odour. On a physical examination, hypertrophy of the hands and feet was noted (figure 1). In the feet, the subject had diminished sensation bilaterally. On a motor examination, the ankle dorsiflexors had a muscle power of 3 bilaterally, with no ankle and knee reflexes.

TREATMENT

The subject was evaluated for any possible absolute or relative contraindications with laser therapy. Before irradiation, the procedures were explained to the subject and a written consent was obtained.

The accuracy for output dosage of the laser machine was tested before irradiation using a dosimeter (Newport, hand-held optical power meter, model 840). After deciding the parameters for laser irradiation, the nature of treatment was explained to the subject and he was asked to wear wavelength-specific goggles throughout the treatment sessions to prevent any accidental application of laser beams into the eyes. Before therapy, the subject's foot was cleaned using a povidone–iodine antiseptic solution and distilled water following which laser scanner for irradiation was used. An He–Ne scanner manufactured by Transmed Healthcare Systems (Kerala, India) was used for treatment. A frequency of 632.8 nm generating a power of 24 mW, at a distance of 50 cm, scanning along the x and y

axes of the ulcer area, yielding a total dosage of 1.58 J/cm^2 for 15 min to an area of 13.68 cm^2 at a frequency of 15 Hz. Following this, a hand-held class 4 LED (gallium aluminium arsenide; LX 2 model, manufactured by Thor) was used at a distance of 1 cm from the ulcer. The probe was a collection of 69 such LEDs, of which 34 LEDs of a wavelength of 660 nm had a spectral width of 50 nm at a 50% intensity, an average power of 10 mW, a spot size of 0.2 cm^2 and a power density (irradiance) of 50 mW/cm^2 . The remaining 35 LEDs of a wavelength of 950 nm with a spectral width of 50 nm at 50% intensity, generating a total power of 865 mW and a frequency of 156 Hz.

The dosage for irradiation was decided according to the formula: $D = P \times T/A$, where D is the dose in Joules per square centimetre; P is the laser power output in watts, T is the irradiation time in seconds and A is the area of wound measured in square centimetres. LEDs were used for 6 min, yielding an energy density of 22.8 J/cm^2 .

The subject was irradiated twice a week with the He–Ne scanner and LEDs (approximately 7 months from the commencement of irradiation) until complete healing. Usually an interval of 10 minutes was followed between the irradiations of two lasers. During each visit, the wound area was photographed along with an evaluation of the PUSH score to determine the healing of ulcer.

OUTCOME AND FOLLOW-UP

From the second week, proliferating granulating tissue was seen in the wound bed; the wound edge was well defined with no foul odour (figure 2). Initially, the PUSH score increased to 12 but by the second month it declined to 11 again. It further decreased to 7 by the fourth month and finally became 0 in the 7th month (figure 3) with complete closure of the ulcer site (figure 4). Moreover, after 8 months of follow-up no recurrence of ulcer at the right medial malleolus was found.

DISCUSSION

The PUSH tool was developed by the National Pressure Ulcer Advisory Panel as a quick, reliable tool to monitor the change in pressure ulcer status over time. Gardner *et al*⁶ did a prospective study in 2011 to assess the validity of PUSH when used to evaluate pressure ulcers in clinical

Figure 2 A wound area of 13.68 cm^2 , with well-defined wound margins and proliferation of healthy granulating tissue at the second week of laser irradiation.

Figure 3 The graph illustrates decrease in the Pressure Ulcer Scale of Healing score over 7 months following irradiation with laser.

practice and concluded that PUSH provides a valid measure of pressure ulcer healing over time and accurately differentiates a healing ulcer from a non-healing ulcer.

In KTS, the most common limbs involved are the lower extremities (88–95%), followed by the upper extremities (5%).⁷ Unilateral involvement occurs in 85% of cases. The combined involvement of the upper and lower extremities occurs in 15% of cases.⁸ Uncommonly, one may observe upper extremities (unilateral or bilateral) and crossed bilateral involvement (crossed dissociation). Very rarely, the involvement of all four extremities has been reported.¹ The subject in this study had the involvement of all four extremities (figure 1). KTS can affect blood vessels, lymph vessels or both.⁷ These problems commonly merge to present a mixture of two. Those with venous involvement experience excruciating pain and complications such as ulcers.⁷ Usually, surgical exploration is considered to be the mainstay in the management of KTS. Procedures like debulking are most commonly used. Invasive procedures used are known to have many complications.⁹

In 1998 in the *Mayo Clinic Proceedings*, Jacob *et al*¹⁰ reported about the largest experience in managing KTS with major surgery. For a follow-up of 39 years, the surgery team at Mayo Clinic evaluated 252 consecutive cases of KTS, of which all the procedures demonstrated a

Figure 4 Complete closure of the wound defect at 7 months, after irradiation with lasers.

high recurrence rate. Major surgery including amputation and debulking did not seem to offer any benefit on a long-term basis.¹⁰ In the present study, it was found that LLLT can be a superior tool in the management of chronic ulcers in KTS, as there was no recurrence of ulcer reported after the closure of wound site in the follow-up for 8 months, indicating an ambience of LLLT, which can be of greater importance in non-healing ulcers than other invasive procedures.

In 1965, Lindenauer¹¹ reported that subjects treated with multiple ligations and stripping appear to have been made worse by these procedures. He recommended the subjects merely wear elastic hose for symptomatic control of their varicosities and oedema,¹¹ indicating conservative treatment to be superior to explorative procedures.

The most striking feature during irradiation with He–Ne and LED lasers in the subject with KTS was eradication of foul smell and development of healthy granulating tissue (figure 2) as well as closure of the ulcer site (figure 4) without any surgical or drug therapy intervention. This suggests that laser can play a vital role in treating chronic non-healing ulcers in KTS.

In conclusion, irradiation with a combination of He–Ne and LED lasers can be a novel method and may be a modality of choice in the management of acute and chronic ulcers in KTS. Even after 8 months of follow-up, in this case study, after irradiation with LLLT no recurrence of ulcer was found at the previously irradiated site. Above all, a multidisciplinary approach should be considered to possibly make a difference in the management of ulcers in KTS.

Learning points

- Irradiation with He–Ne and LEDs can be a novel method and an effective treatment of choice in the management of chronic ulcer in KTS.
- After irradiation with lasers, the recurrence of ulcer was not observed on the treated site.
- A multidisciplinary approach should be considered in treating KTS.
- In future, a more structured study design should be pursued to provide rigorous evidence regarding the efficacy of LLLT in the management of chronic and acute wounds in KTS.

Competing interests None.

Patient consent Obtained.

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