Photobiomodulation with Blue Light in non-healing wounds: case series evaluation

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This article reports the clinical observations made on 19 patients affected by chronic wounds of diverse aetiologies, not responding to standard treatment who were treated with a Blue LED Light medical device (EmoLED). There exists important scientific literature supporting the evidence that light stimulates tissue regeneration and skin repair owing to the ability to interact with tissue through the photobiomodulation (PBM) process (Anders et al, 2015). Over the past few years, LED sources have proven to be effective solutions for the development of new medical devices based on PBM, allowing a more accurate selection of wavelengths, including the range of visible blue light that has generated growing interest for its potential in terms of wound healing (Lubart et al, 2007; Ishikawa et al, 2011; Landau et al, 2011).

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Chronic skin lesions represent a serious nursing and medical problem worldwide, having a significant impact on health and patient quality of life, alongside the substantial social costs associated with them. An overall quantification of the problem is made difficult by the diverse aetiologies of chronic skin lesions; ulcers of venous origin alone affect 1% of the adult population and 3.6% of people over the age of 65 in industrialised countries (Avruscio et al, 2017).

The search for a therapy that stimulates and accelerates ulcer healing is, therefore, a medical priority. In the context of research for new therapies that support and stimulate the healing processes of wounds, a medical device (EmoLED) has been developed that uses LED sources emitting blue light with 400–430 nm range wavelengths, with a power density of 120 mW/cm^2 and a fluence of 7.2 J/cm^2 at 4 cm from the light source. The functioning of the medical device is based on a light energy transfer from the device to the patient, without the intervention of mediators (chemical additive or medicines). Through the interaction with some endogenous chromophores of blood and skin, it is able to activate the photobiomodulation mechanism, stimulating the physiological processes of wound healing. The blue LED light medical device has been studied extensively in animal models, which demonstrated its efficacy and safety (Cicchi et al, 2016; Rossi et al, 2017a; 2017b; Magni et al, 2018; Mosti et al, 2019). In humans, the medical device reduced acute wound healing time (skin grafting harvesting area) and significantly improved chronic ulcer healing (Mosti et al, 2017; Mosti and Gasperini, 2018).

Patients

Clinical observations were conducted on patients (average age 75 years) with ulcers of diverse aetiologies, older than 2 months or more, and not responding to standard of care treatments, including compression therapy for venous leg ulcers. Eleven patients with venous ulcers, six patients with post-traumatic skin lesions, three patients with cutaneous vasculitis, one patient with wound dehiscence and four patients with peripheral arterial disease (PAD) ulcers, of which three had already undergone revascularisation, were observed.

For the purpose of evaluating the blue LED light treatment's effectiveness, the percentage of reepithelisation achieved over a maximum 10-week observation period was taken into account. The evaluation was carried out on 19 patients of the 25 enrolled. Five patients (two patients with PAD lesions, one patient with post-traumatic lesions and two patients with chronic venous insufficiency (CVI) ulcers were excluded due to treatment discontinuation for the following reasons: patient withdrawal, collateral events unrelated to the treatment and adoption of alternative therapy. One patient affected by a

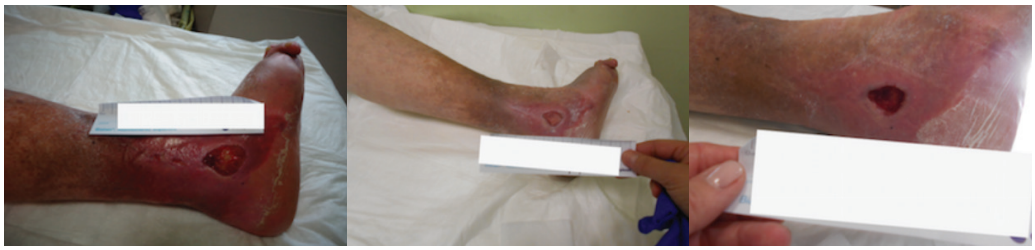

Figure 1. Cutaneous vasculitis on the medial malleolus of the left leg. (a) Beginning of observation (b) Week 5 (c) End of observation.

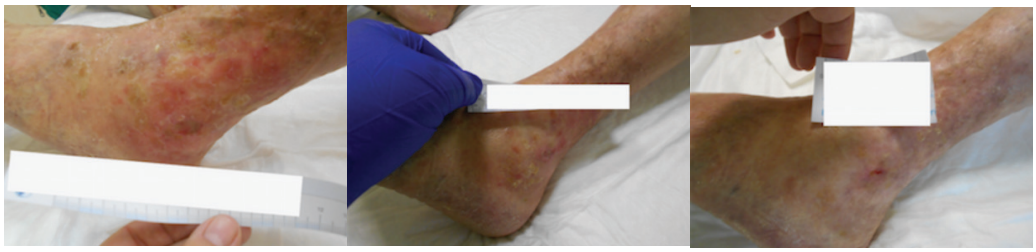

Figure 2. Venous ulcer on the lateral malleolus of the left leg. (a) Beginning of observation (b) Week 4 (c) End of observation.

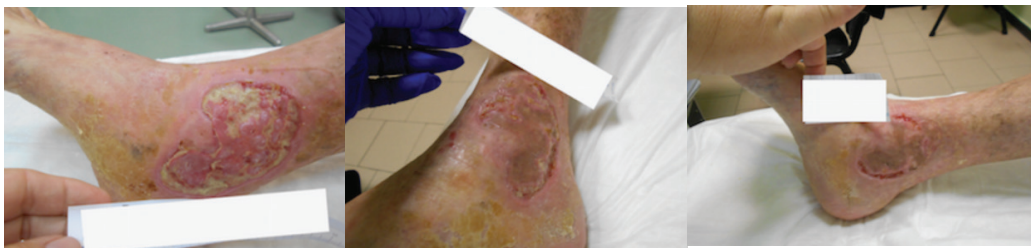

Figure 3. Venous ulcer on the medial malleolus of the right leg. (a) Beginning of observation (b) Week 4 (c) End of observation.

post-traumatic lesion who achieved total healing during the blue LED light therapy was also excluded from the final evaluation, as he showed a marked improvement only after a change of medication.

Materials and methods

The treatment schedule adopted was the application of blue LED light (400–430 nm) for 60 seconds once a week for a maximum period of 10 weeks, on every 50 mm diameter circular sub-area, at the time of dressing change and after wound cleaning. Subsequently, treatment suited to the type of lesion was applied in accordance with the standard of care adopted prior to enrollment, including compression therapy where necessary.

The use of blue LED light is complementary to conventional therapies and is part of wound bed preparation. Blue LED light is able to promote physiological wound-healing processes in a natural and non-invasive way, owing to the presence of elements that are sensitive to it in blood and tissues; in particular, cytochrome C, a haemeprotein component of the electron transport chain, which is sensitive to blue light due to the presence of chromophore protoporphyrin IX, with an absorption spectrum peak of around 410 nanometres. Once activated by the blue light, cytochrome C interacts with the last two mitochondrial transport chain complexes, and contributes to strengthening the cellular respiratory process, therefore, increasing the production of adenosine triphosphate, energy currency of the cell; this results in an increase in the cell's energy which can intensify its metabolic activity. Blue light has the effect of supporting wounded tissue with an increase in energy supply. Further important effects can be associated with EmoLED through the action of reactive oxygen species (ROS), signal transducers of numerous cellular pathways involved in tissue repair; in particular, an increased production of ROS induces a controlled increase of inflammatory functions sufficient for stimulating tissue response (Romagnani, 2000; Zadeh et al, 2000; Naik and Dixit, 2011; Racz and Prens, 2015; Landén et al, 2016), overcoming ulcer inflammatory stasis while promoting angiogenesis (Hong et al, 2014; Mistry and Brewer, 2017).

Results

The evaluation of reepithelisation was made through the clinical observation of lesion dimension and depth and perilesional skin. Of the 19 wounds observed, 16 responded to the treatment (84%) reaching an average 50% reepithelisation within the maximum 10-week observation period. Five wounds reached between 50–80% reepithelisation and six wounds reached over 80% reepithelisation (of these, half reached total reepithelisation over an average 7-week period). In the group of patients with venous

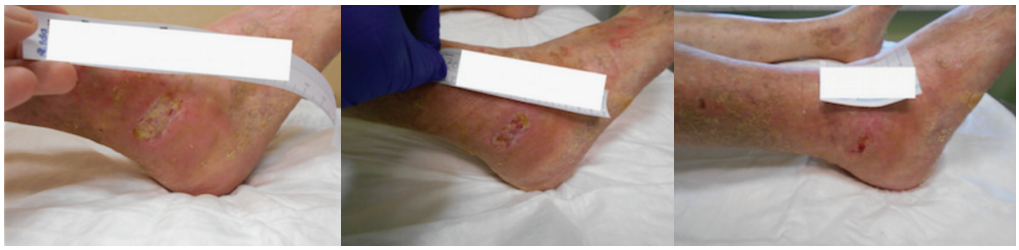

Figure 4. Venous ulcer on the lateral malleolus of the right leg. (a) Beginning of observation (b) Week 4 (c) End of observation.

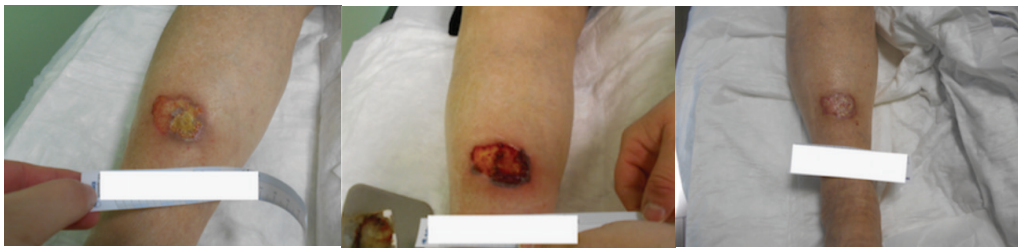

Figure 5. Post-traumatic skin lesion. (a) Beginning of observation (b) Week 2 (c) End of observation.

ulcers, seven out of nine ulcers responded to the treatment, with an average 65% reepithelisation. In two cases, there was no response to the treatment; both patients had diabetes, which may have had an effect on the treatment's lack of efficacy. Of the three post-traumatic ulcers evaluated, all responded to the treatment, reaching an average 77% reepithelisation. The three patients with vasculitis all responded to the treatment with an average 43% reepithelisation. Of the two PAD lesions, only one responded to the treatment. The patient with wound dehiscence responded to the treatment (85% reepithelisation reached). The treatment was well tolerated by all patients and a higher compliance was recorded. No adverse events occurred.

Three cases are described below that are particularly interesting from a clinical point of view, for the results obtained given the initial lesion conditions. The patient in *Figure 1* is a male affected by PAD, CVI and diabetes with chronic Charcot Foot. He had a recurrent cutaneous vasculitis on the medial malleolus of the left leg, that had been present for 2 months and worsening, with a surface area of around 12 cm^2, exuding, with lipodermatoslerosis of the perilesional skin. Before blue LED light therapy was initiated, the lesion was treated with a carboxymethylcellulose (CMC) dressing with Ag and polyurethane foam, after the removal of necrotic tissue (courettage). Moreover, the patient was wearing an inelastic compression garment to control the oedema. The compression exerted on the patient's limb was less than 20 mmHg (measured with a portable pneumatic pressure transducer), insufficient to further compromise the arterial framework and useful to partially reduce the oedema present on the limb. Blue LED light therapy was added to the aforementioned treatment for 60 seconds at every weekly dressing change session. After four treatments, the lesion was reduced by around 47%, was clean, with a normal exudate and proliferative edges, and the perilesional skin showed marked improvement. A decision was made to continue blue LED light treatment and to substitute the previous dressing with a collagen dressing, polyurethane foam and bandage. After 10 weeks and 10 blue LED light treatments, the lesion surface was reduced by 75%, presenting a clean base, proliferative edges, a normal exudate and reddened perilesional skin.

The patient in *Figures 2,3 and 4* is a female who presented with PAD, CVI, psoriasis and mild chronic kidney disease (CKD). The diagnostic angiography shows arterial line patency of lower extremities to plantar arches, with non-significant multiple local stenosis. She had three venous ulcers that had been present for years, and that had undergone grafting 1 month before. She presented with a lateral malleolus lesion of the left leg with a surface of 1.7 cm^2, as well as a medial malleolus lesion with a surface of 51 cm^2 and a lateral malleolus lesion of 24.5 cm^2, both on the right leg. The lesions, stable, with small red patches and small pustules, were treated with hyperoxidised oil-based medication, absorbent dressing pads and bandage. Blue LED light therapy was added to the aforementioned treatment for 60 seconds at every weekly dressing change session.

After five treatments, the lesions showed a marked improvement in terms of surface reduction; a decision was made to continue treatment and to substitute the previously used therapy with a CMC dressing with Ag, non stick gauze and bandage. At the end of Blue LED Light therapy, after 10 treatments in a 10-week period, the lesions were clean, with proliferative edges and intact perilesional skin.

The patient in *Figure 5* is a female affected by hypertension, gallstones and arthritis. At presentation, she had a lesion of traumatic origin that had been present for months, with a surface area of 12.6 cm^2, yellow sloughy tissue at the base, firm edges, highly exuding, with a perceived pain equal to 8 on Numerical Rating Scale (NRS). The lesion had undergone debridement surgery and heterologous graft, and was treated with Ag and polyurethane foam medication.

The patient was wearing a non-elastic compression brace to control the swelling. Blue LED light therapy was added to the aforementioned treatment for 60 seconds at every weekly dressing change session. After four treatments and 5 weeks, the lesion showed improvement with no signs of infection and critical colonisation, normal exudate, reduction of necrotic tissue, even if the lesion surface had not decreased. At the end of the blue LED light therapy, after eight treatments, the lesion reduced by 34%, showing no signs of infection, with proliferative edges and granulating tissue with the presence of slough.

Conclusions

To evaluate the efficacy of photobiomodulation with blue light as a chronic skin lesion therapy, patients with ulcers of diverse aetiologies not responding to standard treatment were chosen. Blue LED Light treatment was added to the standard treatment. Of the 19 ulcers evaluated, 84% responded to the treatment during the 10-week observation. Photobiomodulation with blue light contributed significantly to the healing process of the ulcers observed. The blue LED light medical device, EmoLED, proved to be safe and easy to use. WINT

Disclosure

The authors report that the Blue LED Medical Device was provided by EmoLED for a product test.

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