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

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).

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). 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/cm² and a fluence of 7.2 J/cm² 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...
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
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 cm², as well as a medial malleolus lesion with a surface of 51 cm² and a lateral malleolus lesion of 24.5 cm², 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 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 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 cm², 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.

The blue LED Medical Device was provided by EmoLED for a product test. The authors report that the Blue LED Medical Device, EmoLED, proved to be safe and easy to use.