Effects of photobiomodulation with blue light on diabetic foot ulcers: a case series report


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Abstract: Due to the poor circulatory system, a wound in a person with diabetes can demonstrate a persistent and protracted inflammatory response that results in reduced cellular proliferation and production of growth factors. Photobiomodulation (PBM), also known as low-level light therapy, is an application of light to promote beneficial effects such as reduction of inflammation and tissue regeneration. Promising results have been obtained with the use of blue LED light in the treatment of hard-to-heal wounds, which led us to assess its efficacy on patients with diabetic foot ulcers (DFU), in five patients undergoing treatment at the Kuala Lumpur Hospital Wound Care Unit. All the patients responded to the treatment reaching complete healing or a significant reduction of wound size during the treatment period. Our positive results obtained must be validated by further larger studies.

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Diabetes mellitus is a complex metabolic disorder with 25% of people with diabetes developing ulcers on the foot (Alavi et al, 2014), diabetic foot ulcers (DFU). Furthermore, one in every three people with neuropathic DFU has an amputation, representing the most prevalent cause of lower extremity amputation (Rastogi et al, 2020). The pathogenesis of DFUs is complex. An increased plantar stress due to foot deformity is the common cause of DFU occurrence, delayed healing can be caused by local ischaemia, prompting poor circulation and decreased neurovascular functions (Cavanagh, 2005). Due to the poor circulatory system, people with diabetes and a wound have a persistent and protracted inflammatory response, which results in reduced cellular proliferation and the lower expression of growth factors (Ponnusamy et al, 2020). Current treatment of a patient with a DFU includes systemic glycaemic control, pressure-relieving or off-loading strategies, local wound care (debridement) and infection control and where possible revascularisation (Hinchliffe et al, 2020). Despite the standard of care for DFUs being well described, often treatments are not sufficient and the rate of infection and amputation due to DFUs is still very high. There is a need to implement novel treatments to improve clinical outcomes in patients with DFUs.

Photobiomodulation (PBM), also known as low-level light therapy, is application of light (usually visible to infrared wavelengths) to stimulate or inhibit cellular functions leading to beneficial effects. The mechanisms behind the interaction between skin tissues and light has been extensively studied and Photobiomodulation has been acknowledged as an advanced physical therapy in wound management (Anders et al, 2015). In this context, the range of visible blue light was beneficial to treat skin wounds, reduce inflammation, and promote tissue regeneration (Lubart et al, 2007; Landau et al, 2011).

Objective

To assess the therapeutic effect of blue LED light used as adjuvant therapy in patients with DFUs.

Methods

We randomly selected patients with a DFU undergoing treatment at the Wound Care Unit, Hospital of Kuala Lumpur (WCUHKL). Blue light treatment was applied as adjuvant therapy, in addition to the most suitable primary dressing, according to the WCUHKL standard of care. The treatment was performed with a portable Medical Device (EmoLED; *Figure 1*) that employs

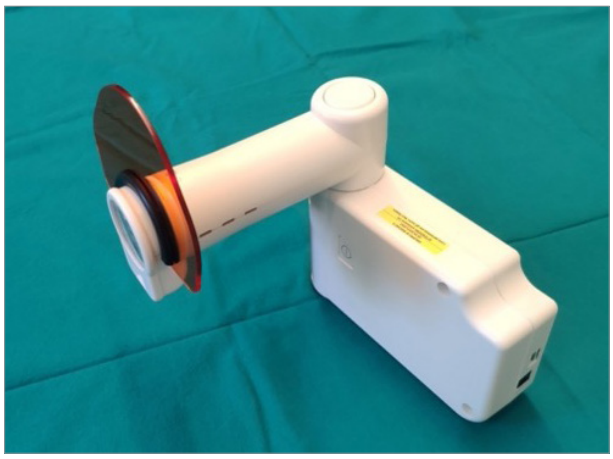

Figure 1. The medical device (EmoLED) used for Photobiomodulation with blue LED light

LEDs sources emitting blue light (410–430nm) with an optical power density of 120 mW/cm^2 and an energy density of 7.2 J/cm^2 at target. The blue LED light medical device illuminates a circular 5cm diameter area, at a distance of 4cm. The DFUs were irradiated twice a week for 2 minutes on each wound area of 5cm^2, until all the surface was covered. Then the dressing and offloading was re-applied. Wound bed tissue type, size reduction and wound healing, were assessed. Reduction of pain wasn't measured due to the high incidence of sensory neuropathy in patients with DFU.

Results

We recruited five patients into this case series, of these three patients had previously undergone amputations and two DFUs had been present for 12 months before the beginning of blue LED light treatment.

In a maximum treatment period of ten weeks all the five patients showed DFU wound bed improvement, size reduction and three of them achieved complete healing.

Case 1

A 75-year-old male with diabetes and underlying hypertension, presented with a DFU over the right toes that he had for almost one year before presentation at the foot clinic *(Case 1)*. He started blue light therapy in March 2020 in addition to collagen-based dressing and the wound achieved complete healing after 10 weeks of treatment.

Case 2

A 72-year-old male with diabetes and underlying hypertension. The patient presented with a DFU over left foot that he had for almost one month before presentation at the foot clinic *(Case 2)*. The wound showed granulation tissue with minimal slough and moderate serous exudate.

He started blue light therapy in addition to honey-based cream (WoundKreme, Feuilleorganix Sdn Bhd); after eight treatments the wound showed no more slough and low serous exudate associated with size reduction and it achieved complete healing after ten weeks of treatment.

Case 3

A 76-year-old male with diabetes and underlying hypertension. The patient presented with a DFU

Case 1. A diabetic foot ulcer (DFU) during treatment with blue LED light

- A 75-year-old male with diabetes and hypertension, presented with a DFU over right toe
- After almost a year he began blue LED light therapy and in addition to collagen-based dressing and the wound
- The wound healed after 10 weeks of treatment.

a. 9 March 2020 Size: 1.6 x 1.3cm	b. 11 March 2020 Size: 1 x 0.6cm	c. 4 May 2020 Reepithelialisation
		

over right foot, which had previously undergone Ray amputation of the 2nd toe. He had the ulcer for one week before presentation to the foot clinic *(Case 3)*. At the first observation the wound showed granulation tissue with minimal slough, high serous exudate and mildly macerated surrounding skin. He started blue light therapy in addition to honey-based cream (WoundKreme); after eight treatments the wound had no more slough, moderate exudate and no maceration, with an associated wound size reduction. The wound size was reduced by 94% after ten weeks of treatment.

Case 4

A 54-year-old female with diabetes and underlying hypertension. She presented with a DFU over right foot that had previously undergone transmetatarsal amputation; she had the ulcer for almost two years before presentation at the foot clinic *(Case 4)*. She started blue light therapy in January 2021 in addition to Urgostart dressing and Calmoseptine cream. Initially the wound showed high exudate, macerated wound edges and surrounding skin, as well as 1cm undermining. After 10 weeks of treatment the

Case 2. A diabetic foot ulcer (DFU) during treatment with blue LED light

- A 72-year-old male with diabetes and hypertension who presented with a DFU over left foot
- He started blue light therapy in addition to honey-based cream
- The wound healed after 10 weeks of treatment.

a. 25 January 2021 Size: 10.1 x 2.2cm	b. 15 February 2021 Size: 4.8 x 1.1cm	c. 17 March 2021 Reepithelialisation
		

Case 3. A diabetic foot ulcer (DFU) during treatment with blue LED light

- A 76-year-old male with diabetes and hypertension, presented with a DFU over right foot with a previous Ray amputation (and toe)
- On presentation the wound showed granulation tissue with minimal slough, high serous exudate and mildly macerated surrounding skin.
- He started blue light therapy in addition to honey-based cream
- The wound size was reduced by 94% at 10 weeks of treatment.

a. 11 January 2021 Size: 8.5 x 2.9cm	b. 3 February 2021 Size: 7.0 x 1.7cm	c. 15 March 2021 Size: 2.1 x 0.7cm
		

Case 4. A diabetic foot ulcer (DFU) during treatment with blue LED light

- A 54-year-old female with diabetes and underlying hypertension. She presented with a with a DFU over right foot. The wound had high exudate, macerated wound edges and surrounding skin and 1cm undermining
- She started blue light therapy in January 2021 in addition to Urgostart dressing and Calmoseptin
- After 10 weeks of treatments the wound remained highly exudative with macerated surroundings. The undermining had resolved; wound had reduced in size by 36%.

a. 12 January 2021 Size: 4.1 x 3.8cm	5 February 2021 Size: 4.0 x 3.3cm	c. 30 March 2021 Size: 4.5 x 2.2cm
		

wound remained highly exudative with macerated surroundings, however the undermining had resolved and the wound had reduced in size by 36%.

Case 5

A 63-year-old male with diabetes and underlying hypertension. He presented with a DFU over right foot that had previously undergone amputation of the 5th toe. He had the ulcer for almost one year before presentation at the foot clinic *(Case5)*. He started Blue Light therapy in January 2021 in addition to honey-based cream (WoundKreme) and Melolin. After 7 weeks (14 treatments) the wound achieved an estimated 90% size reduction.

Discussion

The mechanism of action of blue LED light is due to the light absorption by enzymes in the electronic transport chain (Cytochromes C, Cytochrome C Oxidase) and by flavoproteins that are sensitive to this wavelength; through these photoacceptors should this be photoreceptors, photochemical events are elicited that are able to trigger important therapeutic effects such as alleviation of pain and inflammation, and the promotion of wound healing and tissue regeneration (Prindeze et al, 2012). Previous results showed that blue LED light was able to induce a faster

Case 5. A diabetic foot ulcer (DFU) during treatment with blue LED light

- A 63 year-old male with diabetes and hypertension. Presented with a DFU over right foot that had undergone amputation of the 5th toe
- He started blue light therapy in addition to honey-based cream (WoundKreme) and Melolin
- After 7 weeks (14 treatments) there was an estimated 90% size reduction.

a. 22 January 2021 Size: 5.5 x 2.5cm	b. 18 February 2021 5 x 2cm	c. 17 March 2021 Reepithelialisation
		

wound healing process due to an accelerated transition of the inflammatory phase (Cicchi et al, 2016). Moreover, a rapid onset of inflammation was observed, probably the main process promoting a better recovery of wounds after irradiation (Magni et al, 2020a). Blue light was also able to modulate the activity of fibroblast cells, main responsible of extracellular matrix and collagen deposition during tissue remodeling (Magni et al, 2020b; Rossi et al, 2021). Blue LED light was also effective in resolving inflammation, promoting wound healing progression and reducing pain in patients affected by venous leg ulcers (VLU), cutaneous vasculitis and traumatic ulcers not responding to standard treatments (Mosti et al, 2018, Marchelli et al, 2019, Dini et al, 2020). Safety and efficacy of blue light in promoting reepithelialisation of long-term VLUs in ten weeks was confirmed in a multi-centre clinical study (B.L.U.R. - ClinicalTrials.gov Identifier: NCT04018924). Previous promising results obtained with blue LED light stimulated us to assess the efficacy in patients with DFUs. The blue LED light therapy was well tolerated, did not produce unpleasant or undesirable reactions for the patient and it promoted the lesion's healing process. The treatment was fast, from 2 up to 4 minutes: as far as DFU are quite small, repetition of treatment to cover the entire wound area wasn't an issue.

Conclusion

According to this preliminary experience blue LED light treatment used as adjuvant therapy is promising in terms of promoting wound healing in patients with DFUs. As this was a small case series, further studies must be done to validate our results.

Declaration of interest

The authors have no conflicts of interest to declare and received no funding for this study.

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