Use of photobiomodulation with blue light in the treatment of ulcers of various etiology in spinal cord injured patients: a case series

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ABSTRACT

The case study sought to validate the efficacy of Photobiomodulation with Blue Light as a therapy for promoting the healing of skin lesions resistant to conventional therapies in patients with spinal cord injuries. 25 patients were treated for a total of 32 skin lesions of various etiologies, primarily 2nd, 3rd, or 4th-degree pressure ulcers (ref. EPUAP/NPUAP classification), that had been present for more than 90 days and showed no clinical signs of evolution toward healing, despite having already received advanced medication treatment in the Spinal Unit for more than 4 weeks. For photobiomodulation therapy, a class IIa medical device (EmoLED) was employed, which uses LED sources that generate blue light in the 410-430nm region. Blue Light treatment restarted the healing process in 68.7% of the ulcers treated, with an average level of re-epithelialization of 72.8%. Blue Light, based on our prior experience, is a therapy that can assist shorten treatment and hospitalization times while also improving patients' quality of life; it can also be utilized for frail patients because it is well tolerated and readily deployed.

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Introduction

Photobiomodulation represents a new therapeutic method for the treatment of acute and chronic wounds. In photobiomodulation therapy, the injured skin tissue is illuminated by a source of non-ionizing electromagnetic radiation (emitted by laser or LED) to stimulate photochemical reactions; this process results in beneficial therapeutic outcomes including, but not limited to, the reduction of pain or inflammation, immunomodulation, and the promotion of wound healing and tissue regeneration.[1] The literature indicates that photobiomodulation is used for the treatment of inflammatory conditions, wound healing, and pain management.[2] Photobiomodulation has recently been employed for the treatment of coronavirus (including COVID-19) and related inflammatory diseases such as pneumonia, acute respiratory distress syndrome (ARDS), chronic obstructive pulmonary disease (COPD), and acute lung injury.[3]

The development of photobiomodulation has been possible thanks to lasers, "monochromatic" light sources with a very low spectral amplitude, which have allowed studying the interactions between biological tissues and specific wavelengths. An important acceleration in the development of this therapeutic method was provided by the subsequent advent of light emitting diodes (LED): these light sources allow obtaining monochromatic emissions similar to those of low-power lasers and they behave equally well in terms of therapeutic effects, whilst having a higher safety profile and being easier to use. Blue LED Light is a relatively recent technological achievement and

has attracted increasing interest both for its potential as a wound-healing therapy and for its antimicrobial effects. Our objective was to verify the efficacy of Photobiomodulation with Blue Light as an adjunctive therapy to promote the healing of ulcers unresponsive to conventional therapies, in spinal cord injured patients, using a Medical Device equipped with LED sources emitting Blue Light in the 410-430 nm range, possessing the features of easy clinical application and handling.

Materials and Methods

For the photobiomodulation therapy, a class IIa Medical Device (EmoLED) was used, produced by Emoled S.r.l, Florence, which uses LED sources that emit Blue Light in the range 410-430 nm, with a power density equal to 120mW/cm^2. It consists of a rotatable optical head (up to 180°) connected to a body; the optical head contains the LED sources and a distance sensor; the body is equipped with a touchscreen display for controlling the device and a multifunction button. The optical system allows obtaining a homogeneous and controlled light emission over a surface of approximately 20 cm^2; for larger lesions, the user will have to perform several successive applications; the number of applications needed to complete the treatment of a wound is automatically calculated by the device after switching it on and entering the approximate dimensions of the wound surface. The treatment distance must be 4 cm (+/- 1cm) and the device is activated only if placed at the correct distance; an indicator on the screen during application helps the user to identify and maintain its correct positioning. The duration of the single application (60 seconds) is pre-set.

The selection of the patients took place through an interdisciplinary and interprofessional evaluation, both clinical and of the patient's case history, which involved the collaboration of the physiatrist, the plastic surgeon, and the nurse. The study included spinal cord injured patients between the ages of 20 and 80, both hospitalized and attending day hospital, at the Spinal Unit Complex Structure. The selected patients had skin lesions of various aetiologies, mainly 2nd, 3rd, and 4th-degree pressure ulcers (ref. EPUAP/NPUAP classification), present for more than 90 days and showing no clinical signs of evolution towards healing, already having undergone treatment with advanced medication in the spinal unit for more than 4 weeks. Patients with the following were excluded from the study: fever and/or other systemic symptoms of infection and antibiotic therapy in progress; ongoing loco-regional infection; critical contamination of the skin lesion for which surgical debridement was required; cavity-like pressure wound. As the outcome of the case study, we chose the reactivation of the healing process with a level of re-epithelialization of the wound surface achieved >40%.

The patients underwent Blue Light treatment for 60 seconds over the entire surface of the lesion, once a week, when changing the dressing and after adequate cleansing with a preparation based on poly hexamethylene biguanide (PHMB).

Results and Discussion

25 patients were treated, 21 males and 4 females, with a mean age of 57.4 years. 32 skin lesions were treated: 29 pressure wounds (classified 2nd, 3rd, and 4th according to the EPUAP/NPUAP classification), 2 venous ulcers, and one surgical dehiscence. The mean ulcer size was 11.89 cm^2; the maximum size was 101.20 cm^2; the minimum size was 0.32 cm^2. The age of the skin lesion averaged 171.6 days; the maximum age was 360 days; the minimum age was 90 days. The wounds were located in the ischiatic (6), sacral (9), and coccygeal (2) regions; the buttocks (4); the external malleolus (2); the heel (2); the foot (2), respectively the sole and the stump at plantar level; the leg (5). The number of Blue Light treatments carried out varied from a minimum of 2 sessions to a maximum of 20 with an average of 10 treatments per patient. Table 1 shows the data per patient while Figures 1-5 show the evolution of the ulcer during treatment in 5 patients.

In our case, Photobiomodulation with Blue Light reactivated the healing process in 68.7% (22 out of 32) of the ulcers treated, achieving a level of re-epithelialization of the lesion area >40% and a percentage of mean re-epithelialization of 72.8% (average 85%; SD 32; $p<0.001$). In particular, 10 wounds achieved full recovery (100% re-epithelialization). No significant improvements were observed in 5 ulcers: one wound remained stationary while 4 ulcers recorded a worsening with enlargement of the wound area and two cases also the onset of a perilesional phlogistic state and a worsening of the wound bed. The 4 patients who worsened had important comorbidities (mainly diabetes, obesity, and allergic diathesis) even though the correlation between the therapeutic failure with the comorbidities is unclear.

Blue Light can stimulate specific molecules, involved in the tissue repair process, which are not normally reached by conventional therapies. Photobiomodulation is the biophysical mechanism by which light on specific wavelengths interacts with the biomolecules present in living cells and cellular organelles to induce a photochemical reaction. The photons that strike a biological tissue must be absorbed by specific photosensitive molecules to influence their physiological function. These photon-absorbing molecules, called chromophores, typically comprise transmembrane proteins, ion pumps, and channels located on the surface or within cells and cellu-

Table 1. Patients' data.

Patient	Age	Sex	Wound age (days)	Etiology	Location	Underlying pathology	Final re-ephitelialization	Treatments number
1	78	M	240	Pressure ulcer 3°	Left ischium	Paraplegia	24.24	9
			240	Pressure ulcer 2°	Sacrum	Paraplegia	27.27	9
			240	Pressure ulcer 2°	Left buttock	Paraplegia	83.33	9
2	60	F	360	Pressure ulcer 2°	Sacrum	Paraplegia	-380	8
3	20	M	360	Pressure ulcer 3°	Ischium	Tetraplegia	16.67	14
4	49	M	90	Pressure ulcer 3°	Left external malleolus	Paraplegia	46.67	8
5	42	M	540	Pressure ulcer 3°	Sacrum	Paraplegia	-60	14
6	71	M	240	Pressure ulcer 3°	Sacrum	Paraplegia	85	14
7	78	M	300	Pressure ulcer 2°	Left ischium	Tetraplegia	20	4
8	62	F	90	Pressure ulcer 4°	Left ischium	Paraplegia	-80	2
9	59	M	90	Pressure ulcer 3°	Right buttock	Tetraplegia	20	9
10	72	M	270	Pressure ulcer 3°	Coccyx	Tetraplegico	70.67	14
11	24	M	90	Pressure ulcer 2°	Heel	Paraplegia	100	18
12	66	M	90	Pressure ulcer 2°	Tibial	Tetraplegia	-16.67	8
13	47	F	90	Pressure ulcer 2°	Left buttock	Paraplegia	98	10
14	53	M	30	Pressure ulcer 2°	Right heel	Tetraplegia	99.44	2
15	60	F	90	Pressure ulcer 2°	Coccyx	Paraplegia	100	2
16	51	M	120	Pressure ulcer 2°	Foot sole	Tetraplegia	100	5
			90	Pressure ulcer 4°	Right ischium	Tetraplegia	100	8
17	62	M	180	Pressure ulcer 4°	Ischium	Paraplegia	25.33	10
			180	Pressure ulcer 2°	Sacrum	Paraplegia	100	6
18	43	M	360	Pressure ulcer 3°	Left external malleolus	Paraplegia	62.50	12
19	57	M	180	Pressure ulcer 2°	Right buttock	Paraplegia	100	2
20	58	M	90	Pressure ulcer 3°	Right leg	Tetraplegia	100	8
			90	Pressure ulcer 3°	Right leg	Tetraplegia	100	6
21	53	M	120	Pressure ulcer 4°	Sacrum	Paraplegia	70.36	20
22	49	M	90	Pressure ulcer 3°	Sacrum	Tetraplegia	100	12
23	61	M	90	Pressure ulcer 3°	Sacrum	Paraplegia	100	13
			90	Venous leg ulcer	Upper leg	Paraplegia	0	13
			90	Venous leg ulcer	Lower leg	Paraplegia	43.75	13
24	62	M	180	Pressure ulcer 2°	Stamp	Paraplegia	75	5
25	50	M	90	Pressure ulcer 3°	Sacrum	Tetraplegia	96.67	4

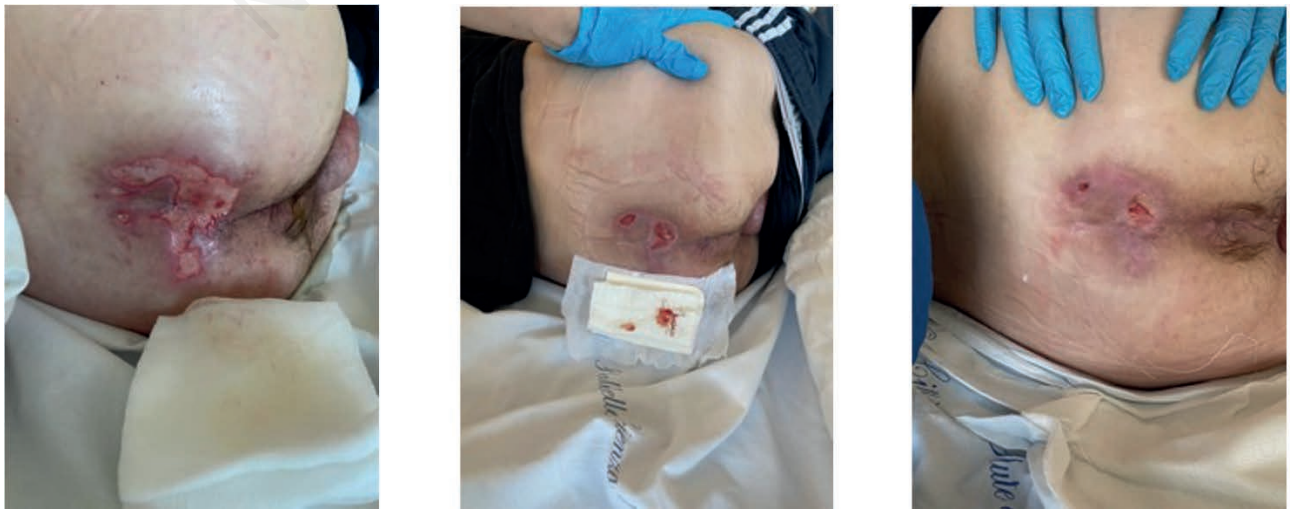

Figure 1. Patient No. 25 (ref. Table 1). Evolution of sacral pressure ulcer during treatment with Blue Light.

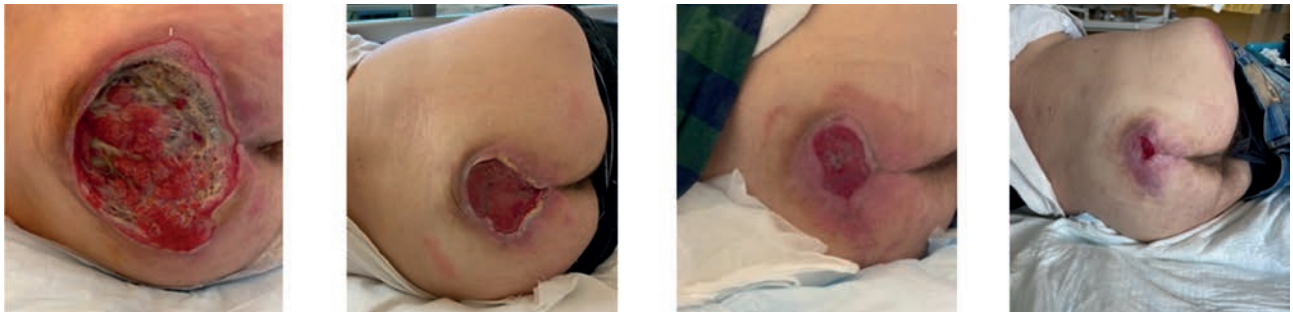

Figure 2. Patient No. 21 (ref. Table 1). Evolution of sacral pressure ulcer during treatment with Blue Light.

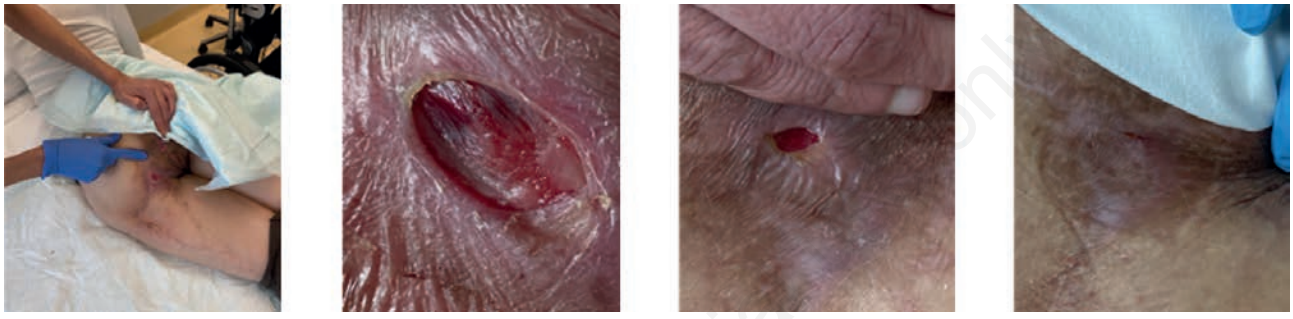

Figure 3. Patient No. 13 (ref. Table 1). Evolution of pressure ulcer on the left buttock during treatment with Blue Light.

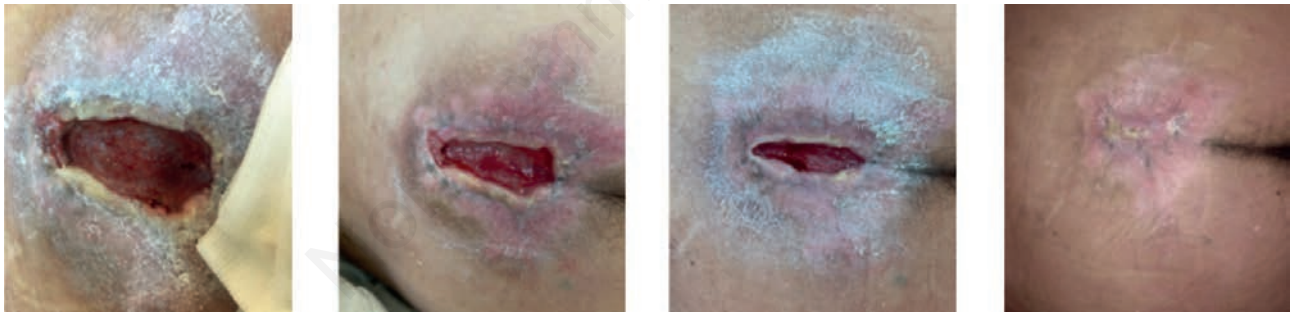

Figure 4. Patient No. 10 (ref. Table 1). Evolution of coccygeal pressure ulcer during treatment with Blue Light.

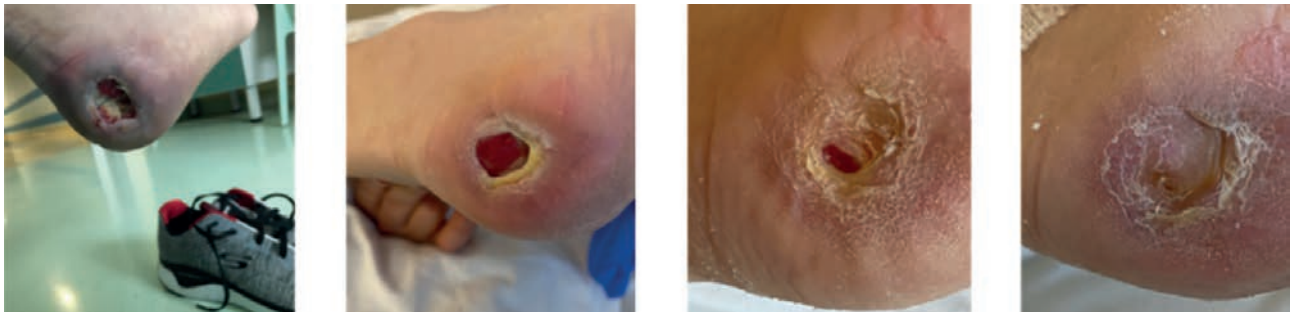

Figure 5. Patient No. 11 (ref. Table 1). Evolution of the ulcer on the heel during blue light treatment.

lar organelles (including mitochondria). The wavelengths in the range 410-430 nm (Blue Light) are absorbed by Protoporphyrin IX and act on Cytochrome C which, once activated by the Blue Light and interacting with the last two complexes of the mitochondrial transport chain, contributes to strengthening the cellular respiratory process and to increase the production of ATP; this results in an increase in the energy of the cell which can intensify its metabolic activity. The Blue Light, therefore, supports the injured tissue with an increase in the supply of energy, mainly necessary during the phases of proliferation and remodeling. Another phenomenon observed is the sensitivity of Fibroblasts to Blue Light, particularly relevant for the remodeling phase of the injured tissue: the fibroblasts modulate their activity (metabolism) based on the exposure time, suggesting a possible positive action of the Blue Light during the collagen formation process.[4,5] Further important effects can be associated with Blue Light through the action of ROS (reactive oxygen species), the signal transducers of numerous cellular pathways involved in tissue repair. By activating Flavins, Blue Light stimulates the production of ROS; the increase in ROS stimulates the production of the T lymphocytes present in the wound bed which can favor the phenotypic transition of macrophages from M1 (pro-inflammatory) to M2 (pro-healing),[6,7] promoting overcoming the inflammatory phase. Through the production of HIF-1α (Hypoxia-inducible factor 1-α) and the subsequent release of pro-angiogenic factors and the induction of eNOS (endothelial nitric oxide synthase), ROS promote angiogenesis and therefore a greater supply of nutrients and oxygen in the wound bed, greatly important during the proliferation phase.[8,9]

The duration of treatment with Blue light was defined as 60 seconds based on the protocol followed in the multicentre prospective controlled study "B.L.U.R."[10] which demonstrated the effectiveness of Blue Light in the treatment of vascular ulcers present for at least 8 weeks; image analysis demonstrated a mean residual wound area at week 10 that was significantly lower in the treated wounds than in the control wounds (48% less residual wound area; $p<0.016$), a trend in the likelihood of healing at week 10 41% greater for the treated wounds. Based on these encouraging results, we decided to try the therapy on our patients, and in particular on pressure ulcers, since, regardless of the etiology of the wound, healing proceeds according to the same sequence of articulated and complex events.

Conclusions

Blue Light therapy is a safe and simple therapy, not in contact with the patient, which directly stimulates tissue repair, enhancing cellular metabolism. It can also be used for frail patients, as it is well tolerated and quickly implemented. Blue Light treatment, controlled and safe, can help reduce treatment and hospitalization times and improve patients' quality of life. These preliminary results indicate that Blue Light could be an effective and safe therapy in the management of ulcers that do not heal with conventional therapies in spinal cord-injured patients. Further clinical investigations are needed to confirm these results.

References

1. Anders JJ, Lanzafame RJ, Arany PR. Low-level light/laser therapy versus photobiomodulation therapy. Photomed Laser Surg 2015;33:183–4.
2. Enwemeka C. Therapeutic Light. Rehab Manag 2004; 17: 20-7.
3. Williams RK, Raimondo J, Cahn D, et al. Whole-organ transdermal photobiomodulation (PBM) of COVID-19: A 50-patient case study. J Biophotonics 2022;15:e202100194. Erratum in: J Biophotonics 2022;e202190015.
4. Rossi F, Magni G, Tatini F, et al. Photobiomodulation of human fibroblasts and keratinocytes with blue light: implications in wound healing. Biomedicines 2021;9:41.
5. Magni G, Banchelli M, Cherchi F, et al. Experimental study on blue light interaction with human keloid-derived fibroblasts. Biomedicines 2020;8:573.
6. RomagnaniS.T-cellsubsets (Th1versusTh2). Ann Allergy Asthma Immunol 2000;85:9-18;quiz 18,21.
7. Landén NX, Li D, Ståhle M. Transition from inflammation to proliferation: a critical step during wound healing. Cell Molec Life Sci 2016;73:3861-85.
8. Mistry RK, Brewer AC. Redox regulation of gasotransmission in the vascular system: A focus on angiogenesis. Free Radical Biol Med 2017;108:500-16.
9. Hong WX, Hu MS, Esquivel M, et al. The role of hypoxia-inducible factor in wound healing. Adv Wound Care 2014;3:390-9.
10. Fraccalvieri M, Amadeo G, Bortolotti P, et al. Effectiveness of blue light photobiomodulation therapy in the treatment of chronic wounds. Results of the Blue Light for Ulcer Reduction (B.L.U.R.) Study. Ital J Dermatol Venerol 2022; 157:187-194.