Blue light therapy.
An alternative approach for treatment of vascular skin ulcers

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Managing non-healing wounds is nowadays a challenging issue because of costly burden for each national health care system and the important disability of patients in terms of increased pain and decreased overall quality of life. Chronic skin lesions are usually stucked in the inflammatory phase of reparative cycle and defined from absence of a clinical improvement in a temporal span ranging from four weeks to three months.
Improvement of wound microenviroment can play a leading role in the enhancement of chronic ulcers' healing process, as well as the standard care application on the basis of etiopathogenesis of ulcer.
Hereafter, we will focus on the interesting use of blue light therapy as therapeutical option on wound microenviroment, in order to unblock repair process and promote healing in stubborn wounds.

KEY WORDS: Advanced Medications, Blue Light Therapy, Vascular Ulcer

Introduction

Chronic vascular ulcers represent nowadays an increasing concern because of costly burden for each national health care system and the important disability of patients; elevated levels of cytokines and proteases, common findings in the chronic phlogosis, stuck skin lesions in the inflammatory step of wound healing process. Even if compression therapy is the gold standard for treating venous leg ulcers, many patients aren't able to adhere to this regimen of treatment. Nevertheless, in case of peripheral artery disease or also microvascular damages linked to diabetes mellitus, inadequate blood supply undermines normal healing process of skin ulcers, that sometimes occur as banal traumatic wounds or vesicles related to lower extremities' lymphedema. Use of blue light therapy (BLT) by photobiomodulation [1] of phlogosis mechanisms may help to prompt healing of stubborn wounds. Hereby, in this brief report we will describe two different clinical cases, a venous vascular ulcer and an arterial one, treated successfully with BLT as therapeutical strategy in order to unblock repair process.

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Case Reports

CASE STUDY N. 1

A 86-year-old woman was admitted at our hospital with non revascularizable popliteal-tibial arterial occlusive disease complicated by 2 very painful skin ulcers above the lateral malleolus of right leg, the largest one with diameter 1,3x2,8 cm close to another satellite microlesion of 0,7x1,2 cm (Fig. A). Microbiological cultures were negative. Doppler ultrasonography showed very reduced anterior and posterior arterial flows in accordance with a long, calcified femoro-popliteal-tibial occlusion. Patient had skin lesions for the last 9 months secondary to lymphedema caused by congestive heart episode, with no clinical signs predicting healing, although prostanoids intravenous infusions. Therefore, blue light therapy was applied once weekly just one minute for each treatment, whilst regular medications were performed with topical hyaluronates every two days. After 3 weeks of treatment, recalcitrant wounds completely healed (Fig. B).

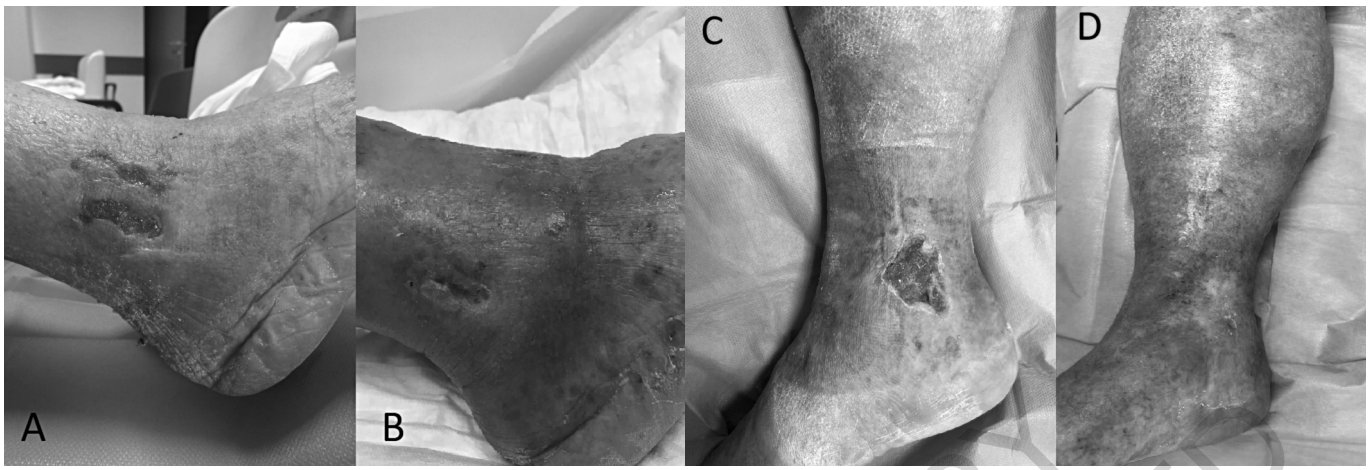

Fig. 1: A) View of skin ulcers located above the right lateral malleolus; B) Whereas a complete repair was observable only after 3 applications of BLT; C) Internal perimalleolar ulcer of the right leg with phlebostatic etiology; D) Complete healing process of skin lesion after about 8 weeks of BLT.

Case Study n. 2

A 51-year-old woman was referred to our division for a chronic phlebostatic ulcer at internal perimalleolar level with diameter 3x2,5 cm (Fig. C). The patient had already undergone total internal saphenectomy and also a second operation in order to correct recurrent varices. The ulcer didn't change over the subsequent 3 months after treatment with conventional medications. A normal pedal arterial pulse was detected. Moreover, the patient doesn't adhere easily to the classical compression therapy. An infection related to Enterococcus was found and eradicated through appropriate antibiotic therapy with carbapenemes. Once performed a correct debridement with the aim of removing necrotic tissue, we started an approach based upon 1 weekly application of blue light therapy associated to dressing changes with matrix of oxidized regenerated cellulose, collagen and silver.
Ulcer's view improved very quickly with clear size reduction just by week 3 (diameter 2,4x2 cm), whereas the goal of a complete healing of skin lesion was obtained after eight weeks (Fig. D).

Discussion

Dealing with a chronic ulcer, the first essential step is represented by the etiopathogenetic study of the lesion and the analysis of previous treatments' failure [2], in order to address the correct care.
Nevertheless, functional role of wound microenviroment is a concept of ongoing interest in the management of a recalcitrant wound, identifying a significant microscopic level able to substain or impair repair processes [3]. The relationship between inflammation and a chronic wound is well-known; phlogistic phase, typical of chronic ulcers, leads to a biochemical shift of wound microenviroment towards higher proinflammatory cytokines and proteases rates, that strengthen the inflammatory bioburden[3] impairing growth factors and proteins of extracellular matrix balance.
Then, development of biofilm represents a critical step in the healing cycle of a wound, warranting mainly a protection of bacteria towards a local antiseptic and systemic antibiotics; therefore, high frequency of superinfections due to increase of bacterial load requires a clinical and microbiological assessment of stalled skin lesions, in accordance with a correct antibiotic stewardship in terms of simple colonization or critical clinical infection. Together to appropriate wound bed preparation and eradication of frequent superinfections, advanced therapies are suggested with the aim of achieving the closure of a chronic wound. We should learn to look at the wound microenviroment as the level where the most important clinical battle of an *hard-to-heal* wound takes place.
Blue light therapy (BLT) induces a photothermal activity by interaction with photoreceptors targeted from Protoporphyrin IX in the epithelial and red blood cells in the wound bed; otherwise, in the first seconds of each treatment, hemoglobin activation promotes hemostasis, something very useful especially after a bloody surgical debridement. Mytochondrial enzymes and flavoproteins of tissues absorbe energy of blue light inducing chemical reactions and changing conformation of active biomolecules.
Even in case of reduced vascularization and lack of bleeding, such as often found in arterial and diabetic ulcers, cytochrome C protein activation, an emoprotein usually located on the surface of endothelial cells, increases ATP-mediated mitochondrial cellular respiration, improving healing process in relation to higher metabolic cellular activity. Simultaneously, photochemical stimulation of flavins from BLT determines reactive oxygen

species activation, allowing to overcome phlogistic stasis by TNF-alfa, IL-6 and Il-8 cytokines modulation and macrophages transition M1-to-M2 promotion beyond a specific neoangiogenetic effect due to VEGF release and NOS induction.
Therefore, BLT represents an innovative, non-invasive and easily reproducible option, that may be performed once weekly for at least six-eight times, improving cellular and biochemical level in the wound bed [4], with the aim of restarting the healing process of a chronic wound. In conclusion the description of this short report emphasizes that BLT may represent a therapeutic advancement as adjuvant tool in the modern day care of vascular wounds, showing encouraging results and shortening repair processes thanks to improvement of the wound microenviroment.

Riassunto

La gestione delle ferite croniche che non mostrano tendenza a guarigione resta ai nostri giorni un'avvincente sfida clinica e una problematica di serio rilievo in considerazione dell'elevato costo di cure a carico del sistema sanitario nazionale e soprattutto dell'importante impatto sulla qualità di vita dei pazienti che ne risultano affetti.
Le lesioni ulcerative croniche sono abitualmente bloccate nella fase infiammatoria del ciclo riparativo e convenzionalmente vengono definite dall'assenza di un miglioramento clinico tangibile in un arco temporale compreso tra quattro settimane e tre mesi.
Il miglioramento del "wound microenviroment", ossia il microambiente della ferita, potrà giocare un ruolo determinante nell'avanzamento del processo di guarigione della ferita cronica, in associazione all'applicazione dello standard care una volta identificata con chiarezza l'eziopatologia della lesione, mantenendo un approccio olistico in quanto l'eziologia è talora multifattoriale.
In questo articolo noi focalizzeremo l'attenzione sull'interessante uso della terapia con la luce blu come opzione terapeutica in grado di agire sul microambiente di ferita, al fine di sbloccare i processi riparativi e promuovere la guarigione di ulcere vascolari croniche, laddove le convenzionali terapie di base non abbiano determinato un concreto beneficio clinico.

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