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Case report

Application of photodynamic therapy, laser therapy, and a cellulose membrane for calcaneal pressure ulcer treatment in a diabetic patient: A case report

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ABSTRACT

Diabetes mellitus is a metabolic disorder in which a person has high blood glucose levels due to inadequate insulin production by the pancreas. Wounds in these individuals cannot heal properly over time due to circulatory changes that hinder and stagnate the healing process. We report the case of an 82-year-old female type 2 diabetes mellitus carrier, presenting to clinical-dermatological examination pressure ulcer (PU) in the right calcaneus region. The patient was treated with photodynamic therapy using curcumin and blue light-emitting diodes (LEDs), laser therapy, and the application of a cellulose membrane in order to promote ulcer decontamination by local action, accelerate wound healing, and maintain favorable conditions of asepsis and moisture, respectively. The ulcer healing occurred after 30 days of treatment and total epithelialization was observed. From the results obtained in this case report, we conclude that the combination of photodynamic therapy, laser therapy, and coating with a cellulose membrane is a promising treatment for the healing of PU in diabetic patients.

1. Introduction

Diabetes mellitus is a metabolic disorder in which a person has high blood glucose levels due to inadequate insulin production by the pancreas [1]. Wounds are difficult to heal in individuals affected by this condition due to circulatory disorders that interfere with the healing process [2]. Pressure ulcer (PU) is a localized injury to the skin and/or the underlying tissue, usually over a bony prominence, as a result of pressure or pressure in combination with shear, frequently seen in immobile hospitalized patient [3]. In such cases, infections are common complications often associated with the increased risk of amputation [3].

Overuse of local and systemic antibiotics has contributed to the high prevalence of multi-drug resistant infections in diabetic patients. Furthermore, the limited penetration of drugs into infected areas, which is aggravated by ischemia, reduces the effectiveness of conventional therapies [4]. Photodynamic therapy (PDT) is considered a promising new treatment method for the eradication of microbes, and has been clinically approved for the treatment of several infectious skin diseases, such as acne and viral warts [5]. In addition, several studies have confirmed the efficacy of PDT in the treatment of bacterial infections and their biofilms [6].

Of the various methods shown in literature to accelerate the healing process, the use of lights with low energy intensity has garnered an increase in interest. Some studies have reported beneficial effects of laser biostimulation for wound healing in cell cultures, animal models, and in clinical applications in humans [7]. These effects include increased local blood circulation, cell proliferation, enhanced cellular and subcellular processes required for the formation of collagen type I and III, and increased ATP synthesis and lymphocyte action [8].

Although there are various types of biological and synthetic dressings available, the search for an ideal dressing is still in progress. According to modern methods for wound healing, an ideal system should be structurally and functionally similar to the skin autograft.

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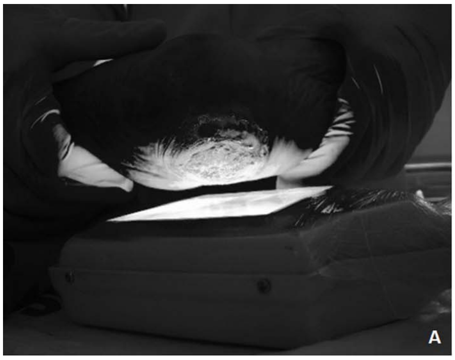

Fig. 1. (A) PDT; (B) low level laser therapy.

Recently, advancements in bioengineered materials have led to the development of an artificial skin polymer made from cellulose produced by the bacteria *Gluconacetobacter xylinus*. These skins have the ability to protect burn wounds and lesions on human skin, allowing gas exchange and respiration of the body and preventing the passage of liquid and impurities. Because of its unique properties, several studies have shown that microbial cellulose has great efficacy in improving the healing process in chronic wounds [9].

Our objective was to present a case report of one pressure ulcer (PU) in the calcaneal region in diabetic patients treated by a combination of PDT, laser therapy, and the application of a cellulose membrane.

2. Case report

A Caucasian 82-year-old female patient with type 2 diabetes mellitus, chronic venous insufficiency and hypertension using Metformin hydrochloride (1700 mg/d) and Captopril (50 mg/d) was hospitalized due to the presence of venous ulcers in the left lower limb. The ulcers were treated topically with no success, and the left limb was amputated. In addition to this condition, she presented chronic venous insufficiency and hypertension. During her hospital stay (30 days), the patient developed a grade III PU in the right calcaneal region measuring 7.4 cm^2 in the clinical-dermatologic examination.

Prior to the treatments, the PU was cleaned with sterile saline (0.9% NaCl). To perform the PDT, the photosensitive agent curcumin [1,7-bis (4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione] (PDT Pharma Industry and Trade Pharmaceuticals LTDA, Cravinhos, SP, Brazil) in a 1.5% emulsion base was used [10]. The emulsion formulation consisted of: BHT (0.05 g), Nipazol (0.05 mL), Crodabase CR-2 (12 g), Nipazim (0.15 mL), dissodic EDTA (0.14 g), Germal (115 0.44 g), and distilled water q.s. to prepare 70 g of the emulsion used in this case. Curcumin was applied across the surface of the ulcer, and immediately, the region was occluded with PVC film and aluminum foil to prevent exposure to ambient light. After 30 min of application, the surplus emulsion was removed with sterile saline and gauze. To activate the curcumin, we used the Lince (MMOptics, São Carlos, São Paulo, Brazil) device that is composed of an active plate (8.0 cm × 7.7 cm) with 30 LEDs of 450 ± 10 nm wavelength (visible blue) distributed in 6 rows of 5 LEDs each. The light was delivered continuously over 12 min with an irradiance of 30 mW/cm^2, and the total dose of energy delivered to the tissue was 22 J/cm^2. The light was applied from a distance of 5.0 cm from the surface of the ulcer. The concentration, time of impregnation and activation of curcumin with light was determined by the previous work of Andrade et al. [10], who observed better curcumin impregnation and activation with higher times for yeast biofilm inactivation.

Swabs were taken before and immediately after the PDT and were seeded in Petri dishes containing the following culture media: blood agar (for total count of microorganisms growth), MacConckey agar for enterobacteria growth, Mannitol salt agar for selective *Staphylococcus* spp. growth, and Sabouraud dextrose agar with chloramphenicol for yeast growth. The plates were incubated in a B.O.D. at a temperature of 35 ± 2 °C under aerobic conditions and ambient CO_2 concentrations for 24 h to 48 h. After incubation in B.O.D. the plates of Sabouraud dextrose agar with chloramphenicol were left for another 5 days in capped containers with a moistened cotton, at room temperature, to create favorable growth conditions of humidity for the yeasts that did not grow in B.O.D. incubation. The colonies developed in the culture media were analyzed for shape and staining and submitted to optical microscopy to observe the morphological characteristics of the microorganisms. The colonies were then counted and the number of colony forming units (CFU) was obtained. In the samples collected before PDT, we observed microorganism growth in blood agar and Sabouraud dextrose agar with chloramphenicol. The samples collected after PDT did not show microorganism growth. After seven days, new microbiological sampling was carried out under the same conditions as those described above, and there was no microbial growth. Thus, only one PDT session was required.

Low level laser therapy was performed with a 660 nm (visible red) laser in a punctual and continuous manner, twice a week. The beam size and power was 0.04 cm^2 and 40 mW, respectively. The irradiation time was 10 s, generating a fluence of 10 J/cm^2 and an irradiance of 1000 mW/cm^2. The procedures are shown in Fig. 1.

The cover of the PU was made with the cellulose biomembrane Nanoskin® (Innovates Biotechnological Products Inc., São Carlos, São Paulo, Brazil) and was placed over the entire surface of the ulcer not exceeding the limit with normal skin, and covered with gauze and bandages. The biomembrane was changed every 3 days.

The progression of ulcer healing was evaluated with digital images obtained prior to initiation of treatment and at each dressing change with a digital camera of 5-megapixel definition. The area was measured in square centimeters with the UTHSCSA Image Tool program, version 1.28 (University of Texas Health Science Center, San Antonio, Texas, USA).

3. Discussion and conclusion

The presence of infection in wounds may lead to increased healing time due to the “paralyzation” of the epithelial cell repair mechanisms [10]. The concept of disinfecting wounds using a noninvasive and localized strategy such as PDT with limited damage to the host tissue is well documented in literature [11]. The bactericidal effect of PDT reduced the bacterial load on the ulcer surface and assisted the healing process. The anti-bacterial pathway of PDT is different from traditional antibiotics; therefore, this therapy may have uses on drug resistant or multi-drug resistant strains and does not induce new drug resistance [12]. In addition to its antibacterial effect, PDT has also been shown to decrease the amount of bacterial toxins [13], increase production of proinflammatory cytokines [14], increase fibroblastic activity with the production of neocollagen, modulate matrix metalloproteases, increase collagen synthesis, promote the production of both the vascular endothelial and keratinocyte growth factors, and encourage remodeling [15].