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Fluorescence biomodulation in the management of acute traumatic wounds in two aged dogs

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Abstract: Traumatic wounds represent a fairly common reason for the admission of dogs to a veterinary practice. In elderly patients, the management of wound healing can be challenging due to both the concurrent diseases and impaired physiological states, potentially resulting in delayed healing and chronic or non-healing wounds. The aim of this article is to describe an innovative therapy based on photobiomodulation (PBM) for the management of acute traumatic wounds with significant tissue loss in aged dogs. Two mixed breed dogs were presented with similar wounds in the cervical region and were managed with a fluorescence biomodulation system, a form of PBM, which consists of a photoconverter topical gel that is illuminated with a blue light-emitting diode lamp, applied on a weekly basis. Wound closure was achieved after 9 and 16 weekly treatments, respectively, with a complete re-epithelisation of the skin. This fluorescence-generating system is an innovative, non-invasive, wound care therapy and these results indicate it could be successfully applied in the management of acute traumatic wounds with tissue loss in dogs.

Keywords: canine; moist wound therapy; photobiomodulation therapy; injury; wound healing

Acute traumatic wounds with tissue loss are not infrequent in dogs and could be related to a number of causes such as bites, a penetrating or blunt trauma, and shearing and degloving injuries (Dernell 2006). Once the patient is clinically stable, the goal of managing the injury is to achieve healing as quickly as possible to minimise the risk of infection and restore normal skin function (Devriendt and de Rooster 2017).

Surgical procedures should be always considered at first; whenever not applicable, the choice of an alternative treatment protocol is influenced by several factors such as the time delay between the injury and treatment, the degree of contamination, the extension and depth of the wound, the clinical status and the age of the patient, requiring a patient-specific approach (Percival 2002; Devriendt and de Rooster 2017). In elderly patients, the physiological state, which may be compromised by a concurrent disease, the medical history, the wound, and the environment may contribute to a malfunction or interruption of the reparative healing process potentially resulting in chronic, difficult-to-heal or non-healing wounds (Amalsadvala and Swaim 2006). Moreover, in aged dogs, anaesthesia-related risks and the failure or dehiscence of a surgical treatment (i.e., skin grafting, secondary healing, etc.) may impair the healing process outcome and could sometimes lead the veterinary practitioner to a conservative approach rather than a reconstructive-surgical therapy (Campbell 2006; Pavletic 2018). When surgical intervention is not appropriate, wound dressings may be considered as an effective option in an elderly patient (Krahwinkel and Boothe 2006). Different types of bandaging and treatments have

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been developed with the aim to provide a physical barrier against contamination, to decrease the risk of infection and necrosis, thus, creating an ideal environment for the wound healing (Campbell 2006; Krahwinkel and Boothe 2006). Distinctive materials and types of dressings have been effectively used to manage open wounds in dogs, such as conventional bandages, negative pressure wound therapy (NPWT), highly absorptive dressings, moisture-retention dressings, and extracellular matrix dressings, including those containing platelet-rich plasma (PRP) and collagen (Campbell 2006). Each option presents different features and is suited to different types of wounds and visit schedules. There is a growing interest and evidence to support new approaches, such as NPWT (Pitt and Stanley 2014; Nolff et al. 2018) and PRP (Tambella et al. 2014; Tambella et al. 2018).

Some authors consider moist wound therapy the best option for the care of all types of skin wounds that cannot be promptly closed surgically (Campbell 2006; Fahie and Shettko 2007). In these contexts, therapies based on photobiomodulation (PBM) are widely employed in humans for their benefits in tissue regeneration, the reduction of discomfort and control of the inflammation (Langella et al. 2018; Ramos et al. 2019). PBM consists in the stimulation of different biological functions through the use of visible to infrared light (from 415 nm to 810 nm) which stimulates the endogenous molecules called chromophores. These chromophores are particularly expressed in the dermal layer and are able to promote the skin healing process once illuminated by a specific light wavelength. In fact, previous studies have demonstrated how PBM especially impacts the skin, decreasing inflammation, promoting neoangiogenesis, and manipulating the signal transduction pathways that recruit the transcription factors activating several genes involved in skin healing (Shnitkind et al. 2006; de Freitas and Hamblin 2016; Scapagnini et al. 2019). The Fluorescence Biomodulation (FB) system consists of two components, a light source made of diodes and emitting blue light (LEDs; with a peak wavelength between 440 and 460 nm) and chromophores embedded in a topical photoconverter gel, which produce fluorescence light energy (FLE) when activated by the LED light. Fluorescence Biomodulation is a form of PBM that uniquely employs fluorescence light energy and has been demonstrated to advance the healing of both acute and chronic wounds in humans, shortening the time to resolution and improving the quality of the healing (Fogacci et al. 2018; Romanelli et al. 2018). In humans, FB has shown to be very well tolerated and efficacious in the management of chronic wounds such as diabetic foot ulcers and venous leg ulcers (Nikolis et al. 2016; Romanelli et al. 2018) and has been used in acute wounds and burns (Fogacci et al. 2018; Luca-Pozner et al. 2019). FB has also been shown to stimulate mitochondrial production of adenosine triphosphate (ATP), which is responsible for the acceleration of tissue regeneration; moreover, FB increases the collagen production and decreases the inflammatory status of the skin due to the downregulation of the TNF alpha and IL-6 (Edge et al. 2019; Scapagnini et al. 2019).

In veterinary patients, FB has successfully been used for the management of surgical wounds and interdigital pyoderma in dogs (Marchegiani et al. 2019; Salvaggio et al. 2020; Tambella et al. 2020). In interdigital pyoderma, there was a significant reduction in the clinical scores and the time to a clinical resolution in patients treated with an antibiotic plus FB, when compared to patients treated with an antibiotic alone (Marchegiani et al. 2019). In a different study conducted on dogs, histology of surgical lesions treated with FB showed a significant improvement, with a hastened re-epithelialisation of the skin with less inflammation throughout the healing process (Salvaggio et al. 2020). In canine otitis externa, FB has been shown to be effective in improving the clinical condition while increasing the therapeutic compliance (Tambella et al. 2020).

The presented case report is the first reporting of an acute traumatic wound management using an FB system in dogs.

Clinical presentation

Two aged, mixed breed dogs were presented with similar wounds in the cervical region due to a road traffic accident (case 1) and a bite (case 2).

The routine clinical work (CBC, serum biochemistry, electrophoresis, abdominal and cardiac ultrasound, thorax x-ray examination) as the screening process for trauma in elderly patients did not highlight any concurrent diseases in either subject.

A 17-year-old, male mixed breed dog (case 1, Figure 1), with a body weight of 6 kg and a body

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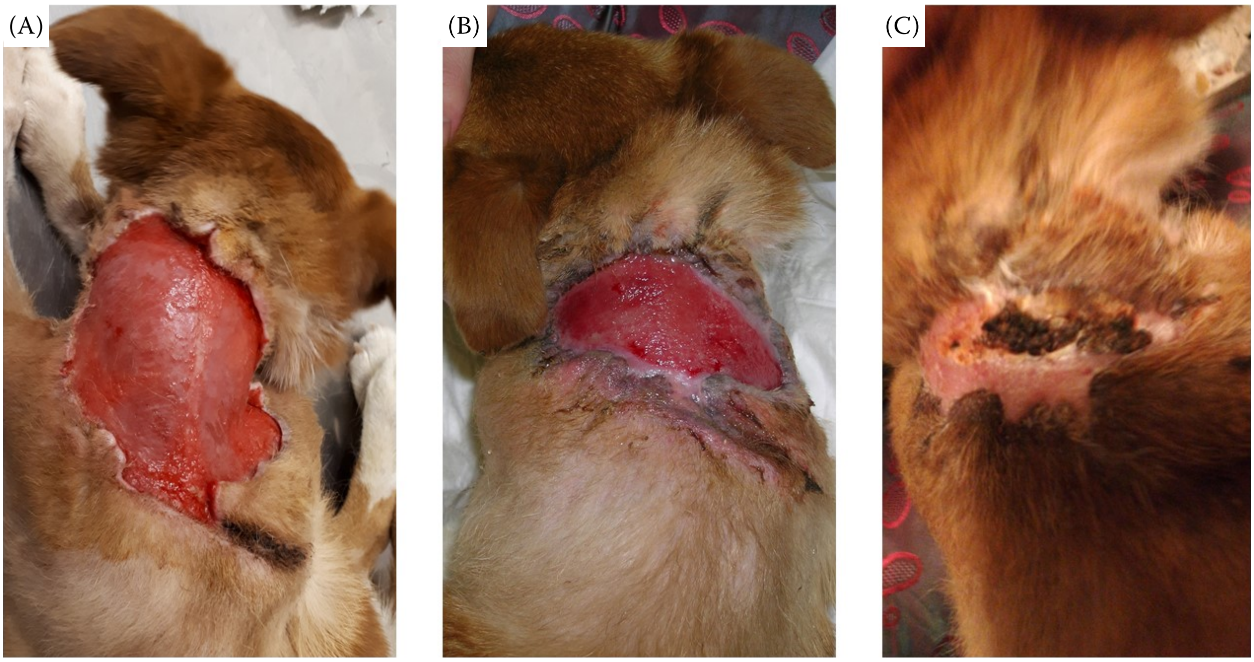

Figure 1. The 17-year-old, male mixed breed dog, before the PBM (photobiomodulation) initiation (A), after 4 weeks (B) and at the end of the PBM management (ca 9 weeks)

condition score (BCS) assessed as 5 on a 9-point scale, presented with a full-thickness shearing injury from a road traffic accident that occurred a week prior which caused significant loss of substance in the dorsal region of the neck and extending from the right shoulder joint area to the left axillary region with the abundant presence of foreign material. The minimum-maximum wound length was about 9–16 cm and the wound edges and subcutaneous tissue were ischemic and necrotised.

A 15-year-old, female mixed breed dog (case 2, Figure 2), weighing 25 kg and assessed as 2 out of 9 in the BCS, presented with an infected wound resulting from a dog bite that occurred five days

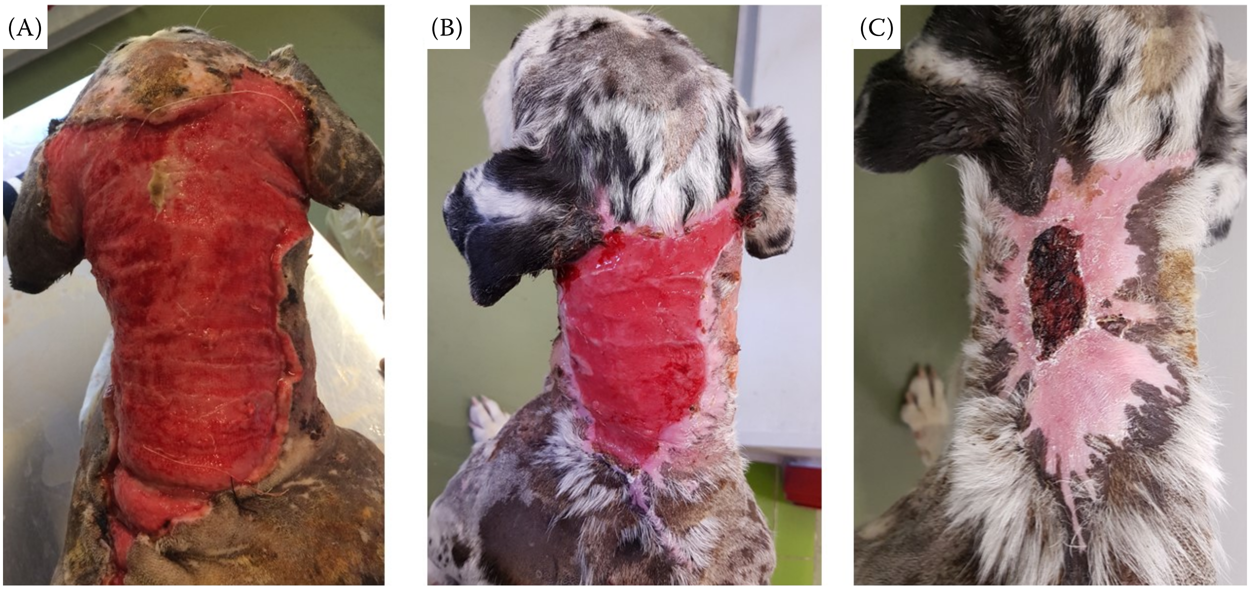

Figure 2. The 15-year-old, female mixed breed dog, before the PBM (photobiomodulation) initiation (A), after 4 weeks (B) and at the end of the PBM management (ca 16 weeks)

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before presentation. The wound affected the dorsal region of the neck, both ears, both cheeks, with the abundant presence of a purulent discharge, necrosis of the skin, subcutaneous and fascia, and with the substantial undermining of the adjacent tissues. The wound bed extended down through the deep hypodermal fascia to the muscle layer; the minimum-maximum wound length was about 15–26 cm.

Upon their arrival at the veterinary hospital, both dogs received culture swabs before the surgical debridement and curettage of the wounds with the removal of the necrotic and contaminated material. The culture and sensitivity testing revealed the presence of *Staphylococcus pseudintermedius* in case 1 and *Staphylococcus pseudintermedius,* gamma haemolytic *Streptococcus,* and *Klebsiella* spp. in case 2, respectively. All these bacteria were susceptible to amoxicillin and clavulanic acid, which were administered at a dose of 12.5 mg/kg twice daily for twenty days to control the bacterial infection once the granulation tissue completely covered the wound bed (Pavletic 2018), and carprofen (2 mg/kg twice daily) was administered for seven days to control the inflammation and pain. A surgical approach to attempt a secondary wound closure was proposed to the pet owners, but it was refused in both cases due to economic restrictions.

Photobiomodulation therapy and outcomes

The FB therapy was started five days after the initial presentation in both dogs and consisted of spreading an approximately 2 mm layer of the photoconverter gel (Phovia™; Klox Technologies Ltd., Dublin, Ireland) on the wounds and illuminating the gel with an LED lamp (KT-V50™; Klox Technologies Ltd., Dublin, Ireland) at a distance of approximately 5 cm for 2 min; once the illumination was completed, the gel was removed. After a one-minute rest period, this procedure was repeated with the gel being left in place until the next treatment, to help moisten the environment and prevent bandage adhesion. The wound was then covered with a bandage to prevent contamination. Other types of ointment and self-preventive adhesion bandages were not used to avoid any possible cruciate reaction with the FB therapy. The whole procedure was repeated once a week until the wound closure was achieved. The investigators considered the FB procedure easy to apply and suitable for broad clinical use. No signs of discomfort were displayed by both animals either during the illumination or after the treatment.

At week one of the FB treatment, both wounds presented a very healthy and clean appearance with no clinical signs of infection or necrosis; the early granulation tissue already began to develop. By the end of the third week, a very healthy granulation tissue filled the entirety of the wound bed, healthy wound borders without maceration signs and clearly advancing re-epithelisation edges were notable, as it could be expected with other wound management techniques (Figures 1 and 2). The bandages were successfully kept in place after each weekly treatment with the help of an elastic net bandage. When the bandages were removed, it was noted that part of the gel was still in place in the wound bed and it was partially adsorbed by the bandage. A wound closure was obtained after 9 and 16 weeks, respectively in both dogs (Figures 1 and 2), with the complete restoring of the skin's barrier and function. The slight degree of wound contraction, unavoidable in such large wounds, did not hamper the free movements and apparently did not bother the dogs who showed no signs of suffering or propensity to self-trauma.

DISCUSSION AND CONCLUSIONS

The effective management protocol for acute traumatic wounds should be established on a patient's needs and it should include surgical approaches to be more effective (Campbell 2006). When this is not possible, alternative techniques should be chosen, aimed to protect the wound from external contamination and the patient itself, manage the wound exudate, provide support and comfort, and create an environment that actively promotes healing. The removal of harmful debris and necrotic tissue and the control of the bacterial burden are mandatory to obtain a satisfactory result even in the case when surgery cannot be practiced (Hosgood 2006; Fahie and Shettko 2007).

Aged patients could present concomitant diseases which can impact on the healing process and limit the management options (Amalsadvala and Swaim 2006). Aging has been shown to potentially affect the wound healing by decreasing the collagen density, impairing the dermal vascularisation, low-

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ering the epithelialisation turnover and decreasing the tensile strength in the remodelled tissue (Hanks and Spodnick 2005).

Many therapeutic agents and procedures have been tested and are marketed with the attempt to address the vast array of different needs in wound care that arise due to the variability in the wounds and the implicated host factors (Balasch et al. 2016).

Surgery should be always the first option for acute traumatic wounds; when it is not applicable, an FB system could be considered as a valuable option since it positively influences all the phases of the healing process through the modulation of the inflammatory profile, the activation of growth factors, the stimulation of collagen depositions, and helping to control the bacterial growth (Shnitkind et al. 2006; Romanelli et al. 2018; Scapagnini et al. 2019). In fact, *in vivo* and *in vitro* studies conducted on human fibroblasts have shown that FB stimulates growth factors (such as TGF-ß, FGF, PDGF and VEGF) that play active roles in epithelial growth and collagen deposition, thus, enhancing the healing process (Edge et al. 2019; Scapagnini et al. 2019).

In veterinary patients, FB has shown to be a promising adjunct therapy in the management of canine interdigital pyoderma, significantly accelerating the time to a clinical resolution stimulating the same growth factors of humans (Marchegiani et al. 2019; Salvaggio et al. 2020). The immuno-histological analysis of the FB treated wounds has shown significantly greater expression of Factor VIII, Epithelial growth factor (EGF), Decorin, Collagen III, and Ki67, all of which have crucial roles in the process of correct epithelial growth and collagen deposition/maturation (Salvaggio et al. 2020).

The preliminary findings of the cases presented in this paper suggest that FB is well tolerated and may have a positive effect in the management of acute traumatic wounds with a loss of substance in aged dogs, although further clinical reports and controlled studies are needed to better determine the therapeutic potential of the FB application in veterinary wound healing, particularly when compared with current conventional wound care therapies.

A fluorescence-generating technology may, in the future, become a useful tool in the management of acute traumatic wounds in dogs, in particular, aged patients where wound management is often more challenging and management approaches may be more limited.

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Conflict of interest

The authors declare no conflict of interest.

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