Innovative topical haemoglobin spray helps drive the MOIST concept in saving patients' limbs

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Diabetic foot ulceration (DFU) is a common complication of diabetes mellitus. The treatment of DFU continues to be a challenge for clinicians, especially in chronic, hard-to-heal cases. Effective management of DFU is important to prevent amputation and reduce the additional emotional and psychological stress associated with the loss of a limb. Increasing oxygenation at the site of the DFU wound has been demonstrated to improve wound healing (Frykberg and Banks, 2015). Incorporation of topical haemoglobin spray in the treatment regimen shows positive improvements and reduces the size of the ulceration (Bateman, 2015). In this article, the author describes three case studies to demonstrate the effectiveness of topical haemoglobin spray in severe DFU.

DFU is a serious health burden affecting one in ten diabetes patients (Bateman, 2015). Studies show that patients with DFU have a greater than two-fold increase in mortality compared with non-DFU diabetic patients (Chammas et al, 2016). Loss of sensation due to peripheral neuropathy and/or ischemia due to peripheral vascular disease may lead the development of DFUs. According to the International Diabetes Federation, 9.1 to 26.1 million people will develop DFUs annually (Armstrong et al, 2017). If left untreated, DFUs may cause devastating complications leading to limb amputation and long-term disability. The primary goal in the treatment of DFU is to reduce the risk of amputation and the incidence of new ulcers. The Gold Standard for care for DFU includes wound debridement, management of any infection, vascular assessment, and off-loading of the ulcer (Alexiadou and Doupis, 2018). The acronym TIME (Tissue, Infection/inflammation, Moisture balance and Edge of wound) is a wound healing concept that attempts to improve parity in the management of DFUs. This has recently been adapted/changed modified to the MOIST (Moisture balance, Oxygen balance, Infection control, Support and Tissue management) concept, which is a new, improved protocol for the local treatment of wounds (Dissemond et al, 2017).

Oxygen: a key component of the MOIST concept

Oxygen plays an important role in the process of wound healing. It is widely recognized that hypoxia is a rate-limiting step. If the partial pressure of oxygen falls below 20 mm Hg, nicotinamide adenine dinucleotide phosphate oxidase — the enzyme that generates reactive oxygen species for signal transduction necessary to promote healing —stops functioning (Gordillo and Sen, 2009). DFU can be treated with oxygen therapies including hyperbaric oxygen therapy (HBOT), topical oxygen therapy (TOT) and topical haemoglobin spray as an adjust to standard treatment.

Hyperbaric oxygen therapy

Hyperbaric oxygen can be delivered systemically to the ulcer with short-term, high dose oxygen inhalation. HBOT is administered in a compression chamber (pressurized >1 atmosphere absolute [ATA]) that provides 100 percent oxygen (Alexiadou and Doupis, 2018). Each session lasts for 1–2 hours and a full course is made up of 30–40 sessions. HBOT increases oxygen concentration in a patient's bloodstream, thereby, accelerating the wound healing process. Although HBOT has demonstrated many benefits, it is contraindicated in cases of patients with cataracts, history of pneumothorax or thoracic surgery, central nervous system toxicity and seizures, inability to equalize pressure in the middle ear, fetal complications from pregnancy, and claustrophobia.

Topical oxygen therapy

TOT is a localized oxygen delivery method for treating DFU. Topical oxygen therapy may be administered by any of the following methods: delivery of 100 percent oxygen either under

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Case study 1

A 66-year old male with a past medical history of type 2 diabetes mellitus, coronary artery disease, chronic kidney disease, hypertension, hypothyroidism, vitamin D deficiency and recent subarachnoid haemorrhage. He underwent coronary artery bypass grafting in the year 2000. The patient complained of a chronic infected wound in his left heel for 6 weeks prior to presentation.

Diagnosis

Chronic infected wound of the left heel.

Treatment

Subsequent to a comprehensive assessment of the wound, the patient was treated with an antibiotic regimen (biapenem), and the wound was debrided hydrosurgically with continuous wound care and adjuctive topical haemoglobin spray.

Results

The patient presented with gangrenous heel with macerated edges; initial debridement revealed underlying sloughy necrotic wound base deep to the bone. Within 10 days following the start of treatment with standard wound care plus topical haemoglobin spray, a decrease in wound depth, wound base granulation tissue coverage of some of previously exposed to bone area and decrease of pain intensity was observed *[Figures 1A, 1B and 1C]*.

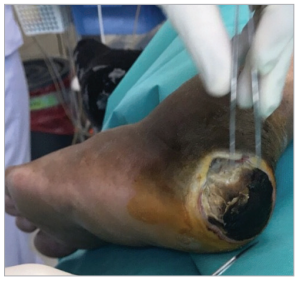

Figure 1a. Day 0, before treatment

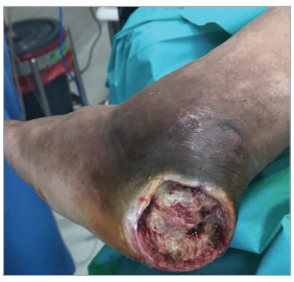

Figure 1b. Day 0, after debridement

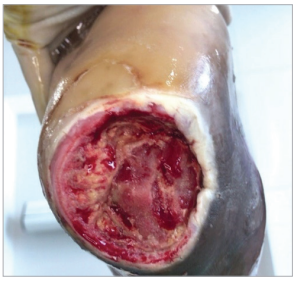

Figure 1c. Day 10, after treatment with standard care plus topical haemoglobin

Case study 2

A 68-year old female with a past medical history of type 2 diabetes mellitus and dyslipidemia. The patient had necrotizing fasciitis of the right leg with gangrenous third and fourth right toes. According to a previous medical report from her country, aggressive wound debridement and treatment with antibiotics (no detail of microbiological culture and antibiotic attached) resulted in no improvement, therefore, a below knee amputation was advised. However, the patient and her family refused amputation — hoping to save the limb — and she was referred to the author's hospital.

Diagnosis

Necrotizing fasciitis of the right leg with gangrenous toes.

Treatment

The patient was started on an empirical regimen of a broad-spectrum antibiotic (biapenem). Debridement was performed and her fourth right toe was amputated. It was then decided to treat the wound with topical haemoglobin spray every 2 days.
After appropriate wound base preparation, the patient underwent a split thickness skin graft on day 45.

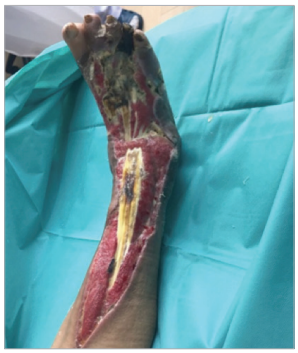

Figure 2a. Day 0, initial wound

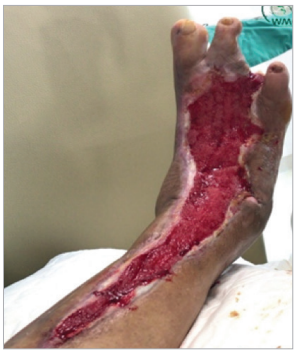

Figure 2b. Day 44, after standard care plus topical haemoglobin spray

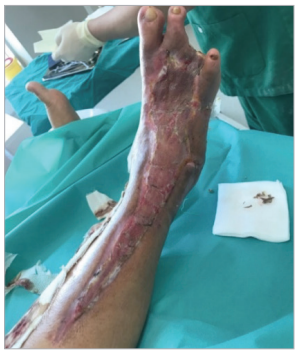

Figure 2c. Day 49, status post split thickness skin grafts

Results

Six weeks following the treatment, the patient showed remarkable improvement in terms of wound healing. The wound decreased significantly in size and increased granulated tissue. A split thickness skin graft was performed on day 45; with the graft taken well *[Figures 2A, 2B and 2C]*.

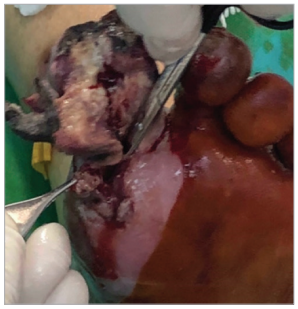

Figure 3a. Day 0, initial wound

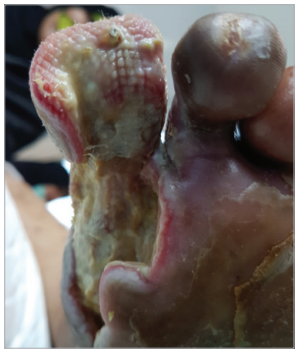

Figure 3b. Wound exposed to bone (post debridement)

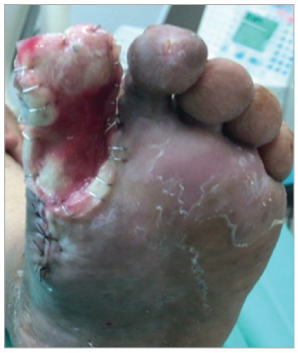

Figure 3c. Treated with acellular dermal matrix and haemoglobin spray

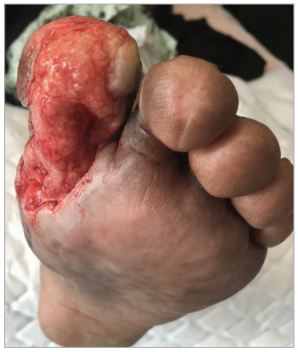

Figure 3d. Day 29, after removal of silicone sheet from acellular dermal matrix

Case study 3

A 75-year old female with a past medical history of type 2 diabetes mellitus, peripheral arterial disease, hypertension, and dyslipidemia presented with gangrene in her left first and second toe and chronic wound of her left leg 2 months prior to admission. Physical examination revealed necrotic wound with bony exposure of left first toe status post debridement and wound of second toe and left leg.

Diagnosis

Gangrenous first and second left toe with osteomyelitis s/p debridement and chronic wound of left leg.

Treatment

Board-spectrum antibiotics was started after wound debridement and dressing. Intensive wound care treatment with topical hemoglobin spray was also started with the goal of keeping as much as viable tissue as possible. After controlling infection with intensive multimodality debridement. Acellular dermal matrix and topical haemoglobin spray were applied.

Results

After 4 weeks of treatment, there was significant increase in granulation tissue and a concurrent decrease in the wound's length and width *[Figures 3A,3B,3C and 3D]*.

pressurized or ambient condition, chemical release of oxygen via an enzymatic reaction or increase of oxygen by facilitated diffusion using oxygen binding and releasing molecules (Dissemond et al, 2017). Studies indicate that TOT increases vascular endothelial growth factor protein expression which accelerates vessel growth at the ulceration site. Furthermore, TOT has been shown to increase the rate of wound epithelialization, increase collagen deposition, and decrease wound infection (Yu et al, 2016).

Topical haemoglobin spray

Topical haemoglobin spray is an innovative oxygen-delivery system that delivers oxygen to the wound site. The spray comprises of purified haemoglobin that binds oxygen from the atmosphere facilitating diffusion of oxygen and transporting it directly to ulceration site (Hunt and Elg, 2017). Recent studies demonstrate that the incorporation of haemoglobin spray in standard wound care resulted in improvements in wound closure, slough elimination, and reductions in exudate levels in DFU patients (Bateman, 2015). Compared to standard care alone topical haemoglobin spray resulted in a higher number of healed wounds and a faster wound healing rate (Hunt and Elg, 2017).

Pros and cons

One of the major advantages of topical haemoglobin spray is:

- The convenience and ease of use
- Safe to use for the healing of complicated chronic wounds
- Compatible with most breathable dressings.

However, it has the following disadvantages:

- Has to be stored at 2 to 8°C
- Carries a potential risk of allergy and anaphylaxis reaction.

Conclusion

Standard wound care plus a haemoglobin spray result in improvements in wound closure, wound size reduction, pain, slough, and exudate levels in patients with chronic wounds. WAS

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