NATROX® — Let the topical oxygen flow for healing complex wounds

Oxygen has a critical role in wound healing including the production of energy to fuel cell metabolism, angiogenesis, fight infection, collagen synthesis and re-epithelialization. Natrox® represents a new development in topical oxygen therapy. It provides a more practical and patient-friendly mode of delivery for oxygen therapy. Its lightweight, the size of a mobile phone and portable, and can provide continuous oxygen therapy for up to 26 hours. It is suitable for patients with wounds under clothes and can be positioned to be used comfortably at night, facilitating continuous use in a way that a patient’s everyday life becomes easier. Clinical evidence and research suggest it can help heal chronic wounds such as diabetic foot and venous ulcers with high patient satisfaction. However, more research is required to help position this device in the wound healing arena and identify when it is indicated.

The presence of a wound increases the body's requirement for oxygen. For a patient with a closed wound and by 50% for an infected wound (Grimbal, 2019). Oxygen is critical in many of the processes required for wound healing including the production of energy to fuel cell function and metabolism, angiogenesis, collagen synthesis and cross-linking, epithelialization and resistance to infection (Caudill et al, 2012).

Wound oxygen is often multi-factorial and is due to either reduced oxygen delivery to tissues or tissue demand and/or increased oxygen demand due to infection and inflammation. One way to increase wound oxygen delivery to wound tissues include:

- Systemic disease, e.g. reduced arterial blood flow due to peripheral vascular disease, heart disease or diabetes (Jen, 2009). Other factors that may contribute to tissue hypoxia include pulmonary disease, sympathetic dysregulation, hypoxemia and hypomaturic insufficiency requiring the need for oxygenation.
- It is important to assess for underlying factors that contribute to tissue hypoxia whilst keeping in mind that chronic wounds are an important driver of impaired oxygenation. Tissue hypoxia is an important driver of impaired oxygenation. Tissue hypoxia is an important driver of impaired oxygenation.

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- Increased delivery of oxygen to wound tissues through increased arterial blood flow and oxygen delivery to wound tissues include:
- Osmotic oxygen delivery to tissues is diffusion, and oxygen is used in metabolic reactions.
- Neutrophil and macrophage infiltration in the wound bed are increased by the delivery of oxygen.
- Increased delivery of oxygen to wound tissues through increased arterial blood flow and oxygen delivery to wound tissues include:
- The energy produced by the battery creates a positive charge on one face of the membrane and a negative charge on the other. The enzyme, prolyl hydroxylase is maximal at oxygen levels due to respiratory disease, and cross-linking, epithelization and resistance to infection (Castilla et al, 2012).
- NATROX® can be used in patients with diabetes, fibrin deposition in chronic wounds, which can be due to either reduced oxygen delivery to infection (Castilla et al, 2012).
- Hypoxia is due to the high oxygen levels and factors that form water, pulling the positive ions through the membrane and the negative ions in the opposite direction.
- Normal mobility (hence 'ambulatory') while doing daily activities, including dressing changes, was achieved. The device can even penetrate healthy skin and deliver oxygen to the wound bed.
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The graph shows that tissue oxygenation improved with the use of the NATROX® device. A significant increase in tissue oxygenation was observed within 4 weeks of treatment. The device was well tolerated and there were no signs of wound infection or adverse events.

The device was easy to use and the patient was able to continue with their daily activities, including dressing changes, without any difficulty. The device was well tolerated and there were no signs of wound infection or adverse events.

Figure 2. It shows lower levels of oxygen delivery to tissues, which is significant for healing.

The current clinical data for Natrox® is based on a study involving 10 patients with chronic DFU who were recruited and treated with the Natrox® device. The device was used for 4 weeks and the patients were followed up for an additional 4 weeks post-treatment. The results showed a significant improvement in wound healing.

Case Study 2

A 55-year-old Chinese male who was known to be home ambulant with limited mobility due to "normal" advanced wound dressings till complete wound closure. Due to the high risks of further complications and infections, a transtibial amputation was considered as the most rational option. However, the patient was not willing to undergo amputation.

Case Study 1

An 85-year-old woman who was known to be home ambulant with "normal" advanced wound dressings till complete wound closure. Due to the high risks of further complications and infections, a transtibial amputation was considered as the most rational option. However, the patient was not willing to undergo amputation.

In conclusion, the use of Natrox® in chronic wounds can be a beneficial addition to current wound care regimens, especially in cases where traditional approaches are ineffective. Further research is needed to determine the optimal use and role of Natrox® in the management of chronic wounds.
Although the rate of decrease in wound area is statistically significant, the small number of patients, lack of a control arm, short study period and other factors require that much larger studies are needed to draw any definitive conclusions. The study increased in wound size when some non-healing wounds were observed in both groups, indicating that for some patients, oxygen therapy is not effective. Further research is needed to understand the role of oxygen in wound healing. The potential of NATROX® to promote the healing of chronic wounds was demonstrated in a cohort study.

Yu et al. (2016) performed a small randomised controlled trial of NATROX® in venous leg ulcers and diabetes patients. Mean duration of DFU prior to enrolment into the study was 76 weeks. Standard of care for both groups included offloading. After 2 months of treatment, 46% of wounds treated in the NATROX® group healed compared with only 29% in the control group.

Khor et al. (2018) reported the experience of using the NATROX® device on wounds of non-healing wounds including venous leg ulcers (VLU), diabetic ulcers and pressure ulcers. They found that 10% of patients that the therapy was very well tolerated and with a mean treatment duration of 38 days, there was a 91% reduction in wound area, either with VLU or DFU.

Carril and Hayles (2016) demonstrated how the therapy has changed the patient’s quality of life, who benefited from healing wounds due to critical limb ischaemia for a total duration of more than 25 years. All patients had healing during the treatment with NATROX® and duration time to achieve closure was 2-4.5 weeks. Patients achieved high satisfaction levels with the device and from a health economic viewpoint total cost of treatment with the device for the few patients was less than 10% compared with the total cost of previous standard treatments (Carri and Hayles, 2016).

An observational study using the new technology to patients with VLU in Malaysia showed a wound area reduction by a mean of 58.9% over the 4-week period study with an increase in wound healing and pain scores decreased in all patients (Khor et al., 2018). However, all the above-mentioned studies were using Caucasian patient cohorts. The blood vessels in Asians are generally smaller and the circulation more dense than in our Caucasian counterparts because of the higher incidence of diabetes. Furthermore, patients with chronic wound insufficiency generally present with poor quality and larger leg ulcers than in Caucasian patients. Therefore, NATROX® may be beneficial for such patients and improve our local salvage rate. When revascularisation and control of infection, there is still a likelihood of wounds that do not heal even with further revascularisation or major amputation. A new small controlled randomized controlled trial at NATROX® study is currently underway in Singapore General Hospital to investigate the depth of effect of the therapy. However, future research to evaluate NATROX® in mass patients. This study may show that NATROX® or wound wraps are better suited to respond to topical oxygen and what effect it has on the patients per se of tissue repair and improvement of quality of life in the very definitive potential to improve the health care of our patients.

We present two case studies with severe wounds to illustrate good results in post-surgical diabetic foot wounds from two centres in Asia: A 60-year-old diabetic and a 50-year-old non-diabetic, showing proof of concept of the therapy in different geographic locations. An expert working group has previously agreed that the core behind topical oxygen therapy is presumptive and that clinical evidence and experience to date show that NATROX® has a role in managing VLU and DFU with early studies showing an improvement in wound healing times (Wounds UK Expert Panel, 2015). However, there are numerous unanswerable questions regarding its potential role and some of the basic science behind it. To investigate whether or not potential use of the device prior to lower limb vascular intervention in DFU is the hope that natural tissue regeneration can be encouraged and angioplasty enlarge or stents or start the wound healing processes before suppressing the wound supply to the foot. Some of the basic science questions that need to be elucidated include the depth of penetration that oxygen using the device can penetrate to both healthy and the healing wounds with heavy fibrotic, the optimum flow rate of oxygen to maximise wound healing and the optimum pH that oxygen delivery would work best at these wounds.

References