Healing Tough Wounds Using Topical Oxygen Therapy During Hemodialysis Sessions

CNE Continuing Nursing Education

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Topical oxygen therapy (TOT) is used widely in the treatment of difficult-to-heal arterial and venous ulcers in patients with peripheral vascular disease (PVD), diabetic ulcers, and lower extremity venous insufficiency. Successful TOT relies on supplying 100% oxygen at 1.04 atmospheres to the ulcered area. In principle, TOT allows a rapid proliferation of new epithelium over the ulcer. This article describes two case studies with successful wound healing as a result of using this clinical method during hemodialysis sessions.

Key Words: **Topical oxygen therapy, non-healing wounds, hemodialysis, peripheral vascular disease, diabetic ulcer.**

Chronic wounds in individuals constitute a major therapeutic challenge (Gottrup & Apelqvist, 2012), and financially strain patients and the health care system. In Europe, it is estimated that 4% of total health care budgets are due to chronic wounds and ulcers associated with diabetic and vascular diseases (de Smet et al., 2017). In the United States, the burden of chronic wounds is estimated to affect 6.5 million patients, with a cost of $25 billion, annually (Harding, 2015). There is a need to identify and review strategies and treatments for this patient group to reduce the burden of care in an efficient, cost-effective, and evidence-based manner (Gottrup & Apelqvist, 2012). The challenge is to choose the most suitable therapeutic intervention for chronic, non-healing wounds (Gottrup & Apelqvist, 2012) while controlling patients' pain level (Kauric-Klein, 2012). Although the number of innovations in medical fields has increased dramatically over the past 100 years, innovations in the field of wound care have been slow to develop. Novel partnerships between academic, business, and clinical researchers and the health care system have resulted in major advancements pertaining to wound care or wound-healing processes; there is still much to learn about the wound care process (Harding, 2015).

A retrospective review of wound management in medicine began in the years 1900 to 1940, when most wounds were treated with gauze dressings. Since then, medical breakthroughs have been achieved, including the introduction of insulin for diabetes (1922) and the discovery of penicillin (1928) with the first antibiotics coming in 1932 (Harding, 2015). The following three decades (1950 to 1970) led to the first advancements in wound dressing, such as the development of the theory of moist wound healing (1962), with the first film dressings introduced in 1971 (Harding, 2015). From the 1980s until 2000, many different wound dressings were developed, including the first antimicrobials. Hydrocolloid dressings were introduced in 1983, and biological dressings followed in 1995 (Harding, 2015). The greatest advancements in wound management were made in the 21st century with new treatment methods and technologies to treat non-healing wounds, such as new wound dressings, hyperbaric oxygen therapy, topical oxygen delivery, light therapy, warm-up therapies, electrical stimulation, and ultrasound (Harding, 2015).

Recent advances in the understanding of chronic wound biology have led to the development of several new treatments that offer renewed hope to patients with ulcers and other chronic wounds (Ahanger, Woodward, & Cowin, 2018). However, before these advantages can be safely implemented in practice, the effectiveness of different treatments, procedures, and products must be carefully assessed and determined (Gottrup & Apelqvist, 2012). Furthermore, various systemic patient factors, such as advanced age, malnutrition, diabetes, and kidney disease, must also be considered. It is important to quantify the impact of such disease states on healing, so specific treatments can be used to target the particular abnormality in individual patients and lead to healing (Harding, Morris, & Patel, 2002). The types of disease that most commonly lead to severe chronic non-healing wounds in patients are caused by diabetes, peripheral vascular disease (PVD), and calciphylaxis (Blair, 2016). Special caution must be taken when treating wounds in patients with chron-

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Note: *The Learning Outcome, additional statements of disclosure, and instructions for CNE evaluation can be found on page 337.*

ic kidney disease (CKD) (Scholnick, 2016).

Diabetes mellitus is a group of physiological dysfunctions characterized by hyperglycemia resulting directly from insulin resistance, inadequate insulin secretion, or excessive glucagon secretion (Blair, 2016). Diabetes complications can be separated into microvascular and macrovascular complications. The involvement of microvascular complications may lead to kidney failure and diabetic foot disorders, with the latter resulting in infections and amputations. Macrovascular complications include cardiovascular diseases, such as insufficient blood flow to the legs, brain stroke, and myocardial ischemia (Blair, 2016). Diabetic foot ulcers can negatively impact patients' quality of life. Successful management of diabetic ulcers requires a long period of treatment, during which patients' daily activities are severely restricted.

PVD is strongly associated with type 2 diabetes, which in turn, is associated with symptoms of chronic, nonhealing wounds (Formosa, Gatt, & Chockalingam, 2012). PVD is a leading cause of mortality and morbidity in Western countries, and incurs a huge burden in terms of disability, functional decline, and health care costs. Early identification and management of this condition, especially among asymptomatic patients in the primary care setting, are crucial steps in preventing the development of diabetes foot complications, which can lead to amputations (de Franciscis, Metzinger, & Serra, 2016).

Calciphylaxis or calcific uremic arteriolopathy (CUA) is a term that refers to the deposition of calcium in small and medium vessels of the skin that can result in thrombosis and necrosis of the skin, subcutaneous fat, and muscle. The major goal of therapy for patients with CUA is the normalization of calcium, phosphorous, and parathyroid levels (Kauric-Klein, 2012). The disease has been highly reported in patients with CKD who are dependent on dialysis (Nigwekar et al., 2016).

The underlying pathophysiology of CUA is incomplete but appears to be multifactorial, such as high calcium and phosphorus products, biochemical mineral metabolism abnormalities, and disturbances of calcification inhibitors (Jovanovich & Choncol, 2016). CUA is considered a rare disease, and there is a lack of agreement on the appropriate course of treatment because the optimal treatment remains uncertain. Principles of CUA therapy include wound care (sterile dressing, debridement, and preventing secondary infection), nutritional support, and attempts to normalize serum calcium-phosphate levels. Other clinicians considered parathyroidectomy as a dramatic approach for CUA improvement, but the response is inconsistent and unpredictable. Other treatment strategies include the use of non-calcium-based phosphate binders, intensified hemodialysis, and hyperbaric oxygen that may have contributed to the favorable outcome in some cases (Sebastian, Jordaan, Schneider, Moosa, & Davids, 2017). Wound care is important in patients with CUA, and additional trauma to the site should be avoided to prevent any new formations of CUA. Pain associated with CUA can also be excruciating; the slightest touch can elicit extreme pain and may cause severe discomfort to the patient (Foo & Wong, 2007).

Wound treatment requires a multiprofessional approach with input from vascular, plastic, and podiatric surgeons, nurses, and internists (Chung, Modrall, Ahn, Lavery, & Valentine, 2015). Major goals of treatment are controlling risk factors, controlling pain, and preventing wound infection and possible sepsis (Dowsett & von Hallern, 2017).

Most often, the first encounter with patients who present with CUA wounds is in the acute care setting due to the amount of pain associated with the lesions (Hahler, 2001). As mentioned, these wounds are associated with excruciating pain at the slightest touch (Foo & Wong, 2007); as such, they have an enormous impact on patients' daily quality of life (Hahler, 2001).

Wound Treatment Approaches and Methods

There is a large variety of therapeutic approaches and methods to treating a chronic, non-healing wound. Common methods frequently used are hyperbaric oxygen therapy and topical oxygen wound therapy (Kaufman et al., 2018). Commonly available wound dressings include wound contact dressing, alginates, film dressing, hydrogels, foam dressing, hydro-fiber dressing, hydrocolloids, and antimicrobial dressings containing iodine and silver (Newton, 2013). Clinical wound treatment can be significantly affected if the wrong dressing is used; hence, practitioners must have the knowledge, skills, and competence to ensure their wound care practices and wound dressing selections are both safe and effective (Newton, 2013).

Systemic hyperbaric oxygen therapy (HBOT) is a treatment modality in which the patient breathes 100% oxygen at a pressure greater than one atmosphere (Gottrup et al., 2017). This therapy occurs while the patient is entirely enclosed in a stationary pressure chamber. This therapy increases the systemic plasma oxygen levels, and therefore, is dependent on adequate blood flow to the wound (Gottrup et al., 2017). HBOT is systemic and raises the partial pressure of oxygen; thus, there is a risk of complications, such as seizures, damage to the retinal nerve, and oxygen toxicity to the brain, lungs, and sinuses (Orsted et al., 2012). HBOT has been used as an adjunct for healing diabetic foot ulcers for decades; however, because of its relatively high costs, accessibility in some areas, reputed lack of evidence, and partly because of a history of unsubstantiated claims of its effectiveness in treating a variety of ailments, its use remains controversial (Bishop & Mudge, 2014).

Other oxygen-based or pressure-based wound therapies are administered topically rather than systemically. Topical pressurized oxygen therapy is also considered hyperbaric in that is also delivers 100% oxygen at a pres-

sure greater than one atmosphere. However, it is a non-invasive, portable therapy. Humidified pressurized oxygen is delivered directly to the wound bed through a reusable acrylic chamber, vinyl extremity boot, or vinyl multipurpose bag. This method of delivery achieves tissue penetration and increases oxygen levels in the open wound without the risk of systemic oxygen toxicity (Orsted et al., 2012). Topical pressurized oxygen therapy is not dependent on systemic circulation reaching the wound bed (Orsted et al., 2012). Topical continuous oxygen therapy is an additional oxygen-based wound therapy method in which non-pressurized, non-humidified oxygen is delivered to the open wound via a cannula placed over the wound with a dressing topper (Orsted et al., 2012).

Topical negative pressure (TNP) is one of the most interesting emerging methods for treating acute wounds. TNP has been introduced in recent years as a method of treatment for non-healing chronic wounds (Gottrup & Apelqvist, 2012). A significant benefit for both healing rate and healing time has been reported in individuals with diabetes, as well as post-amputation wounds and cavity ulcers (Gottrup & Apelqvist, 2012). Topical negative pressure wound therapy uses a pump device to provide controlled sub-atmospheric pressure to a wound sealed to air. The use of a wound filler, such as foam or gauze dressing, ensures delivery of this sub-atmospheric or negative pressure to the entire wound surface, while the resulting pressure gradient encourages simultaneous removal of wound exudate through the dressing material (Huddleston, 2015).

Topical oxygen therapy (TOT) is not yet widely used. Growing evidence of its effectiveness suggests it has the potential to form a regular part of adjunctive therapies in treatment regimens to speed up healing of chronic wounds (Yu, Lu, McLaren, Perry, & Cross, 2016). During the last two decades, results of various case studies and clinical trials suggest local oxygen therapies are promising options for enhancing wound healing (Dissemond, Kröger, Storck, Risse, & Engels, 2015). Compared with wound therapy using hyperbaric oxygen chambers, TOT has a lower cost and the advantage of being more comfortable for the patient (Lo et al., 2013). Properly administered, TOT can improve wound parameters, such as healing outcomes in the form of higher collagen maturity underneath the surface (Lo et al., 2013). In addition, it is safer, associated with fewer risks and complications, and features a more efficient method for delivering oxygen to the wound surface (Feldmeier et al., 2005).

Figure 1
Topical Oxygen Therapy During Hemodialysis Session

With TOT, the polyethylene bag is sealed around a limb or the trunk by elastic bandage (Gottrup et al., 2017). High flow oxygen (usually at 10 liters per minute) is introduced into the bag and over the wound at a pressure just over 1.0 atmosphere absolute (atm abs), typically 1.004 to 1.013 atm abs (Feldmeier et al., 2005). This pressure rate is recommended because higher pressures could decrease arterial/capillary inflow (Feldmeier et al., 2005). The premise for TOT (i.e., the diffusion of oxygen into the wound to enhance healing) is essential (Dissemond et al. 2015), and its delivery is less complex and expensive than that of hyperbaric oxygen (Feldmeier et al., 2005).

Wound Therapy for Patients on Hemodialysis

Patients with CKD who are treated with hemodialysis (HD) often suffer from calciphylaxis. That occurs due to primary hyperparathyroidism, chronic inflammation, and drugs, such as

Figure 2
Topical Oxygen Therapy Polyethylene Chamber

glucocorticoids, which promotes the transdifferentiation of vascular smooth muscle cells to an osteogenic phenotype with subsequent vascular calcification (Sebastian et al., 2017). As previously mentioned, most cases are characterized by rapid progression of cutaneous plaques to epidermal necrosis, with death in the majority due to sepsis (Foo & Wong, 2007). The pathogenesis of this wound disease is not well understood, and there are very few studied treatment options for this disease (Jovanovich & Choncol, 2016).

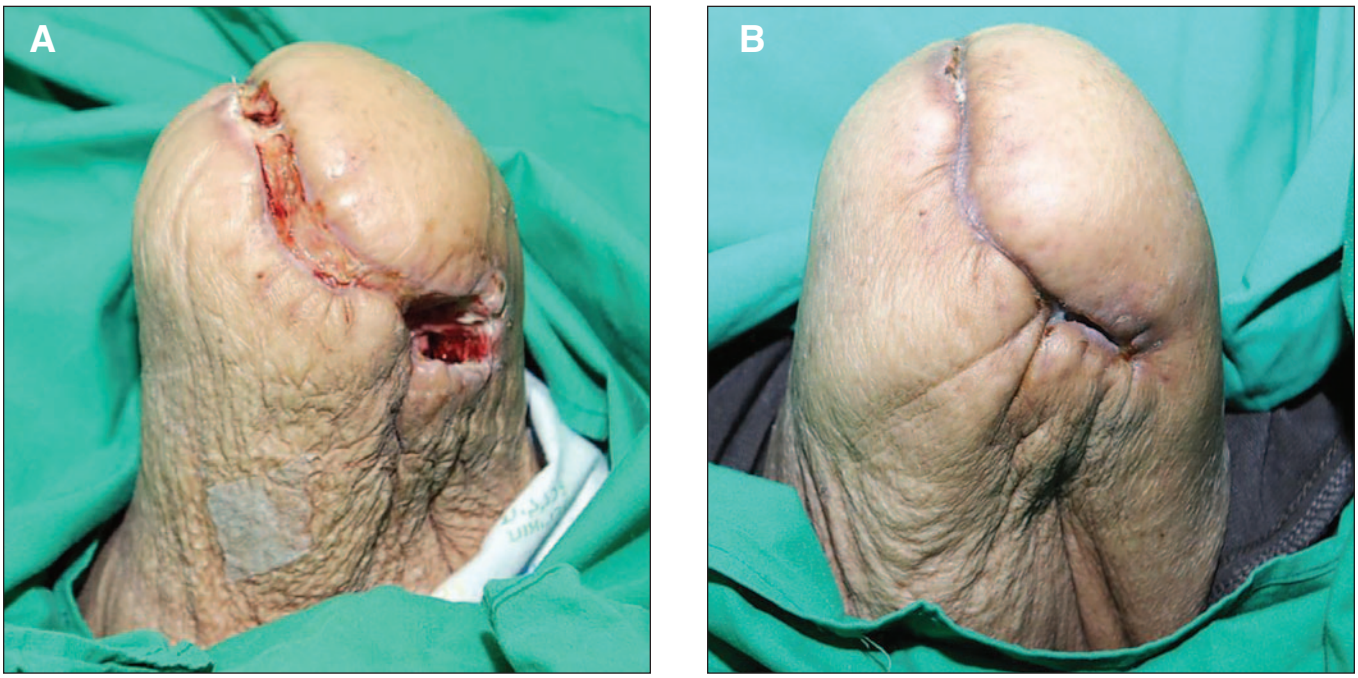
To date, there is no published evidence of a combined therapy approach whereby topical oxygen therapy for non-healing wounds is administered during HD.

Retrospective Case Studies

This retrospective study is based on two cases in which patients received TOT during their HD sessions (see Figure 1).

Figure 3
Patient A: Stump Ulcer Before (A) and After Topical Oxygen Therapy Treatments (B)

Figure 4
Patient B: Stump Ulcer Before (A) and After Topical Oxygen Therapy Treatments (B)



Method of TOT Treatment

TOT treatment involved supplying 100% oxygen via a polyethylene chamber (100x60 cms) placed around the ulcer (after it was cleaned with antiseptic solution), with the chamber's proximal end closed using an elastic bandage. TOT was given during each of the patient's regular HD sessions for the entire time length of the HD session (4 to 5 hours) (see Figure 2).

Patient A. A 72-year-old man with PVD, arterial ulcer, obstructive pulmonary disease, and kidney failure had been receiving HD treatment for a period of 10 years before the amputation of his right leg. TOT treatment was administered during his three weekly HD sessions for a period of four months because of a non-healing wound located on the below-knee stump of his right leg. Intradialytic parenteral nutrition (IDPN) was used simultaneously. The ulcer was dressed with Biatain® Foam at the end of each session.

Patient B. A 77-year-old man with diabetes, ischemic dilated cardiomyopathy, hypertension, kidney failure, and atrial fibrillation had been receiving HD treatment for a period of six years before the amputation of his right leg. TOT and IDPN were administered during his three weekly HD sessions for a period of three months to treat an ulcerated above-knee stump on his right leg. The ulcer was dressed with Biatain® Foam at the end of each session.

Results

As a result of the TOT treatments, the necrotic ulcer in both patients healed and was replaced by healthy granulation tissue. In Patient A, after four months, the initially necrotic ulcer (ulcer grade 4) had improved significantly in appearance to an ulcer grade of 1-2 (pink-red granulated tissue; see Figure 3). In Patient B, when TOT was stopped, the stump was covered with healthy granulation tissue, and the ulcer grade was 1 (pink tissue; see Figure 4). In both cases, no re-amputation was necessary, and narcotic medications dosages were reduced (see Table 1).

Discussion

Tough wounds are a global health care problem. In the industrial world, the risk of non-healing wounds is approximately 1% to 1.5% (Gottrup et al., 2017). In nephrology, PVD and diabetes are the leading risk factors for patients with kidney failure developing a non-healing wound (Meloni et al., 2016). Treating wounds of patients on HD constitutes a medical challenge because of the frequently accompanying conditions of uremia and anemia, as well as poor self-care (Scholnick, 2016). Treating the patient's wounds is usually performed at outpatient clinics or home-based practice where TOT is administered for 1.0 to 1.5 hours, three to seven times a week (Gottrup et al., 2017). Patients on HD, who already have limited free time, must spend additional time beyond their dialysis treatment time away from their preferred daily routines (Gerogianni et al., 2016). Treating wounds during HD sessions enables patients to spend less time at the hospital and in the wound

Table 1
Patient Characteristics and Results of Topical Oxygen Therapy

Patient Characteristics	Patient A	Patient B
Gender	Male	Male
Age (years)	72	77
Diabetes mellitus	No	Yes
PVD	Yes	No
Hgb(mg/dL)*	10.75	10.1
Ca^{2+}/ PO_4- (mg/dL)*	8.75/ 6.97	10/5.8
Albumin (gr/dL)*	3.95	3.43
Glucose (gr/dL)*	87	158
Results of TOT		
TOT duration (months)	4	3
Mean number of treatments	48	36
Ulcer healing	+	+

*During TOT treatment period (mean).

Note: TOT = topical oxygen therapy, PVD = peripheral vascular disease.

clinic, and preserves their time at home. Health-related quality of life has been shown to be a valuable outcome measure in wound care (Woo, Conceição de Gouveia Santos, & Alam, 2018). This therapeutic approach takes into account the impact of health services on the patient's overall experience and quality of life (Harding, 2015).

Conclusion

In these retrospective case studies, TOT was a successful approach to wound care administered to patients on HD by nursing staff during HD sessions. The therapy was efficient and simple, and led to healing and possible closure of arterial ulcers. No adverse effects were related to TOT. Combining TOT with HD improved healing time and reduced hospital length of stay without compromising the level and quality of care.

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