

# Cyclical Topical Oxygen Therapy of Trauma-Induced Venous Leg Wounds in Diabetics – A Case Series

Lou Ann Hall-Matos, DPM, MS<sup>1</sup>; Ivan Vela, DPM<sup>2</sup>; Christopher Japour, DPM, FASPS<sup>3</sup>  
<sup>1</sup>Podiatry Resident, Saint Joseph Health System, Mishawaka IN, <sup>2</sup>Podiatry Resident, DVA Illiana Healthcare System, Danville IL, <sup>3</sup>Attending Physician and Residency Director, DVA Illiana Healthcare System, Danville IL

## Introduction

- The partial pressure of oxygen (pO<sub>2</sub>) within healthy skin tissue is around 100 mmHg, but prolonged periods of poor blood perfusion can cause the pO<sub>2</sub> within a wound bed to become as low as 10 mmHg<sup>1</sup>.
- It has been shown that exposure to oxygen not only upregulates growth factors that are essential for maintaining a well-vascularized wound core<sup>1, 3, 4</sup>, but also aids with enzymatic reactions sensitive to pO<sub>2</sub> levels which are responsible for healing of the skin<sup>1</sup>.
- These necessary processes can be maximized by raising the pO<sub>2</sub> well above the physiologic 100 mmHg, which can be achieved by means of oxygen therapy<sup>2</sup>.
- Hyperbaric oxygen therapy has been established as a common method of oxygen delivery to wounds. However, some disadvantages of this modality include the high cost of treatments, the possibility of oxygen toxicity, claustrophobia, and travel time to facilities for lengthy daily therapy sessions<sup>1,3,4</sup>.
- Cyclical topical oxygen therapy (TOT) is an option in which portable bags or chambers that deliver concentrated oxygen are applied directly over wounds, which further allows for oxygen to diffuse directly over the injured tissue<sup>1-4</sup>. This modality can be utilized from the comfort of the patient's home.
- Combined with the standard of care and regular debridement, TOT saturates the wound base and surrounding tissues with oxygen to induce localized expression of growth factors that result in angiogenesis and upregulation of enzymatic reactions which can lead to a reparative environment<sup>3</sup>.

## Purpose

- Our main goal is to demonstrate the efficacy of TOT to treat chronic traumatic lower extremity wounds complicated by venous insufficiency and diabetes mellitus.

## Methods

- Case review series conducted at the Veterans Affairs Illiana Healthcare System in Danville, Illinois.

- Inclusion criteria:

Lower extremity wounds secondary to trauma	<ul style="list-style-type: none"> <li>Iatrogenic</li> <li>Accidental injury</li> <li>Thermal injury (burn)</li> </ul>
Existing comorbidities	<ul style="list-style-type: none"> <li>Diabetes mellitus</li> <li>Venous insufficiency</li> </ul>
Stalled wound healing	<ul style="list-style-type: none"> <li>Utilizing standard of care</li> <li>Minimum of 4 weeks</li> </ul>
Use of TOT	<ul style="list-style-type: none"> <li>After failing standard of care</li> <li>Weekly debridement</li> <li>Multilayer compression therapy</li> <li>Collagen +/- graft</li> </ul>

- Weekly wound care protocol:

### Clinic visits

- Sharp debridement
- Compressive dressing application
- Wound measurement\*

### Home TOT application (Fig. 1)

- 5-7 days / week
- Up to 90 minutes / session [per manufacturer's protocol]

\*Wounds were measured from initial presentation to time of full epithelialization.



Fig. 1: Topical Wound Oxygen (TWO2<sup>®</sup>) Extremity Chamber (left) and Controller (right); TWO2<sup>®</sup>, Advanced Oxygen Therapy Inc., Oceanside, CA.

## Results

Patient	Wound Type	Failed Healing (weeks)	Wound Volume after Failed Healing (cm <sup>3</sup> )	Time to Healing with TOT (weeks)
1	Iatrogenic	8	0.448	7
2	Accidental injury	14	1.25	8
3	Accidental injury	4	0.624	12
4A	Thermal injury	8	7.2	6
4B	Thermal injury	8	1.5	6
5	Accidental injury	47	1.102	21
6	Accidental injury	12	0.26	12
7A	Accidental injury	4	0.375	4
7B	Accidental injury	4	1.925	4
8	Accidental injury	4	0.182	1

Table 1: Weeks of delayed wound healing and wound size/volume after failing standard of care, and time to healing/full epithelialization after TOT.

- Retrospective chart review from May 2016 to July 2021
- Inclusion criteria met by 8 male patients with 10 wounds:
  - Average age of 76 years
  - Average BMI of 27
  - Average hemoglobin A1C of 8
- Prior to the use of TOT, patients averaged 11.3 weeks of failed healing attempts when treated with the standard of care.
- All wounds achieved 100% healing / epithelialization following TOT.
- The average time to healing was reduced to 8.1 weeks after TOT.
- One wound recurred after 2.5 months in an uncontrolled diabetic patient.
- One patient expired from wound unrelated reasons and was excluded from follow up.
- All other wounds remained closed/healed after an average follow up of 27.5 months up to June 2023.

## Discussion

- Chronic lower extremity wounds have a large impact on health, well-being, and cost to those afflicted.
- Multiple anatomic and physiologic factors ultimately reduce oxygen diffusion to the wound bed, resulting in delayed healing<sup>1-4</sup>.
- Patients carry the physical, emotional, and economic burden of their treatment when the standard of care fails.
- This retrospective review of 10 chronic lower extremity wounds induced by trauma and complicated by venous insufficiency and diabetes mellitus demonstrated effectiveness in healing when treated with cyclical topical oxygen therapy, or TOT.
- Chart review included 8 male patients with 10 wounds, with an average age of 76 years, average BMI of 27, and average hemoglobin A1C of 8, all of which achieved 100% healing.
- When the failed therapies were replaced with TOT, the average time to healing these complicated wounds was reduced to 8.1 weeks.
- Treatment management should be re-evaluated and include the use of TOT when there is less than 40% wound closure in 4 weeks.
- Raw data is limited but shows promising results, keeping in mind comorbidities, medication use, and quality of life.
- Ongoing efforts are intended to expand sample size that will enable statistical significance.

## References

- Fries RB, Wallace WA, Roy S, et al. Dermal excisional wound healing in pigs following treatment with topically applied pure oxygen. *Mutat Res.* 2005;579(1-2):172-181. doi:10.1016/j.mrfmmm.2005.02.023
- Frykberg RG. Topical Wound Oxygen Therapy in the Treatment of Chronic Diabetic Foot Ulcers. *Medicina (Kaunas).* 2021;57(9):917. Published 2021 Aug 31. doi:10.3390/medicina57090917
- Sun XK, Li R, Yang XL, Yuan L. Efficacy and safety of topical oxygen therapy for diabetic foot ulcers: An updated systematic review and meta-analysis. *Int Wound J.* 2022;19(8):2200-2209. doi:10.1111/iwj.13830
- Lavery LA, Killeen AL, Farrar D, et al. The effect of continuous diffusion of oxygen treatment on cytokines, perfusion, bacterial load, and healing in patients with diabetic foot ulcers. *Int Wound J.* 2020;17(6):1986-1995. doi:10.1111/iwj.13490