Real-world Analysis of the Effect of Adjunctive Vaporous Hyperoxia Therapy on the Healing of Chronic Wounds

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Introduction

In the United States, 1.6 million people are affected each year with a diabetic foot ulcer (DFU), comprising one-third the annual cost of diabetes care and contributing to >80% of all lower extremity amputations,[1-4] Less than a third of DFUs treated with standard wound care heal.[5] Safe and effective treatments for chronic wounds are desperately needed.

VHT® [vaporous hyperoxia therapy (VHT), Vaporox, Inc., Lone Tree, CO] is a patented, FDA-510(k) cleared technology for the adjunctive use in chronic wounds, surgical wounds, amputations, infected ulcers/gangrene, skin grafts, burns, and frostbite. VHT delivers a low-frequency, noncontact, nonthermal, ionic, hydrating mist that alternates with concentrated oxygen, providing an optimal wound healing environment that hydrates and oxygenates tissue, reduces bioburden, and promotes angiogenesis to boost the healing process.[6] In a recent study of chronic DFUs in 29 patients, an 83% healing rate at 20 weeks was observed after adjunctive VHT treatment.[6] The current study retrospectively evaluated the impact of VHT in chronic wounds of various types and etiologies.

Figure 1. Vaporous hyperoxia system (VHT)

The VHT system is shown below, which emits a low-frequency, noncontact, nonthermal, ionic, hydrating mist to the wound that alternates with concentrated oxygen.

Table 1. Patient (n = 40) and Wound (n = 53) Characteristics

Variable	n (%)
Patient age, years	
• 45-54	• 1 (2%)
• 55-64	• 8 (20%)
• 65-74	• 21 (52%)
• 75-80	• 6 (15%)
• >80	• 4 (10%)
Sex	
• Male	• 26 (65%)
• Female	• 14 (35%)
Race/ethnicity	
• White	• 39 (98%)
• African American	• 1 (2%)
• Hispanic	• 4 (10%)
Mean (SD) HbAlc, mg/dL, *n = 16*	6.8 (2.2)
Mean (SD) no. of wounds/patient	1.6 (0.8)
Mean (SD) no. of comorbidities/patient	4.6 (2.5)
Most common comorbidities	
• Diabetes	• 37 (93%)
• Peripheral neuropathy	• 29 (73%)
• Hypertension	• 21 (53%)
• Peripheral vascular disease	• 18 (45%)
Wound area, cm^2	
• Mean (SD)	• 5.6 (12.3)
• Median (IQR)	• 1.5 (3.9)
Wound age, months	
• Mean (SD)	• 8.0 (22.5)
• Median (IQR)	• 2.0 (3.0)
Wound type, n (%)	
• Arterial ulcer	• 2 (4)
• Burn	• 1 (2)
• Diabetic foot ulcer	• 47 (88)
• Pressure injury	• 3 (6)
Wagner grade, n (%)	
• 1	• 4 (7)
• 2	• 38 (72)
• 3	• 11 (21)

Methods

We performed a retrospective chart review of patients with chronic wounds treated with VHT, in conjunction with standard of care. From February 28, 2020 through August 30, 2022, adults with chronic wounds >4 weeks at multiple outpatient centers received VHT with standard of care. The patient had to be able to maintain reasonable nutrition, hydration, and home care between visits (or had a caregiver who could assist); and they had to give their written informed consent. Exclusion criteria were one-time visits, Wagner 4/5 DFUs, being pregnant, having sepsis, having a wound with cancerous etiology, wounds whose end could not be probed, and wounds treated with >5 cellular and/or tissue-based products (CTPs). The primary endpoint was complete healing (defined as complete epithelialization and granulation) at 16 weeks. Secondary endpoints were time to heal (weeks), percentage area reduction (PAR), percentage volume reduction (PVR), and the average number of treatments administered.

At the initial visit, patient demographics, comorbidities, and wound age were recorded. There were 2 weekly treatment visits for ≤4 weeks and until the wound healed, or until 16 weeks. Each treatment visit included a comprehensive wound assessment and laboratory tests. Before VHT, the wound was debrided (if needed) and wound measurements were taken. Arterial ulcers were revascularized as needed. The index foot was then placed in the treatment chamber (Figure 1) and underwent 1 hour of VHT, involving 4 alternating cycles of a proprietary ultrasonic mist for 9 minutes and then 5 minutes of concentrated oxygen. The wound was dressed with moist dressings and received offloading with felt-to-foam modalities, CAM boot, or diabetic shoes. Burns received silver alginate and dry, sterile dressings. Arterial ulcers also received compression.

Any patient that did not receive on average 1.7 to 2.3 treatments per week or did not complete ≥4 weeks of VHT treatment was withdrawn from analysis.

Providers used an electronic medical record system (VapApp, Vaporox Inc.) to collect patient/wound data and wound photographs at point of care. The system stores data in a HIPPA-compliant cloud database (Amazon Web Services, Amazon, Seattle, WA). A data visualization tool (Microsoft Power BI, Microsoft, Redmond, WA) generated outcomes data. Data were analyzed with PASW 28 (IBM, Armonk, NY). Means and standard deviations (SD) summarized continuous variable data [medians and interquartile ranges (IQR) values for non-normal distribution). Categorical variable data were summarized with counts and percentages. Kaplan-Meier analysis evaluated time to heal.

Figure 2. Kaplan-Meier plot of time to heal (weeks)

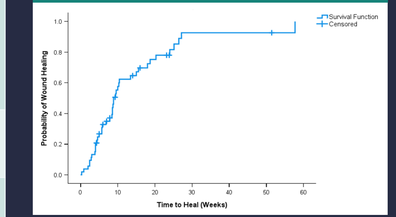

Figure 3. Percentage Area Reduction over 16 weeks, using a window of ±2 days for each week.

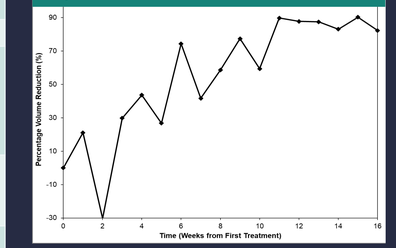

Figure 4. Percentage Volume Reduction over 16 weeks, using a window of ±2 days for each week.

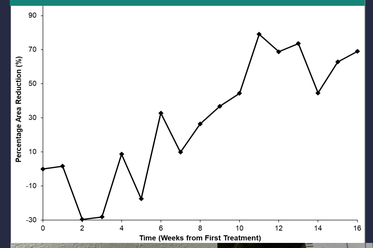

Figure 5. Pressure Injury (PI) Case

A White, female patient aged 45-54 years presented with a PI with a duration of 6 weeks. She also had hypertension, dyslipidemia, renal insufficiency, and spina bifida. Baseline wound volume was 3.4 cm^3 (6A). The PI was treated with 14 vaporous hyperoxia therapy treatments (~1.7 treatments/week). After 2 weeks, the wound volume decreased to 3.0 cm^3 (6B). At 7 weeks, the wound volume was 1.9 cm^3 (6C). The wound was healed at 9 weeks (6D).

Figure 6. Diabetic Foot Ulcer (DFU) Case

A White, male patient aged 55-64 years presented with a DFU with a duration of 2 months. He had diabetes, peripheral neuropathy, obesity, and a prior amputation. Baseline wound volume was 36 cm^3 (6A). The DFU was treated with 30 vaporous hyperoxia therapy treatments (~2/week) and one application of amniotic membrane. After 4 weeks, the wound volume decreased to 15.6 cm^3 (6B). At 7 weeks, the wound volume was 5.4 cm^3 (6C). The DFU was healed at 15 weeks (4D).

Results

Among 249 patient retrospectively screened for eligibility; 206 (83%) were excluded for not receiving on average 1.7-2.3 treatments per week or for not completing ≥4 weeks of treatment. Forty patients with 53 chronic wounds were analyzed. About half (53%) of the patients were 65-74 years old, and the majority (65%) were males (Table 1). The mean comorbidity count was 4.6 (SD: 2.5) per patient, with diabetes, peripheral neuropathy, hypertension, and peripheral vascular disease being the most common comorbidities. There were on average 1.6 (SD: 0.77) wounds per patient (Table 1). Most wounds were DFUs (n = 47, 88%). At baseline, the mean wound area was relatively large at 5.6 cm^2, with an average age of 8 months. The median wound area and age at baseline was 1.5 cm^2 and 2 months, respectively. Thirty-eight DFUs (72%) were Wagner grade 2.

Twenty-seven (68%) patients completed VHT treatment in an average of 81 days [SD: 78.9; median: 60; interquartile range (IQR): 76.5]. Among the 13 patients withdrawn, 7 patients (54%) were ultimately treated with ≥5 CTPs. The other 6 patients were withdrawn due to death (n = 1), hospitalization (n = 1), surgery (n = 1), protocol nonadherence (n = 1), and other (n = 2).

The mean number of VHT treatments applied per patient was 22.9 (SD: 20.8); the median was 18 (IQR: 21). Patients received on average 2.2 weekly treatments (SD: 0.71, median: 2; IQR: 5.3). Five patients were also treated with <5 CTPs, including 1 with dehydrated human amnion/chorion membrane, 2 with human connective tissue matrix, 3 with amniotic membrane grafts, and 5 with unknown CTPs. The wounds of all 5 patients treated with combination VHT/CTP therapy healed.

A total of 41 out of 53 (77%) wounds healed by 16 weeks. The mean time to heal was 14.5 weeks (95% CI: 9.9-18.1); the median time to heal was 8.9 weeks (95% CI: 7.6-10.1). Figure 2 depicts the Kaplan-Meier plot.

The mean PAR at 16 weeks among healed wounds was 69% (SD: 156.7) (Figure 3). The mean PVR at 16 weeks among healed wounds was 82% (SD: 70.3) (Figure 4).

Figures 5 depicts a pressure injury that healed after adjunctive VHT treatment. Figure 6 depicts a very large DFU that healed after combined VHT/CTP therapy.

Discussion and Conclusion

In this real-world analysis, 77% of chronic wounds treated with VHT healed by 16 weeks, with an average time to heal of 14.5 weeks. The mean PAR and PVR at 16 weeks was 69% and 82%, respectively. These findings suggest that VHT accelerates healing in chronic wounds and are consistent with a previous study evaluating adjunctive VHT on chronic DFUs.[6] That study reported an 83% healing rate by 20 weeks, with an average healing time of 9.4 weeks. In the current study, we included a variety of wound types and etiologies beyond DFUs to assess the real-world impact of VHT, which could account for slight differences in healing rates. Also, the average wound area at baseline in our study was 5.6 cm^2 and much larger than the wounds in the previous VHT study, which had a mean baseline area of 3 cm^2.[6]

Ultrasound therapy improves wound healing, by altering the activity of the cell membrane via cavitation and microstreaming.[7] In a meta-analysis of 463 chronic wounds treated with noncontact, low-frequency, ultrasound therapy, 41.7% closed, and and the average PAR was 85.2%.[8] The healing rates obtained from combined oxygen therapy and ultrasound provided by VHT in our study thus exceed the outcomes reported in the literature with noncontact, low-frequency ultrasound alone.

VHT combines a low-frequency, noncontact, nonthermal, ultrasonic mist with concentrated oxygen to optimize the therapeutic benefits of both treatments and accelerate wound healing. Microcapillaries absorb VHT, so that tissue reperfusion occurs without applying direct pressure to the wound bed.[6] VHT optimizes wound bed preparation and also facilitates the wound bed response to CTP application, as demonstrated by the 5 patients who healed following combination VHT/CTP therapy (and depicted in Figure 6). Forty-one wounds completely healed with only adjunctive VHT, and so VHT alone also has an accelerated effect on wound closure.

The retrospective design of our study is limited by an inability to control for patient selection bias, and it was not possible to assess all the prohealing factors. Another limitation is the relatively small number of patients enrolled. However, the heterogeneity and severity of the cases evaluated in this study present real-world evidence and represent challenges faced daily in clinical practice. Patients were very sick with nearly 5 comorbidities each, and large wounds were included (Figure 5). Unsurprisingly, a third of patients did not complete this study, but, importantly, none of the early terminations were related to VHT. Thus, it appears to be safe, as well as beneficial to wound healing. Further study of the use of VHT on chronic wounds is therefore warranted, especially larger, RCTs that compare VHT to standard of care and/or evaluate its use in combination with CTPs.

In conclusion, this real-world analysis demonstrated that the use of VHT with standard of care appeared to optimize wound bed preparation and accelerate healing rates, with the majority of wounds closed before 16 weeks. VHT also appears to boost healing rates in wounds that are also treated with CTPs, but this finding warrants further investigation. The use of VHT as an adjunctive therapy for chronic wounds appears to be safe and effective in a real-world population with multiple comorbidities and various wound types.

References

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