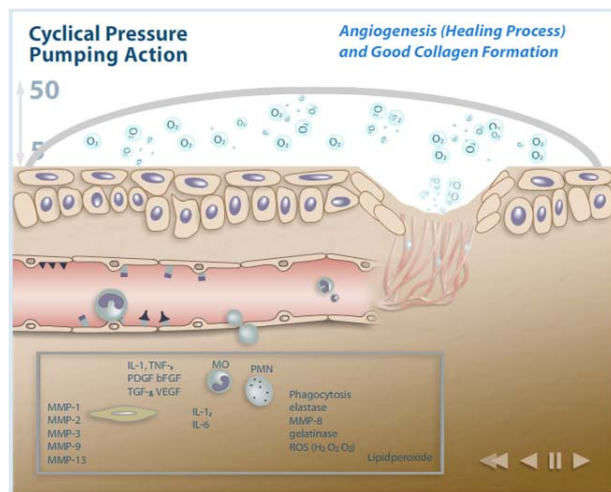


FACT SHEET - Topical Wound Oxygen Therapy (TWO₂)

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Why do wounds need Oxygen?

Oxygen (O₂) and their reactive oxygen species are involved in all stages of wound healing; modulating cell migration, adhesion, proliferation, neovascularization, remodeling and apoptosis^(1; 2). It is well established that O₂ is vital in the synthesis of collagen, enhancement of fibroblasts, angiogenesis and leukocyte function^(3; 4; 5; 6). O₂ also has key functions in energy metabolism^(7; 8) and in the inhibition of microbial growth⁽⁹⁾. As a consequence, tissue hypoxia, caused by disrupted or compromised vasculature, seems to be a key factor that limits wound healing^(10; 11)



Does TWO₂ support the diffusion of oxygen into the tissue?

Topical oxygen therapies increase the tissue pO₂ of superficial wound tissue in pigs⁽¹²⁾. Using a special probe designed to measure superficial pO₂ at 2 mm depth at the center of the wound bed Fries et al. saw an increase of pO₂ from less than 10 mmHg to 40 mmHg in as little as 4 minutes. Additional indirect evidence of the penetration of oxygen into the tissue with topical wound oxygen (TWO₂) devices comes from Scott and Reeves⁽¹³⁾ in which TWO₂ was shown to increase the most crucial angiogenesis related growth factor, VEGF. Finally Fries et al. could demonstrate by histology that wounds treated with oxygen showed signs of improved angiogenesis and tissue oxygenation in pigs⁽¹²⁾.

What are the clinical benefits of TWO₂?

Fisher treated 52 patients with diabetic, venous and pressure ulcers with topical oxygen as early as 1969⁽¹⁴⁾. All of them had had been treated from several months to several years utilizing conventional treatment regimes without improvement.

Topical oxygen treatment healed 88% of the cases. In 4 out of 6 patients without healing there was an underlying osteomyelitis, unknown at the start of therapy. However, in 6 other patients, with almost identical lesions on both lower extremities and hips, one side was treated conventionally while the contra lateral lesion was exposed to topical oxygen. All wounds in the TWO₂ group healed within 7 weeks, while only two out of 6 control wounds showed mild improvement. When the TWO₂ treated wound had healed, TWO₂ was then applied to the control wounds. All control wounds subsequently healed when treated with TWO₂, with healing times remarkably similar to those of the originally treated wounds. A randomized prospective study utilizing TWO₂ was published by Heng et al. ⁽¹⁵⁾ showed healing rates of 90% in the TWO₂ group, compared with 22% in the control group. In a cohort study examining the cost-effectiveness of TWO₂ in the healing of necrotic ulcers ¹⁶ none of the control group ulcers healed during the 4-week observation period compared with 100%, 80% and 83% of Level 2, 3 and 4 topical oxygen treated ulcers healed, respectively. In the most recent study on venous wounds, Tawfick et al ⁽¹⁷⁾ studied 80 patients with refractory non-healing venous ulcers. At three months, 80% of TWO₂-managed ulcers (n = 37) were completely healed, compared to 25% (n = 9) in the control group. Seventeen ulcers were MRSA-positive, which became MRSA-negative after TWO₂ treatment. This is compared to 18 MRSA ulcers managed in the control group, all of which remained positive after treatment. The pain score threshold in the TWO₂ managed patients improved from eight to three by 13 days. After 3 months follow-up, three of the nine healed ulcers in the control group showed signs of recurrence compared to none of the 37 TWO₂ healed ulcers.

What additional clinical evidence is on its way?

AOTI is currently conducting a prospective multicenter randomized double blinded placebo controlled clinical trial in the US and Canada. A prospective cohort study in diabetic foot ulcers has been submitted for publication to a major US wound care journal. Several smaller studies evaluating questions like; the antibacterial potential, the optimal treatment regime and the pain diminishing potential of TWO₂ therapy are in process.

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