Beneficial uses of HBOT in Wound Healing

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Wound healing is achieved through four phases: hemostasis, inflammation, proliferation, and remodeling. Many factors can interfere with one or more phases of this process, thus causing improper or impaired wound healing. Oxygen is important for cell metabolism, especially energy production utilizing ATP, and is critical for nearly all wound-healing processes. It prevents wounds from infection, induces angiogenesis, increases keratinocyte differentiation, migration, and re-epithelialization, enhances fibroblast proliferation and collagen synthesis, and promotes wound contraction.[1,2]

Due to vascular disruption and high oxygen consumption by metabolically active cells, the early wound's microenvironment is depleted of oxygen and is quite hypoxic. Chronic wounds are notably hypoxic; tissue oxygen tensions have been measured transcutaneously in chronic wounds from 5 to 20 mm Hg, in contrast, to control tissue values of 30 to 50 mm Hg.[3] In wounds where oxygenation is not restored, healing is impaired. Temporary hypoxia after injury triggers wound healing, but prolonged or chronic hypoxia delays wound healing. The proper oxygen level is crucial for optimum wound healing. The key to successful management of any ulceration lies in identifying the underlying cause of the ulcer and the appropriate measures to remove or modify the causative factors interfering with healing.

When wound hypoxia is the systemic cause of the healing failure, providing oxygen at the wound site is, essentially, treating the cause. Hyperbaric oxygen therapy is an adjunctive therapeutic modality in which the patient is given a high volume of pure oxygen to breathe in an environment of elevated atmospheric pressure, which leads to an increase in tissue oxygen pressures at the wound site.

Hyperbaric Oxygen Therapy (HBOT)

Figure 1: Monoplace chamber

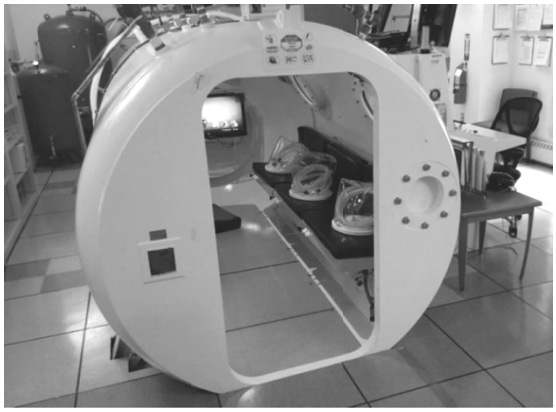

Figure 2: Multiplace chamber

Hyperbaric oxygen therapy (HBOT) is a treatment modality that has been used in chronic wounds for about 40 years.[4] Treatment involves placing the patient in a compression chamber, increasing the chamber's environmental pressure, and administering 100% oxygen for respiration. In this way, it is possible to deliver a greatly

increased partial pressure of oxygen to the tissues. Typically, treatments involve pressurization between 2.0 and 2.5 atmospheres absolute (ATA) for periods between 60 and 120 minutes once or twice daily. A typical course might involve 15 to 30 such treatments. (Fig. 1 & 2)

Mechanism of HBOT

In HBOT, increasing the partial pressure of oxygen inhaled by a patient by administering 100% oxygen and elevating the pressure increases the amount of oxygen that can be dissolved in a patient's blood serum by Henry's law, which states that the amount of ideal gas dissolved in the solution is directly proportional to its partial pressure.[5]During treatment, arterial oxygen tension often exceeds 2000 mm Hg, and oxygen levels of 200 to 400 mm Hg occur in tissues.[6] The increased oxygen supply to hypoxic tissues has multiple beneficial effects on wound healing. Because oxygen cannot be stored in tissue, daily HBOT supports an adequate oxygen supply to the injury site to promote wound healing progression from the inflammatory phase to the proliferative phase. Increased oxygen concentrations lead to increased production of reactive oxygen species and reactive nitrogen species, which play essential roles in signalling pathways for promoting neovascularization, matrix formation, and decreasing inflammation.

Extracellular matrix formation is an oxygen-dependent process linked closely to neovascularization. Fibroblast growth factor production is also increased by HBOT, promoting fibroblast migration and proliferation.[7] Increased oxygen stimulates the proliferating fibroblasts to produce collagen at increased rates and enhances collagen cross-linking to improve tissue tensile strengths. Hyperoxia also promotes decreased inflammation by impacting three major inflammatory cell types macrophages, leukocytes, neutrophils, and inducing vasoconstriction to reduce local edema. (Fig. 3)

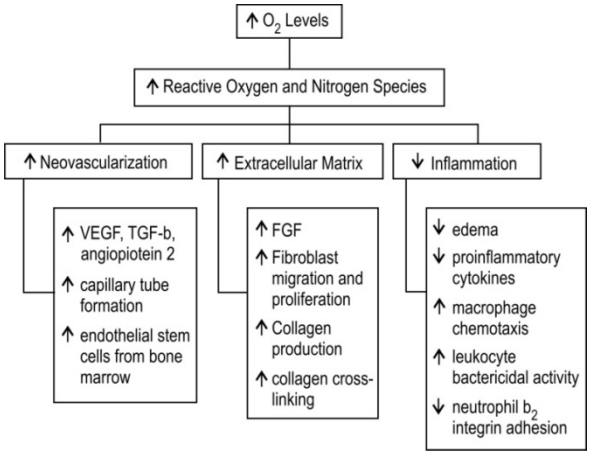

Figure 3: Mechanism of HBOT

Uses of HBOT in wound healing

Treatment of diabetic and ischemic foot ulcers requires a multimodal approach involving local wound care, reasonable glycemic control, revascularization of ischemic limbs, treatment of infections, and pressure off-loading. Unfortunately, complete wound healing rates can be as low 60% a year, even with optimal care. Hyperbaric oxygen therapy has been used as adjunctive therapy for patients with refractory ulcers. It involves inhalation of 100% oxygen inside a pressurized hyperbaric chamber and has been used successfully in humans at varying pressures to treat various conditions. [8]HBOT treatment showed the improved healing rate of DFU in the short term but not in the long term, and it was well recognized that the change in wound size at two weeks and four weeks is a predictor of complete healing after 12 weeks. [9,10] Studies showed that prolonged treatment of HBOT should be avoided as it increases oxidative stresses, which are considered important pathogenesis of chronic nonhealing wounds.[11,12] An only a limited number of studies is available regarding the short-term administration of HBOT to DFU patients.

A prospective study provides evidence that HBOT fastens the healing rate of DFU.

Besides, it suggests the possibility of shortening hospitalization time. The patients on HBOT treatment achieved a favourable healing rate after 14 days of the treatment was evident from histopathological features.[13] A significantly greater percentage of HBOT-treated wounds (33.3%, 5/15) achieved complete closure than conventional therapy–treated wounds (0%, 0/15; P = .014) at the end of treatment. This significant difference was maintained throughout the eight weeks of follow-up.[14]

Conclusion

HBOT allows the reversal of a hypoxic state by increasing the oxygen diffusion within the plasma, consequently promoting angiogenesis, encouraging fibroblastic activity and supporting the tissues to resist against bacteria. HBOT plus conventional therapy appears as safe as and probably more effective than conventional therapy alone for the non-healing wounds.

References

1. Bishop A. Role of oxygen in wound healing. J Wound Care. 2008 Sep;17(9):399-402. doi: 10.12968/jowc.2008.17.9.30937.
2. Rodriguez PG, Felix FN, Woodley DT, Shim EK. The role of oxygen in wound healing: a review of the literature. Dermatol Surg. 2008 Sep;34(9):1159-69. doi: 10.1111/j.1524-4725.2008.34254.x.Epub 2008 May 29.
3. Tandara AA, Mustoe TA. Oxygen in wound healing--more than a nutrient. World J Surg. 2004 Mar;28(3):294-300. doi: 10.1007/s00268-003-7400-2. Epub 2004 Feb 17.
4. Kulonen E, Niinikoski J. Effect of hyperbaric oxygenation on wound healing and experimental granuloma. Acta Physiologica Scandinavia 1968; 73(3):383–4.
5. Howard MA, Asmis R, Evans KK, Mustoe TA. Oxygen and wound care: a review of current therapeutic modalities and future direction. Wound Repair Regen 2013;21:503-11.
6. Thom SR. Hyperbaric oxygen: its mechanisms and efficacy. PlastReconstr Surg 2011; 127(Suppl 1):131S-41S.
7. Stoekenbroek RM, Santema TB, Legemate DA, Ubbink DT, van den Brink A, Koelemay MJ. Hyperbaric oxygen for the treatment of diabetic foot ulcers: a systematic review. Eur J VascEndovasc Surg 2014;47:647-55.
8. Sheffield, P.J., and Smith, P.S. 2002. Physiological and pharmacological basis of hyperbaric oxygen therapy. In: Bakker DJ, Cramer FS (eds). Hyperbaric Surgery Perioperative Care, 63-110.
9. Sheehan, P., Jones, P., Giurini, J.M., Caselli, A., and Veves, A. 2006. Percent change in wound area of diabetic foot ulcers over a 4-week period is a robust predictor of complete healing in a 12-week prospective trial. Plast Reconstr Surg, 117(7), 239-244.
10. Kranke, P., Bennett, M. H., Martyn-St James, M., Schnabel, A., and Debus, S. E. (2012). Hyperbaric oxygen therapy for chronic wounds. Cochrane Database Syst Rev, 4, 41-23.
11. Schafer, M., and Werner, S. 2008. Oxidative stress in normal and impaired wound repair. Pharmacol Res, 58(2), 165- 171.
12. Le Ma, M. D., Pingsong Li, M. D., Zehong Shi, M. D., Tuanjie Hou, M. D., Xiao Chen, M. D., and Jin Du, M. D. 2013. A Prospective, Randomized, Controlled Study of Hyperbaric Oxygen Therapy: Effects on Healing and Oxidative Stress of Ulcer Tissue in Patients with a Diabetic Foot Ulcer. Ostomy Wound Manage, 59(3), 18-24.
13. Ezhilarasi K, Abirami P, Vijay V. Healing effect of hyperbaric oxygen therapy as an adjunctive treatment on diabetic foot ulcer patients in short duration – A brief report. Asian J Sci and Tech. 2018;9:7743–6.
14. Salama SE, Eldeeb AE, Elbarbary AH, Abdelghany SE. Adjuvant Hyperbaric Oxygen Therapy Enhances Healing of Nonischemic Diabetic Foot Ulcers Compared With Standard Wound Care Alone. Int J Low Extrem Wounds. 2019 Mar;18(1):75-80. doi: 10.1177/1534734619829939. Epub 2019 Mar 5. PMID: 30836807.