

HYPERBARIC OXYGEN AND DIABETIC CONDITIONS

Okamoto, N. et al. "Effect of hyperbaric oxygen on ophthalmic artery blood velocity in patients with diabetic neuropathy." *Jpn J Ophthalmol*, 1998, 42(5): 406-10.

To assess the relationship between blood flow and the complications of diabetes mellitus, we investigated the changes in the velocity of blood flow in the ophthalmic artery before and after hyperbaric oxygen therapy (HBO), one of the treatments for diabetic neuropathy. Color Doppler imaging was used before and after HBO. Seven diabetic neuropathy patients, 3 diabetics without neuropathy, and 7 normal, control subjects were enrolled. The patients were subjected to breathing 100% oxygen at 2.0 atmosphere absolute (ATA) for 1 hour. Hyperbaric oxygen therapy resulted in an average decrease in blood velocity by 15.0 +/- 9.0% (mean +/- SD) in normal subjects and 10.7 +/- 8.6% in diabetics without neuropathy. Blood velocity returned to the baseline level 4 hours after discontinuation of HBO. In contrast, blood velocity increased by 20.6 +/- 9.5% in diabetic patients with neuropathy irregardless of the severity of the diabetic retinopathy. The resistance index of the ophthalmic artery was not changed during HBO in the group with diabetic neuropathy, indicating that other mechanisms may be implicated, leading to the compensatory changes of blood flow. These results suggest that the increase in the blood velocity in the ophthalmic artery after HBO in diabetic neuropathy patients could be attributed to an imbalance in autonomic nervous function.

Weisz, G. et al. "Treatment of the diabetic foot by hyperbaric oxygen." *Harefuah* 1993 Jun 1;124(11):678-81, 740.

Diabetic foot wounds are consequences of the neuropathy and the small and large vessel disease that complicate diabetes. At the cellular level, the result is hypoxia which impairs wound healing. Hyperbaric oxygenation (HBO) may be a useful adjuvant to wound care. It leads to enhanced oxygenation of the affected tissues, has an antiseptic effect, reduces edema, and accelerates collagen production and angiogenesis, thus enhancing tissue repair. 14 diabetics with chronic nonhealing wounds which did not respond to treatment for at least 3 months were treated by HBO. All had palpable pedal pulses. Transcutaneous measurements of tissue pO₂ showed elevation from 20 +/- 10 mm Hg during air breathing to 643 +/- 242 mm Hg while breathing pure oxygen at 2.5 ATA. They were treated with HBO in 56 +/- 10 consecutive HBO sessions. In 11 there was complete wound healing, while in 1 there was partial response, in 1 minimal response, and in 1 a transient response. HBO is useful in chronic nonhealing wounds of the diabetic foot and of the diabetic foot with impending amputation.

Lee, S. et al. "Hyperbaric oxygen in the treatment of diabetic foot infection." *Chang Keng I Hsueh Tsa Chih* 1997 Mar;20(1):17-22.

BACKGROUND: This study evaluated multiple healing predictive factors in patients with diabetic foot infections to determine the usefulness of adjunctive hyperbaric oxygen in the treatment of such patients. METHODS: From March 1995 to May 1996, we treated 31 diabetic patients presenting with infected foot lesions with a regimen of adequate metabolic control, frequent wound debridement and hyperbaric oxygen therapy. Age, gender, leukocyte count, total lymphocyte count, hemoglobin, erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), glycosylated hemoglobin A1c (HbA1c), albumin, ankle-brachial index, types of bacterial cultures and number of debridements were compared between successful and failed treatments. Independent t-test and Fisher's exact test were used to identify the prognostic factors associated with outcome of treatment. RESULTS: The mean age of the patients was 63.0 +/- 9.7 years (range 43 to 81). The mean number of hyperbaric oxygen therapies was 35.3 +/- 21.8 treatments (range 5 to 83). Of the 31 patients, 6 received below knee amputation, and 25 had their foot preserved or achieved a lower level of amputation. Elevated leukocyte count and low ankle-brachial index were significantly related to poor outcome. CONCLUSIONS: In the treatment of diabetic foot infection, adjunctive hyperbaric oxygen therapy seems to be a useful tool to enhance wound healing provided that there are preserved circulation and controlled infection.

Faglia, E. et al. "Adjunctive systemic hyperbaric oxygen therapy in treatment of severe prevalently ischemic diabetic foot ulcer. A randomized study. *Diabetes Care* 1996 Dec;19(12):1338-43

OBJECTIVE: To evaluate the effectiveness of systemic hyperbaric oxygen therapy (s HBOT) in addition to a comprehensive protocol in decreasing major amputation rate in diabetic patients hospitalized for severe foot ulcer. RESEARCH DESIGN AND METHODS: From August 1993 to August 1995, 70 diabetic subjects were consecutively admitted into our diabetologic unit for foot ulcers. All the subjects underwent our diagnostic-therapeutic protocol and were randomized to undergo s-HBOT. Two subjects, one in the arm of the treated group and one in the arm of nontreated group, did not complete the protocol and were therefore excluded from the analysis of the results. Finally, 35 subjects received s-HBOT and another 33 did not. RESULTS: Of the treated group (mean session = 38.8 +/- 8), three subjects (8.6%) underwent major amputation: two below the knee and one

above the knee. In the nontreated group, 11 subjects (33.3%) underwent major amputation: 7 below the knee and 4 above the knee. The difference is statistically significant ($P = 0.016$). The relative risk for the treated group was 0.26 (95% CI 0.08-0.84). The transcutaneous oxygen tension measured on the dorsum of the foot significantly increased in subjects treated with hyperbaric oxygen therapy: 14.0 +/- 11.8 mmHg in treated group, 5.0 +/- 5.4 mmHg in nontreated group ($P = 0.0002$). Multivariate analysis of major amputation on all the considered variables confirmed the protective role of s-HBOT (odds ratio 0.084, $P = 0.033$, 95% CI 0.008-0.821) and indicated as negative prognostic determinants low ankle-brachial index values (odds ratio 1.715, $P = 0.013$, 95% CI 1.121-2.626) and high Wagner grade (odds ratio 11.199, $P = 0.022$, 95% CI 1.406-89.146). CONCLUSIONS: s-HBOT, in conjunction with an aggressive multidisciplinary therapeutic protocol, is effective in decreasing major amputations in diabetic patients with severe prevalently ischemic foot ulcers. LinkOut

Brakora, M.J. et al. "Hyperbaric oxygen therapy for diabetic wounds." *Clin Podiatr Med Surg* 1995 Jan;12(1):105-17

Hyperbaric oxygen can be a useful adjuvant in the management of diabetic foot wounds when coordinated with medical-surgical management of the patient. Elevated tissue oxygen tensions improve leukocyte bacterial killing efficiency and enhance connective tissue regenerative systems for wound healing.

Cianci, P. "Adjunctive hyperbaric oxygen therapy in the treatment of the diabetic foot." *J Am Podiatr Med Assoc* 1994 Sep;84(9):448-55

The use of hyperbaric oxygen therapy for the treatment of conditions of local or focal hypoxia is not new. The author discusses the potential benefits of hyperbaric oxygen in the treatment of chronic wounds when used as a part of a multidisciplinary wound care program.

Steed, D.L. et al. "Organization and development of a university multidisciplinary wound care clinic." *Surgery* 1993 Oct;114(4):775-8; discussion 778-9.

BACKGROUND. A multidisciplinary wound care clinic was established to diagnose and treat patients with nonhealing ulcers of the lower extremity. METHODS. The clinic was organized under the direction of the departments of vascular surgery and dermatology with support by the departments of plastic surgery, hyperbaric medicine, orthopedic surgery, and podiatry, and a research nurse. RESULTS. In the first 4 years and 3 months, 683 patients were evaluated. One hundred seventy-one patients underwent outpatient testing in the noninvasive vascular laboratory and 30 patients underwent angiography. Causes of the ulcers were venous stasis, 280 patients (41%); diabetic neuropathy, 182 patients (27%); arterial insufficiency, 119 patients (17%); rheumatologic disorders, 38 patients (6%); trauma, 15 patients (2%); and in 49 patients (7%) a variety of other disorders. One hundred seventy-nine operations were performed including 86 operating room debridements, 48 amputations (43 toe, 4 below knee, 1 above knee), 23 arterial bypasses, 1 venous bypass, 14 skin grafts, 2 pedicle flaps, and 5 excisions of tumor. Fifty-six patients with cellulitis were admitted to the hospital for intravenous antibiotics and 12 patients were treated with hyperbaric oxygen therapy. One-hundred thirty-two patients were entered into randomized prospective trials of topical growth factors on Institutional Review Board approved protocols. CONCLUSIONS. We concluded that a multidisciplinary approach to wound care is beneficial to patients with chronic wounds and provides a mechanism for clinical investigation on the healing of problem wounds.

Doctor, N. et al. "Hyperbaric oxygen therapy in diabetic foot." *J Postgrad Med* 1992 Jul-Sep;38(3):112-4, 111.

To study the effect of hyperbaric oxygen therapy in chronic diabetic foot lesions, a prospective controlled study was undertaken. Thirty diabetics with chronic foot lesions were randomised to study group (conventional management and 4 sessions of hyperbaric oxygen therapy) and control group (conventional management). The patients were assessed for average hospital stay, control of infection and wound healing. The control of infection spread was quicker. Positive cultures decreased from initial 19 to 3 in study group as against from 16 to 12 in the control group. ($p < 0.05$). This difference was most pronounced for *Escherichia coli*. Also, the need for major amputation was significantly less in the study group ($n = 2$) as against the control group ($n = 7$) ($p < 0.05$). The average hospital stay was not affected. We conclude that hyperbaric oxygen therapy can be safely used and is beneficial as an adjuvant therapy in chronic diabetic foot lesions.

Baroni, G. et al. "Hyperbaric oxygen in diabetic gangrene treatment." *Diabetes Care* 1987 Jan-Feb;10(1):81-6

We treated a group of 18 hospitalized adult diabetic patients (all with retinopathy, 17 with symptomatic neuropathy, and 6 with macroangiopathy) presenting with gangrenous lesions of the foot by a combined regime consisting of strict metabolic control, daily debridement of necrotic tissues, and daily hyperbaric oxygen (HBO) treatments given in a multiplace oxygen chamber. Another group of 10 adult subjects with comparable foot lesions (all with

retinopathy, 9 with symptomatic neuropathy, and 4 with macroangiopathy) was treated in exactly the same way except for HBO. In the test treatment group, 16 patients were healed, and the remaining 2 showed no improvement and later underwent amputation. The number of HBO treatments required for healing was significantly related to the size of gangrenous lesions. In the non-HBO-treated group, only 1 patient improved, 5 of 10 showed no change, and 4 of 10 worsened until leg amputation was unavoidable. Comparison of the two groups by chi 2-test revealed a highly significant difference ($P = .001$). In practical terms, HBO treatment drastically reduced leg amputations in patients so treated in the last 3 yr compared with earlier and current figures for patients not receiving HBO treatment.

Giudiceandrea, F. et al. "Diabetic foot. Physiopathology, clinical aspects, and recent therapeutic approaches." *Minerva Chir*, 2000, 55(4): 261-71. (article in Italian)

Diabetic foot is a complication of diabetes mellitus occurring in 15% of patients that is of specific surgical interest. Over the past few years, preventive measures and the use of new therapeutic resources has reduced the number of patients undergoing demolitive surgery. The authors present a concise but at the same time sufficiently detailed picture of modern knowledge of the physiopathology, clinical aspects and current therapeutic guidelines for diabetic foot. In particular, they analyse the validity of various forms of complementary treatment to surgery, including techniques to stimulate tissue repair processes, hyperbaric oxygen therapy and laser therapy, and they underline the importance of using a multidisciplinary approach to this pathology.

Bakker, K. et al. "New developments in the treatment of diabetic foot ulcers." *Ned Tijdschr Geneeskd* 2000, 144(9): 409-12. (article in Dutch)

Diabetic foot ulcers are frequent: 12,000 Dutch diabetes patients have such an ulcer. The ulcers have a multifactorial aetiology: polyneuropathy, biomechanical stress, infection, deficient footwear and to a less extent ischaemia are the major factors. The principles of ulcer treatment are relief of pressure, restoration of skin perfusion, treatment of infection, intensive wound care, metabolic control, treatment of comorbidity, and instruction of the patient. Wound healing is slow. The impaired wound healing is probably caused by deficiencies in local growth factors, changes in the extracellular matrix, diminished fibroblast function, decreased antimicrobial activity of leukocytes and disturbances in the macro- and microcirculation. In recent years several new treatment strategies have been developed to stimulate wound healing in diabetic foot ulcers. These (partly experimental) treatments include: topical growth factors, extracellular matrix products, bioengineered human skin, granulocyte colony stimulating factor and hyperbaric oxygen therapy. In particular recombinant human platelet derived growth factor (becaplermin) has proved to be clinically effective in chronic neuropathic foot ulcer and has been approved in the Netherlands.

Eron, L. J. "Targeting lurking pathogens in acute traumatic and chronic wounds." *J Emerg Med*, 1999, 17(1): 189-95.

The appropriate antimicrobial treatment for skin and soft tissue following acute trauma is determined by the mechanism of injury, time from injury to treatment, environmental wound contamination, pathogenicity of colonizing bacteria, and patient-specific issues. These factors can be used to predict the risk of secondary infection of wounds. Although common skin pathogens (such as *Staphylococcus aureus* and group A *Streptococcus*) cause most secondary wound infections, antibiotic therapy sometimes must be directed against unusual pathogens that are associated with atypical wounds, such as animal bites (amoxicillin with clavulanate for *Pasteurella multocida*) and plantar puncture wounds (ciprofloxacin for *Pseudomonas aeruginosa*). This customized treatment approach is also appropriate for chronic wounds, such as pressure and diabetic foot ulcers. Areas of investigation in wound management include the use of growth factors and hyperbaric oxygen.

Levin, M.E. "Prevention and treatment of diabetic foot wounds." *J Wound Ostomy Continence Nurs*, 1998, 25(3): 129-46.

The diabetic foot ulcer is one of the most common and devastating complications of diabetes mellitus. These ulcers account for most of the hospital admissions for patients with diabetes, and they represent a common precursor for amputation. When a diabetic foot ulcer becomes infected, gangrene and amputation can follow in rapid succession. Recent reviews concerning diabetic foot lesions and amputations have stressed the magnitude and importance of aggressive management. This management is complicated, and typically requires radical debridement, appropriate antibiotics, non-weight-bearing, and vascular surgery when indicated. A variety of adjunctive therapy can be helpful, including hyperbaric oxygen and topical growth factors.