A Monograph for Health Care Providers

Innovative Wound Care Specialists

The Diabetic Foot and Hyperbaric Oxygen Therapy

The diabetic foot ulcer is a result of multi-organ system dysfunction linked to hypoglycemia and its myriad of downstream effects. On the cellular level, diabetes mellitus affects certain cell subtypes that are unable to downregulate glucose transport into the cell in the face of hyperglycemia. Hyperglycemia causes a chronic increase in superoxide, which suppresses endothelial nitric oxide synthase (eNOS), a potent vasodilator, resulting in vasoconstriction and peripheral hypoxia. Hyperglycemia also leads to thickening of capillary basement membranes, reducing oxygen diffusion from the capillary to surrounding tissue, decreased bone marrow eNOS activity required for stem progenitor cell (SPC) mobilization, and repression of hypoxia-inducible factor one (HIF-1) production. Autonomic neuropathy reduces the diabetic's ability to mount a hyperemic response to injury, leading to a functional ischemia on top of anatomical ischemia. Neuropathy in all of its forms (sensory, motor, and autonomic) is responsible for the majority of the pathology of the diabetic foot. Clawfoot deformity, hammertoes, and Charcot arthropathy predispose the diabetic patient to initial ulceration. Dermatologic changes from autonomic neuropathy leads to dry, cracking, callused skin which is a gateway for bacterial invasion. Increased pressure from callus, paired with sensory neuropathy, is a dangerous combination of symptoms initiating the diabetic foot ulcer.

Hyperbaric oxygen delivers oxygen at greater than atmospheric pressure, resulting in increased arterial oxygen tensions in the plasma and drives oxygen into hypoxic tissue. This results in neovascularization and collagen deposition at the site of hypoxic tissue. Local tissue microangiopathy and host SPC mobilization dysfunction are present in diabetics with non-healing ulcers. HBO directly addresses these deficiencies by reversing the hypoxia caused by diabetes mellitus and stimulating growth factors including vascular endothelial growth factor (VEGF), basic fibroblast growth factor (FGF), transforming growth factor beta-1 (TGF-ß), nitric oxide (NO), and platelet derived growth factor (PDGF). HBO systemically stimulates mobilization of endothelial stem progenitor cells through endothelial nitric oxide synthase, increasing nitric oxide without the need for cytokine + receptor complex. Along with the effects of HIF-1a, this bypasses the missing step in diabetics, resulting in elevated levels of serum SPCs (CD34+ and CD45-dim) and improved homing to the site of injury. The recruitment of SPCs *de novo* neovasculogenesis, increased collagen formation, improved granulation tissue formation, and improved healing.

References

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