INTEGRATIVE MEDICINE

Diving In: Hyperbaric Oxygen Therapy in Veterinary Medicine

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Hyperbaric oxygen therapy (HBOT) is the therapeutic administration of oxygen administered at a pressure that exceeds that at sea level (1 atmosphere absolute [ATA]). The treatment pressure can vary but commonly ranges from 1 to 3 ATA to drive a significant increase in arterial oxygen tension and thereby induce a number of physiologic, cellular, and biochemical effects.[1] This article provides a brief overview of the mechanism of action, veterinary applications and evidence, and general treatment mechanics associated with HBOT administration.

MECHANISM OF ACTION

In a healthy patient breathing "room air" at sea level (21% oxygen at 1 ATA), hemoglobin saturation is more than 97% and the plasma oxygen concentration is 0.3 mL/dL.[2] The solubility of a gas is proportional to its pressure, as defined in Henry's law of gas behavior; therefore, as the atmospheric pressure of oxygen rises, so does the plasma oxygen concentration. This concentration jumps fivefold with the administration of 100% oxygen alone without pressure changes, and tenfold when the oxygen is administered at 2 ATA. Increasing the pressure to 3 ATA results in a plasma oxygen concentration of 6 mL/dL, which is more than high enough to meet all resting cellular requirements without the need for hemoglobin-bound oxygen. This extraordinary circumstance proves particularly useful in human patients with exceptional blood loss when suitable blood is not available or transfusion is refused for religious reasons.[3]

Another benefit to increasing plasma oxygen concentration is that oxygen dissolved in the plasma can diffuse up to 4 times further into microcirculation than oxygen transported by red blood cells according to Fick's law, which identifies an increased gas diffusion distance with increasing partial pressure differences.[4] This is particularly crucial in damaged, edematous tissue in which the capillaries are pushed farther apart and are unable to deliver the oxygen necessary for cellular respiration and repair.

By facilitating tissue hyperoxia, HBOT exerts beneficial anti-inflammatory, immunomodulatory, antimicrobial, angiogenic, and barometric effects, which collectively contribute to its myriad clinical applications in veterinary medicine.

CLINICAL APPLICATIONS AND EVIDENCE

Indications for HBOT in human medicine are varied. The most widely accepted and covered by Medicare reimbursement are carbon monoxide toxicity,

decompression sickness, and chronic refractory infections and wounds.[5] Some veterinary indications for which evidence exists include the optimization of tissue repair, neurologic conditions, inflammatory and autoimmune disorders, and cancer.[7]

Tissue Repair

The postulated mechanism of HBOT in enhanced healing is largely related to improved oxygenation and perfusion, as well as increased phagocytosis of bacteria, antimicrobial activity, and angiogenesis.[6,8-10] A number of experimental animal models and clinical studies have shown improvements in healing with HBOT in grafts and flaps, burns, necrotizing fasciitis, bone, cartilage, and muscle.[11-17] In the author's experience, complicated skin wounds—including those that result from envenomation or a fungal, oomycotic, or bacterial infection—are among the more commonly referred indications; in these cases, HBOT is used for attenuation of inflammation and potentiation of concurrent pharmacologic intervention.

Neurologic Applications

The neuroprotective utilization of HBOT is gaining significant clinical and research attention. Based on the expanding favorable evidence in laboratory animals, human clinical trials are under way at Qinghai University in China and Medical University at Graz in Austria using HBOT as an adjunctive treatment for acute spinal cord injury. The suggested mechanisms of HBOT's neuroprotective effects include reduction of oxidative stress, promotion of angiogenesis, modulation of inflammation, and reduction of edema in the central nervous system.[18] Beyond spinal cord injury, HBOT has also been shown to be effective in the management of neuropathic pain, peripheral nerve regeneration, and traumatic and vascular brain injury, as well as some early research into delaying motor neuron disease onset.[19-26]

Modulation of Inflammation and Immune Function

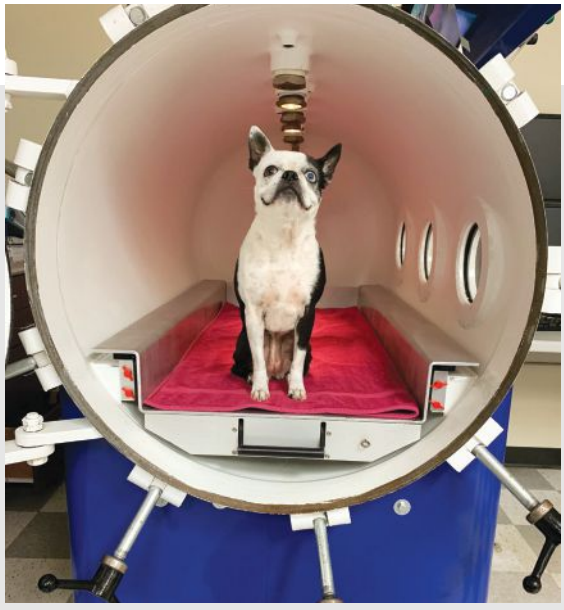
HBOT's ability to modulate neutrophil and macrophage function enables it to elicit positive effects for a number of internal medical conditions, particularly immune-mediated diseases and those characterized by inflammation. Besides ameliorating tissue hypoxia, which is a key trigger of ongoing inflammation, high oxygen concentrations interfere with polymorphonuclear leukocyte adhesion and stimulate the production of endogenous antioxidants. Emerging literature suggests that HBOT is useful in adjunctively managing allergic rhinitis, inflammatory bowel disease, pancreatitis, and inflammatory joint conditions such as rheumatoid and Lyme arthritis.[27-31]

Neoplasia

Given that HBOT promotes angiogenesis and increases tissue oxygen concentration, there is concern that treatment could promote tumor growth in a patient with known neoplastic disease. At present, neoplasia is considered an acceptable indication for HBOT in humans in China and Japan.[32] A 2012 literature review concluded that the use of HBOT in malignancy is safe,[33] and there are data supporting its potential tumor-inhibitory effects in certain cancer subtypes.[34,35] More recent evidence suggests that adjunctive HBOT may enhance the cytostatic effect of certain chemotherapeutic agents and increase the effectiveness of radiation therapy.[36]

MECHANICS AND CONSIDERATIONS

Total treatment times, frequency, and pressure used vary in the literature and between practitioners. The author commonly employs a standard time of about 1.25 hours, including gradual pressurization and



Canine patient in the hyperbaric oxygen chamber preparing for treatment.

depressurization, at 2 ATA; however, specific treatment must be based on the patient's condition.

The risks of HBOT in veterinary patients are minimal with appropriate precautions and operation.[6,35] Patients should be prepared for the chamber by removing or covering materials that are inflammable or pose a risk of spark (e.g., exposed metal implants, synthetic bandages, petroleum-based drugs) and supervised for the entire session by a trained clinician or technician. Gradual pressure changes should be used and patients carefully screened for contraindicated pre-existing conditions (pulmonary bullae, pneumothorax) to minimize the risk of barotrauma.

Oxygen toxicity caused by increased reactive oxygen species manifests as a grand mal seizure and is addressed with monitoring and gradual decompression. The risk is pressure-dependent and low at 2 ATA (<0.4%; unpublished data based on more than 2200 treatment sessions at the author's institution), and there are no reports of a subsequent epileptic predisposition. Patient hyperthermia can increase brain oxygen consumption;[36] hypothetically, pretreatment sedation with medications that cause peripheral vasoconstriction may also have this effect. Based on clinical experience, the author avoids treating patients with a body temperature above 103.5°F as well as using α2-agonists for sedation in HBOT patients.

Given HBOT's safety and wide variety of conditions that could benefit, the major hurdles in clinical veterinary practice are cost, accessibility, and the lack of veterinary clinical trials to guide its evidence-based use for a variety of conditions. Although the modality has seen increased use in the profession,[37] only a few clinics, if any, offer it in each state and the average cost of a treatment session is $100 to $200. The Veterinary Hyperbaric Medicine Society (**vhbot.org**) and Hyperbaric Veterinary Medicine (**hvmed.com**) websites include U.S. location maps of veterinary chambers as a resource for owners and veterinarians seeking referral. Given the possible limitations, it is important to discuss the patient's ongoing HBOT plan in addition to setting realistic goals at the outset.

CONCLUSION

Based on the favorable human and laboratory animal data, HBOT in veterinary medicine is continually expanding. Prospective veterinary clinical research will be key in identifying optimal treatment protocols and clinical implications, as well as further substantiating the modality's utility as an adjunctive or primary treatment option. **TVP**

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