Hyperbaric oxygen therapy in South Africa

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What is HBO and how does it work?

Hyperbaric oxygen therapy (HBO) is the use of 100% oxygen, breathed under pressure and delivered to tissues by the circulation, to achieve a therapeutic benefit. Under hyperbaric conditions oxygen attains medicinal properties. Time and pressure of the exposure provide the specific "dose" and "tissue level" required to achieve the effect. HBO provides a pressure-related increase in plasma-borne oxygen. This increases total blood oxygen content by 20–25%[1] and markedly improves free (i.e. dissolved) oxygen delivery to tissues, increasing the diffusion distance from the capillaries into tissues several fold.[2] At these increased tissue levels, oxygen initiates a series of distinct physiological and pharmacological effects.

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The therapeutic range for oxygen therapy is an inspired oxygen partial pressure (PaO_2) of 1.5 to 3 times atmospheric pressure (ATA). Higher oxygen pressures (> 3 ATA) are too toxic for clinical use. There are five groups of therapeutic mechanisms attributed to hyperbaric oxygen use:

- Hyperoxygenation
- Vasoconstriction
- Neovascularisation (angiogenesis)
- Altered cellular function
- Pressure and gas gradients

1. Hyperoxygenation

Even under normal air-breathing conditions haemoglobin is almost fully saturated with oxygen. The small, but biologically active amount of dissolved oxygen in the plasma can only be increased by increasing inspired oxygen pressure. Under standard treatment pressure (2.5 ATA) the delivery of dissolved oxygen to body tissues is increased from 0.3 mL O_2 per 100mL of blood to 5.5 mL O_2 per 100 mL blood. The latter is enough to sustain life without haemoglobin.[3] Arterial blood gas values exceed 2000 mmHg (263 kPa) PaO_2 under these conditions.[4] HBO not only adds a greater amount of "free" oxygen to the blood, but also establishes steep diffusion gradients from capillaries, driving oxygen further into tissues.[5] Oxygen must be transported by the circulation from the lungs to the tissues.[6] Hyperbaric oxygen therapy does not presume absorption of oxygen through the skin.

2. Vasoconstriction

HBO causes pre-capillary vasoconstriction in non-ischaemic tissues, leaving the capillaries in ischaemic areas unaffected.[7] Unlike the application of ice, HBO produces hyperoxygenation while lowering capillary hydrostatic pressure and thereby reducing ongoing fluid extravasation. The end result is a significant reduction in oedema.[8] This has important implications, particularly in trauma and burns.

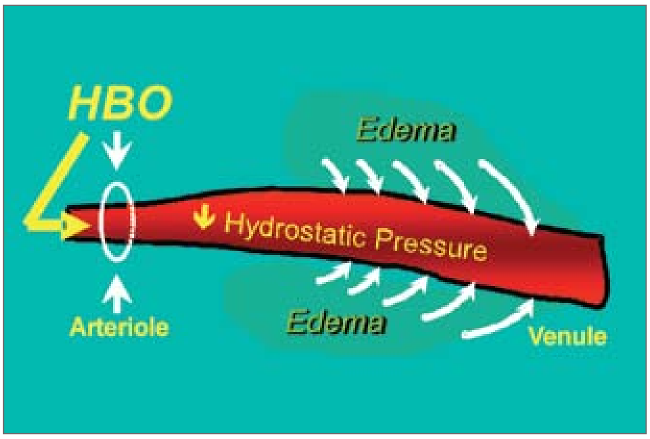

Figure 1: HBO causes vasoconstriction in non-ischaemic tissues. This lowers hydrostatic pressure in capillaries leading to reabsorption of oedema.

3. Neovascularisation (angiogenesis)

A steep oxygen gradient is a fundamental stimulus to angiogenesis.[9] In some abnormal tissues (irradiated, diabetes, etc.), the gradient is so shallow while breathing air or even 100% oxygen at 1 ATA that the stimulus for angiogenesis remains small. Under hyperbaric conditions, the oxygen gradient is raised sufficiently to stimulate angiogenesis in these tissues while normal tissues are unaffected.[9,10] The microvascular revascularisation is long-lasting and affords durable results.[10]

4. Altered cell function

HBO affects all cells involved in healing: normal tissue oxygen levels are necessary for healing to occur. HBO therapy, even once a day, improves healing in chronic ulcers.[11] Intermittent periods of hyperoxia result in extended periods of normal cell function. Periods of tissue hypoxia between treatments encourage the production of cytokines,[12] which stimulate healing, while cellular response to cytokines is again oxygen dependent.[13] This conflicting need for both hypoxia and normoxia is called the "oxygen paradox". Leukocyte defense mechanisms are largely oxygen dependent.[14] Anaerobic phagocytosis can occur, but large amounts of oxygen are necessary for bactericidal activity.[15] Work by Knighton and Hunt has demonstrated that even breathing 45% oxygen is as effective as ampicillin in controlling certain aerobic bacterial inoculations, by stimulating leukocyte function.[16] In addition HBO also enhances the efficacy of certain antibiotics (e.g. penicillins, aminoglycocides, vancomycin, and clindamycin) without increasing their toxicity.[17] Fibroblasts cannot produce collagen anaerobically and the tensile strength of collagen (cross-linking) is also oxygen dependent.[18] Leukocyte adherence to venules is an important pathophysiological mechanism in ischaemia-reperfusion complications that leads to the no-reflow phenomenon. HBO inhibits leukocyte endothelial adherence to venules for a period of 12 hours after one treatment without impairing leukocyte response to infection.[19] In the case of fractures, tissue hypoxia may result in cartilage formation instead of bone, predisposing to delayed or non-union.[20] HBO, if applied early, appears to preferentially stimulate bone formation.[21]

5. Pressure and gas gradients

In arterial gas embolism or decompression sickness, as seen in divers, an increase in ambient pressure can reduce the diameter of inert gas bubbles, lessening their obstructive effects.[22] By breathing oxygen at pressure, the steep gas gradients promote inert gas elimination, ischaemic or hypoxic complications are reduced, and cerebral or spinal oedema is reduced by selective vasoconstriction.[23]

How is HBO provided?

To provide the required environment of increased pressure, HBO therapy is administered in pressure vessels called "hyperbaric chambers". Multiperson chambers are large metal cylinders pressurised with air. Patients breathe oxygen via an oronasal mask or head tent in the chamber. This allows patients to have "air breaks" during treatments, breathing ambient air, thus avoiding cumulative oxygen toxicity.

Single person chambers are small, transparent tubes that are pressurised with oxygen. This avoids the complex gas and oxygen delivery systems required in multiplace chambers. However, by using pure oxygen inside the chamber, there is a greater risk of fire and stringent precautionary measures must be adhered to. Air breaks are provided by a demand valve and oronasal mask. Although no physical patient contact is possible during therapy, invasive and non-invasive monitoring, intravenous infusion, drug administration and even ventilation can be performed safely and effectively.

The use of oxygen under pressure has been likened to it acting as a drug, with implicit factors such as indications, dose, length of use, effectiveness, contraindications and complications.[24]

Which conditions are treatable with HBO

The Southern African Undersea and Hyperbaric Medical Association (SAUHMA) follows the recommendations of the United States based Undersea and Hyperbaric Medical Society (UHMS) with regard to appropriate and ethical indications for the administration of HBO. UHMS is an international peer review and scientific authority of more that 2 500 scientists and clinicians which standardizes therapy

Figure 2: Multiplace HBO chamber

Figure 3: Monoplace HBO chamber

and validates indications with the most up to date literature. UHMS recognizes 13 evidence-based indications for HBO at the present time.[25] These are:

1. Arterial gas embolism
2. Decompression sickness
3. Gas gangrene
4. Carbon monoxide poisoning and smoke inhalation
5. Necrotising soft tissue infections
6. Acute traumatic ischaemias (e.g. crush injuries, compartment syndromes, etc)
7. Compromised grafts and flaps
8. Radiation tissue damage (e.g. osteoradionecrosis [ORN])
9. Chronic refractory osteomyelitis
10. Acute thermal burns
11. Selected problem wounds
12. Acute blood loss anaemia
13. Cerebral abscess

Which protocols are used and what outcomes may be anticipated?

The most common and important indications for HBO are chronic radiation damage and diabetic infections unresponsive to conventional care. No data is presented on decompression illness, arterial gas embolism, carbon monoxide poisoning, exceptional blood loss anaemia and cerebral abscess, as these conditions fall outside the area of interest for wound care practitioners. This leaves the following eight indications for discussion:

1. Gas gangrene

Figure 4: Patient with gas gangrene of the leg. Note the bronze discolouration of the skin (similar to a Betadine stain)

This is the classic indication for hyperbaric oxygen in combination with conservative surgery and antibiotics. When used early (i.e. within 24 hours of diagnosis), and before ablative surgery, HBO reduces morbidity and mortality significantly.[26] Tissue and limbs can often be spared, and spread to the trunk, which carries a high mortality, may be avoided. HBO terminates the production of alpha toxin, the lethal element of gas gangrene, within minutes and prevents ongoing liquefaction of tissue.[27] The need for extensive debridement or amputation is thereby significantly reduced. Following HBO, along with resuscitation and antibiotics, patients are in a better state for surgery, and, important for the surgeon, the demarcation between viable and non-viable tissue is more distinct, thereby avoiding over-excision of tissue in the initial stages.[26, 27]

2. Crush Injuries and acute traumatic ischaemia

Crush injuries, compartment syndromes, thermal burns, compromised flaps and tissue replantations share a number of pathophysiological processes that benefit from adjunctive HBO. In all these injuries a gradient of injury exists, ranging from viable to non-viable tissue. Secondary pathophysiological events, e.g. hypoxia, ischaemia, oedema, reperfusion injury, and sepsis shift the gradient towards further tissue loss. Hyperbaric oxygen, if introduced early, improves outcome, by reducing the effects of ischaemia and hypoxia and reducing oedema and necrosis. This has been confirmed clinically in a prospective, randomised, double blinded and placebo controlled trial by Bouachour et al.[28] Here HBO was able to limit the number of repetitive surgical procedures in relation to severe limb trauma. Based on their findings, patients over 40 years of age with Gustillo grade III soft tissue injuries should receive adjunctive HBO if available.

3. Selected wound care

"Problem wound" implies wounds which fail to respond adequately and timeously to conventional treatment. This includes certain arterial insufficiency ulcers, venous insufficiency ulcers, diabetic wounds and infections, chronic radiation necrosis and decubitus ulcers. Of all the factors involved in healing, oxygen is the most important variable. Tissue hypoxia predisposes to decreased fibroblast proliferation, poor collagen production and cross-linking, impaired leucocyte function and decreased angiogenesis (granulation tissue formation). HBO restores a favourable milieu in which healing and antibacterial mechanisms again become functional or are enhanced. While bypass surgery or angioplasty are more definitive in treating arterial insufficiency ulcers, certain subgroups benefit from adjunctive HBO. These include patients whose wounds do not respond adequately after successful bypass surgery (e.g. diabetics); patients who are inoperable or unsuitable for vascular surgery but are shown to have adequate transcutaneous oximetry values;[29] patients with residual or refractory soft tissue or bone infection; and patients with doubtful long term graft patency who require expedient wound healing. In these cases HBO is often the only remaining way to achieve a good outcome. Transcutaneous oximetry provides a specific and sensitive way of measuring actual tissue oxygenation and thus provides a reliable means of patient selection and prediction of healing in the abovementioned cases.[30,31]

Figure 5: Transcutaneous oximeter (Radiometer – Copenhagen) with placement of the Clark electrode on the peri-wound area

HBO is effective in reducing the number of major amputations in infected diabetic foot wounds and gangrene.[32,33,34,35,36] Patients with Wagner grades III (deep infection) and IV (fore-foot gangrene) foot infections derive the greatest benefit. Oriani et al confirmed a significant reduction in below-knee amputation rates in HBO treated patients (5% vs 33%) compared to matched controls.[32] Similarly Cianci et al achieved 85% long term (average 54 months) limb salvage rates.[33] For HBO to be of value, transcutaneous oximetry values should confirm adequate oxygen delivery to the affected areas (450 mm Hg pO2 at 2.5 ATA).[36,37] For best results, HBO should be combined early in the management of these patients.

Venous insufficiency ulcers rarely require HBO. Attention to the basic pathology indicates appropriate therapy, including surgery if necessary, to the venous system, along with compression bandaging. However HBO, as a stimulus for granulation tissue formation, is of value in the preparation and support of grafting of extensive or intractable ulcers.[11] Decubitus ulcers are primarily managed with good wound care. However HBO should be considered in cases with concomitant osteomyelitis, progressive necrosis or reconstruction problems.[25]

4. Necrotising soft tissue infections

As an adjunct to surgical debridement and systemic antibiotics, HBO directly inhibits anaerobic bacterial growth and indirectly improves the body's response to aerobic infections by potentiating white cell bacterial killing.[38] The principle treatment remains surgical debridement and antibiotics, but HBO is of use in high risk (e.g. perineal and truncal infections) or poorly responding patients. Riseman and Zamboni obtained a mortality reduction from 66% to 23% in such cases, with considerably less debridement required.[39] Hollabaugh, in a recent study on Fournier's gangrene, demonstrated a nine-fold reduction in mortality in matched, randomised patients.[40] If the progression of the disease is not arrested with adequate surgery and antibiotics within 48 hours, patients should be referred for HBO if possible.

5. Refractory osteomyelitis

Chronic osteomyelitis is considered to be refractory when it has persisted or has recurred after appropriate interventions. These normally consist of surgical debridement and a prolonged course of organism-specific antibiotics. Mader, one of the authors of the international Cierny-Mader classification of chronic osteomyelitis, recommends that HBO be added to standard treatment regimens for localised and diffuse osteomyelitis in compromised hosts, e.g. diabetic, elderly, chronically hypoxic, malnourished patients or smokers.[41,42] Only HBO is able to increase medullary bone oxygen tensions, thereby improving leukocyte bactericidal activity, potentiating antimicrobials without increasing their toxicity or side-effects, increasing collagen production and angiogenesis, and improving osteoclast function with subsequent removal of necrotic bone.[43,44] The high morbidity, mortality and limited surgical options for managing malignant otitis externa as well as osteomyelitis of the sternum, cranium and vertebrae, justify the early inclusion of HBO in their management.[25]

6. Radionecrosis

Radiation produces a dose-related, gradual but progressive obliterative endartritis and cellular dysfunction, leading to hypoxic, hypovascular and hypocellular tissue.[10] Such tissues are vulnerable to trauma and unable to heal due to an imbalance between oxygen supply and demand. This results in a non-healing wound, in which the metabolic demands for healing and homeostasis exceed the oxygen and vascular supply.[10] HBO has the unique ability to reverse some of the cellular changes and restore microvascular density to within 75 to 85% of normal.[10,45] This restores the tissue's ability to heal and affords surgical and reconstructive options not otherwise available or reliable. In patients at risk for developing mandibular ORN, or those with established ORN, HBO is of significant value when it is provided before surgery is undertaken.[46,10] Previous treatment failures reported in early South African literature, were the result of inadequate surgery following preparatory HBO.[47] HBO alone cannot resolve established ORN without subsequent sequestrectomy to bleeding bone.

HBO is also of value in the prevention and treatment of soft tissue radionecrosis and is recommended pre and post-operatively in relation to elective surgery in irradiated tissues.[48] In addition, HBO has been shown to be an effective primary treatment for refractory haemorrhagic radiation cystitis.[49]

7. Compromised skin grafts, flaps and reimplantations

Lack of granulation tissue prevents healing and limits plastic surgical options for reconstruction. HBO, by creating steep oxygen gradients, is a powerful stimulus for angiogenesis and fibroplasia.[9,10,12,50] HBO may be indicated when granulation tissue is lacking, either to achieve healing by secondary intention or in preparation for grafting.[11] Early application of HBO is associated with improved tissue salvage in compromised flaps.[51] HBO can improve flap survival and extend the margins of viable tissue while reducing the risk of sepsis.[13,14,15] While revision of vascular anastomoses is required for inflow obstruction, HBO is able to attenuate the ischaemia-reperfusion process that would follow reflow. Flap mottling after surgery is therefore an important emergent indication for HBO.[52] Similarly, in limb or tissue loss followed by reimplantation, HBO attenuates ischaemia-reperfusion, supports the avulsed or degloved tissue after reattachment, and stimulates angiogenesis and healing.[53]

8. Thermal burns

HBO in burns has the ability to maintain microvascular integrity, reduce local and systemic edema and minimise propagation of the burn into adjacent and subjacent tissues.[54] Mortality, hospital stay and graft requirements are reduced.5[5,56] Epithelialisation is also promoted, thereby reducing the incidence of contractures as a time-course related complication.[56] When applied early, HBO appears to prevent partial thickness burns from becoming full thickness.[57]

HBO is not a substitute for established burn care but is a useful adjunct if applied early. Out of facility transfers are not indicated, but patients with 20-80% burns or burns affecting vital areas should be considered for HBO within the first 24 hours if this is available in-house.[58] Approximately 31% of burn units in the USA routinely use HBO as part of their treatment regimens. Standard resuscitation and burn care must be continued in the hyperbaric environment.[58]

How are patients selected for hyperbaric oxygen therapy

For HBO to be successful, the pathophysiology of the condition should match the pharmacological effects of the treatment. This is true for the thirteen recognised indications for HBO. Once a patient is referred they are assessed clinically by a hyperbaric team which usually consists of a hyperbaric physician with either a hyperbaric nurse or a hyperbaric technician. Should the clinical assessment show that HBO will be of value, patients will commence treatment after signing of a fully informed consent form, understanding all possible dangers of this modality.

Dangers, side-effects and special precautions

The most common problem is barotrauma of the middle ear. Patients are taught auto-inflation techniques and sometimes decongestants are used. If necessary, tympanostomy tubes (i.e. grommets) can be inserted. In emergency treatments in unconscious patients, myringotomy is performed. Prolonged exposure to high-pressure oxygen can cause two potentially serious side-effects: seizures and pulmonary oxygen toxicity. Both of these are very rare; safe therapeutic exposure limits have been developed over time. Moreover, oxygen toxicity seizures are not inherently harmful but should be avoided through risk factor identification, the proactive use of air breaks and vigilance.[61] Careful history is taken and prophylactic treatment is given in those with specific risk factors, e.g. those with history of seizures, fever, acidosis, or low blood sugar.

Claustrophobia may be a problem with some patients, and it is reduced by having an attendant inside the chamber (multiplace) or beside it (monoplace). Mild sedatives are sometimes indicated.

Fire risk precautions are mandatory, with unsafe objects not being admitted. Patients are expected to stop smoking for the entire course of HBO therapy. The vasoconstrictive effects of nicotine may interfere with angiogenesis, and raised carbon monoxide levels reduce the full benefit of oxygenation.

Special care should be taken with the selection of dressing materials during the HBO treatment period. Management of fire risk is most important and this eliminates petrolatum and Velcro-containing devices.[62] Most dressings are safe, including water and cotton-based dressings, poly-urethane foams, wet alginates, poly-urethane films, cotton crepe bandages, and paper and plastic strapping products.

The effects of HBO include prompt demarcation, changes in exudate, and increased exudate and granulation formation.[5,7,9,28] Accordingly, caution is required when attributing therapeutic effects to a particular dressing or recommending its use while patients are undergoing HBO therapy. Frequent evaluation of wound progress is necessary whilst receiving HBO therapy and long-term dressings (3–7 days) are inappropriate generally. In general it is wise to change wound dressings after HBO therapy as this practice is less disruptive to the HBO treatment schedules, and patients are less likely to have elevated pain and discomfort in the chamber due to the dressing change which might necessitate early termination of HBO treatment.

Contraindications to HBO

The only absolute contraindications are an untreated pneumothorax and certain anti-cancer drugs, i.e. doxorubicin, bleomycin and cis-platinum, as HBO significantly increases their cytotoxicity. Relative contra-indications include acute viral URTI's, sinusitis, bullous pulmonary disease, history of spontaneous pneumothorax and congenital spherocytosis. Consultation with a physician trained in hyperbaric medicine is important, both for evaluating the indication for HBO therapy and for addressing any possible contraindications.

The Southern African Undersea and Hyperbaric Medical Association (SAUHMA) policy on the clinical application of HBO

In order to provide clear guidelines for medical responsibility, to ensure competence and safety, and to establish a scientifically and financially viable basis for clinical HBO in South Africa, SAUHMA endorses four fundamental principles of HBO practice:

1. Clinical HBO should be provided in a hospital or a registered healthcare facility. Facilities currently in operation in South Africa can be found in Pretoria (Eugene Marais, Pretoria East hospitals), Johannesburg (Milpark Hospital), Durban (St Augustine's Hospital), Cape Town (Claremont hospital) and in Welkom (Welkom Medi-Clinic).
2. A qualified hyperbaric physician must be directly responsible for all aspects of use of a pressure vessel for medical purposes and, as such, must perform the following functions:
    - specifically prescribe HBO for each patient
    - determine if there are any risk factors or contraindications to clinical HBO
    - confirm the suitability of the chamber and oxygen delivery system for each patient
    - supervise the safe and competent operation of the chamber
    - and ensure patient and hyperbaric staff safety
3. A qualified hyperbaric physician should always be in attendance (defined as being immediately available at all times) during treatments to ensure the provisions of par 2 are met and to deal with any medical emergencies that may arise in the chamber.
4. An appointment of Medical Director should be made for each hyperbaric facility. The title represents the chief medical authority at a clinical hyperbaric facility. The Medical Director, in terms of the Occupational Safety Act, is also defined as the user of the equipment.

Conclusion

The past decade has seen a dramatic increase in the understanding of the pharmacological effects of oxygen administered in hyperbaric dosages with a growing evidence base that supports the efficacy and cost effectiveness of this modality.

In acute surgical disorders, HBO reduces morbidity and mortality. Treatments are few in number (7–12) with obvious and significant benefits, including fewer complications, fewer new surgical procedures, better functional outcomes and reduced hospital stay. In chronic refractory disorders and chronic non-healing wound situations, therapeutic options are limited and expensive. The value of HBO lies in improving their effectiveness.

HBO therapy, when applied ethically, properly and safely by a qualified hyperbaric physician, is a powerful and valuable adjunct, and surgeons and wound practitioners should be aware of its capability and potential to assist them in their practice.

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