

Hyperbaric Oxygen Therapy : Current Trends and Applications

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Abstract

Hyperbaric medicine is the fascinating use of barometric pressure for delivering increased oxygen dissolved in plasma to body tissues. Hyperbaric oxygen therapy (HOT) or hyperbaric oxygen (HBO) involves intermittent inhalation of 100% oxygen under a pressure exceeding that of the atmosphere, that is greater than 1 atmosphere absolute (ATA). Therapy is given in special therapeutic chambers which were earlier used primarily to treat illnesses of deep sea divers. There is recently a renewed interest in this field all over the world. Acute traumatic wounds, crush injuries, burns, gas gangrene and compartment syndrome are indications where addition of hyperbaric oxygen may be life and limb saving. Patients who are suffering with non-healing ulcers, decubitus ulcers (bed sores) and all late sequelae of radiation therapy are also benefited with HBO therapy. Acute hearing loss and many neurological illnesses are also now known to possibly benefit from hyperbaric oxygen therapy. This article aims to give a brief overview of the rationale, existing trends and applications of this therapy.

HYPERBARIC OXYGEN THERAPY DEFINITION

A mode of medical treatment in which the patient is entirely enclosed in a pressure chamber and breathes 100% oxygen at a pressure greater than 1 atmosphere absolute (ATA). (Committed on Hyperbaric Medicine, Undersea and Hyperbaric Medicine Society, 1976).

INTRODUCTION

The committee on hyperbaric medicine defines hyperbaric oxygen therapy as "A mode of medical treatment in which the patient is entirely enclosed in a pressure chamber and breathes 100% oxygen at a pressure greater than 1 atmosphere absolute (ATA)". ATA is the units of pressure and 1 ATA is equal to 760 mm of mercury or pressure at sea level.

Over the past 40 years hyperbaric oxygen therapy (HBO) has been recommended and used in a wide variety of medical conditions, often without adequate scientific validation of efficacy or safety. Consequently a high degree of medical scepticism had developed regarding its use.¹ Gabb and Robin in the "Chest" (1987) have highlighted the controversies

relating to HBO and have documented 132 past and present indications for HBO therapy.² Over the last two decades, animal studies, clinical trials have produced reasonable scientific evidence or well validated clinical experience. This has now produced a set of indications for which HBO is beneficial.³⁻⁵ In these conditions early referral is essential.

This has led to a renaissance of HBO, and hyperbaric facilities now form an important part of many hospitals all over the world. In 1996 there were 259 hyperbaric facilities in USA and there has been an annual increase in the number of hyperbaric centers and increase in patients at the rate of 15 and 620 respectively. The number of patients treated annually had increased from 896 in 1971 to 12,047 in 1989.^{5,6}

Experiences with HBO therapy in India have been published in select journals with limited circulation⁶⁻⁸ but there has been no interdisciplinary recognition of hyperbaric medicine at a national level. Thus though sufficient evidence supports use of HBO in certain defined conditions, many patients go untreated because of the physicians unfamiliarity with recent research of HBO as therapy.

PHYSIOLOGICAL BASIS

The usual arterial partial pressure of O₂ is 100 mm Hg, Hb is 95% saturated and 100 ml of blood carries 19 ml of O₂ in combination with Hb and 0.32 ml dissolved in plasma. If the inspired O₂ concentration is increased to 100%, O₂ combined with Hb can increase to a maximum of 20 ml when the Hb is 100% saturated and the amount of O₂ dissolved in

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plasma may increase to 2.09 ml. During HBO in addition to the Hb which is 100% saturated the amount of O₂ carried in solution will increase to 4.4 ml% at a pressure of 2 ATA to 6.8 ml % at 3 ATA which is almost sufficient to supply the resting total oxygen requirement of many tissues without a contribution from oxygen bound to hemoglobin⁹ Table 1. It is this increased oxygen in plasma which is responsible for most of the beneficial effects of hyperbaric oxygen.^{1,5}

Table 1 : Effect of pressure on arterial O₂

Total pressure ATA	Content of oxygen dissolved in plasma (vol %) MmHg	Breathing	
		Air	100% Oxygen
1	760	0.32	2.09
1.5	1140	0.61	3.26
2	1520	0.81	4.44
2.5	1900	1.06	5.62
3	2280	1.31	6.80
4	3040	1.80	O ₂ is not
5	3800	2.30	administered
6	4560	2.80	at pressures

above 3 ATA

All values assume arterial pO₂ = alveolar O₂ and that Hb oxygen capacity of blood is 20 vol %; From Bassett and Bennett (1977)

THERAPEUTIC EFFECTS OF HBO THERAPY

Mechanical

- Reduces bubble size

Hyperoxygenation

- Immune stimulation
- Neovascularisation
- ↑ Fibroblasts
- ↑ Osteoclasts
- Bactericidal
- Reduces edema

Increased pressure by its direct mechanical effect reduces bubble size in conditions such as air embolism and decompression sickness. Hyperoxygenation causes immune stimulation by restoring WBC function, enhanced phagocytic capabilities and neutrophil mediated killing of bacteria. HBO₂ accelerates neo-vascularization in hypoxic areas by augmentation of fibroblastic activity which further promotes capillary growth. HBO causes vasoconstriction in normal tissues but with an over all increased delivery of oxygen due to the hyperoxygenation. This is the basis of use in reducing edema and tissue swelling. In cerebral edema this helps to reduce edema while maintaining hyperoxia. It also reduces the adherence of white cells to capillary walls and is useful in acute brain and spinal cord injury. HBO therapy is bactericidal for anaerobic organisms such as *Clostridi welchii*, and also inhibits the growth of aerobic bacteria at pressures greater than 1.3 ATA. HBO at 2.5 ATA reduces the half-life of carboxyhaemoglobin from 4 to 5 hours in subjects

breathing room air to 20 minutes or less and is the treatment of choice in carbonmonoxide (CO), smoke inhalations and acute cyanide poisoning.^{1,3-5}

METHOD OF ADMINISTRATION

HBO therapy can be given in a "Monoplace chamber" in which a single patient is placed in a chamber which is then pressurised with 100% oxygen. Monoplace chambers are used to treat stable patients with chronic medical conditions. Or it can be given in a "Multiplace chamber" where many patients can be treated at the same time. These chambers are used for acute problems and also for critically ill patients who require a medical attendant within the chamber. These chambers are pressurised with compressed air and the patient breathes 100% oxygen at that pressure through special masks or oxygen hoods. The treatment control panel controls the therapy and monitors the patient during the treatment. Most therapy is given at 2 or 3 ATA and the average duration of therapy is 60 to 90 minutes. Number of therapies may vary from 3-5 for acute conditions to 50-60 for radiation illnesses.^{1,3,5}

TOXIC EFFECTS/COMPLICATIONS

When used in standard protocols of pressures that do not exceed 3 ATA (300 kPa) and the length of treatment is less than 120 minutes, hyperbaric oxygen therapy is safe. Commonest side effect is pain in the ears (aural barotrauma) as a result of inability to equalize pressure on both sides of the tympanic membrane due to a blocked eustachian tube. Pneumothorax and air embolism are more dangerous complications due to tear in pulmonary vasculature due pressure changes but are rare. Other rare side effects are pulmonary and neurological oxygen toxicity (Paul Bert effect), retrolental fibroplasia and cataracts.¹⁰ Transient reversible myopia can also rarely occur after prolonged HBO therapy. Fire is a realistic hazard but preventable by strict safety procedures and the patient may be claustrophobic.¹ Rare instances of hypersensitivity to O₂ are also documented.¹¹ Oxygen toxicity can be prevented in most tissues by using five minutes air in the chamber for every 30 minutes of oxygen. This allows antioxidants to deal with free oxygen radicals formed during the hyperoxic period.^{1,5} A suggested carcinogenic effect of hyperbaric oxygen has not been substantiated in extensive studies.¹²

INDICATIONS FOR HBO THERAPY

Universally accepted indications

These indications are supported with peer reviewed proof of efficacy and early referral is essential.^{1,3} (Table 2)

Non-healing ulcers, problem wounds, compromised skin grafts and flaps : These wounds have the underlying problem of tissue hypoxia, with oxygen tension usually below 20 mmHg, and therefore more prone to infection. The elevation of oxygen tension by hyperbaric oxygen therapy has powerful effects on wound dynamics, by both enhancing leukocyte bactericidal activity and promoting the fibroblast-collagen

Table 2 : Universally accepted indications for hyperbaric oxygen therapy

Acute conditions (where HBO therapy should be given earliest when combined to conventional treatment)

1. Non-healing ulcers, problem wounds, compromised skin grafts and flaps
2. Crush injury, compartment syndrome, and acute traumatic ischemias
3. Gas gangrene / clostridial infections
4. Necrotizing soft tissue infections (subcutaneous tissue, muscle, fascia)
5. Thermal burns
6. Exceptional blood loss (anaemia)
7. Intracranial abscess
8. Post-anoxic encephalopathy
9. Burns
10. Sudden deafness
11. Ocular ischemic pathology
12. Air or gas embolism*
13. Decompression sickness*
14. Carbon monoxide poisoning and smoke inhalation*

*Curative / primary line of treatment

Chronic conditions

1. Non-healing wounds / problem wounds (diabetic / venous etc.)
2. Radiation tissue damage
3. Skin grafts and flaps (compromised)
4. Chronic osteomyelitis (refractory)

support needed for neovascularization. In the United States problem wounds are the commonest indication for adjunctive hyperbaric oxygen therapy and include diabetic and other small vessel ischaemic foot ulcers, dehiscent amputation sites, nonhealing traumatic wounds and vascular insufficiency ulcers and post radiation ulcers. Several studies have shown improved healing and a lower incidence of amputation with 4-30 sessions.^{1,13,14} HBO improves both graft and flap survival compared with routine postoperative surgical care alone. The beneficial role of HBO therapy in plastic surgery and the role in occlusive arterial diseases in the extremities is well known.^{15,16}

Acute traumatic ischaemias ATI (Crush injury, compartment syndromes and others) : ATI occurs when an injury compromises circulation. This may place portions of the extremity or the entire extremity at risk of necrosis or amputation. Secondary complications such as infections, non-healing wounds and ununited fractures frequently develop. The immediate effect of HBO in ATI is enhanced oxygen at the tissue level, increased oxygen delivery per unit of blood flow and reduction of edema. Finally, HBO may mediate the effects of the reperfusion injury in ATIs especially in those where tissue ischaemia is severe and or prolonged (revascularisation, reimplantations, etc.). Surgery and antibiotics remains the corner stone of therapy. Addition of adjunctive HBO has shown to reduce significantly the morbidity and mortality associated with these injuries. Overall cost of management of these injuries is also reduced substantially.^{1,17}

Clostridial myonecrosis (Gas gangrene) : Clostridium

welchii cannot produce alpha-toxin when the patient undergoes HBO therapy. The organism is not killed by hyperbaric oxygen and alpha-toxin is not detoxified by HBO, however, with production shut-off, alpha-toxin is fixed in the tissues within 30 minutes. It also has antibiotic synergy with aminoglycosides, quinolones, sulpha and amphotericin B. A three-pronged approach consisting of HBO, surgery, and antibiotics is essential in treating gas gangrene.^{1,3,6,18}

Necrotizing soft tissue infections : Hyperbaric oxygen therapy may be used as an adjunct treatment of soft tissue infections with tissue necrosis, due to mixed aerobic and anaerobic organisms. Increasing tissue oxygen tension enhances white cell killing of bacteria, promotes inhibition of anaerobic organism growth, and increases the oxidation-reduction potential. These conditions include necrotizing cellulitis, progressive dermal gangrene, anaerobic streptococcal myositis, crepitant anaerobic cellulitis, and necrotizing fasciitis. Primary management remains adequate surgical debridement and antibiotic coverage. The high mortality and morbidity with these conditions warrant the addition of adjunctive hyperbaric oxygen therapy.^{1,2,5,19}

Treatment of late radiation tissue damage (osteoradionecrosis, radiation cystitis, enteritis, etc.) : In a patient who has had between 2,000 and 5,000 rads, there is a possibility that there may be difficulties with subsequent healing. Above 5,000 rads, healing of any subsequent surgical wound will be a definite problem. HBO therapy remains the keystone of treatment of radiation-induced illnesses. Recently, a clearer understanding of its pathophysiology has evolved. The basic physiology of this process is a progressive obliterative endarteritis with resultant hypoxia and tissue ischemia. Hyperbaric oxygen induces neovascularization of tissue and the tissue PO₂ rises to 81% of normal plus or minus 5% between 18 and 30 hyperbaric treatments. Successful surgery and grafting is possible with a PO₂ of 75% of normal. Controlled clinical experience has demonstrated a perioperative staging of hyperbaric oxygenation, termed the "Marx Protocol", has significantly reduced the incidence of post-operative infection, dehiscence, and healing delays. Two reports have specifically addressed the issue of hyperbaric oxygen's cost effectiveness in this disorder: Marx and colleagues and Dempsey *et al.*^{20,21} The authors concluded that in carefully selected patients, managed along algorithmic lines, the addition of hyperbaric oxygen therapy resulted in improved clinical outcomes while greatly reducing the overall cost. The effect of hyperbaric oxygen in radiation-induced bone necrosis, severe laryngeal necrosis, hemorrhagic radiation cystitis, colitis, scleral necrosis is also now well recognised. The cure rate for radionecrosis of the mandible now approaches 94% in those patients treated with hyperbaric oxygen.

Thermal Burns : The burn wound is a complex and dynamic pathophysiologic process characterized by a zone of coagulation, surrounded by a region of stasis, bounded by an area of hyperemia. A significant body of data clearly supports the efficacy of hyperbaric oxygen in the treatment of thermal

injury. Reduction in fluids, less conversion to full thickness injury, preservation of marginally viable tissue, improved microcirculation, reduction in edema, faster epithelialization, less inflammatory response, enhancement of PMN killing, preservation of tissue creatine phosphate, adenosine triphosphate and decreased wound lactate have all been reported with HBO. A significant reduction in hospital stay and cost of treatment with adjunctive hyperbaric oxygen therapy has been reported.²²

Carbon monoxide (CO) poisoning and smoke inhalation : It is recommended that patients with severe CO poisoning, those with neuropsychological changes and those in high risk group be treated with HBO irrespective of their COHb levels. HBO at 2.5 ATA reduces the half-life of carboxyhaemoglobin from 4 to 5 hours in subjects breathing room air to 20 minutes or less. Timely administration of HBO prevents neuronal injury, prevents delayed neuropsychological sequel and terminates the biochemical deterioration.^{1,3,5}

Osteomyelitis (Refractory) : Hyperbaric oxygen provides periodic elevation of bone and tissue oxygen tensions from hypoxic to normal or hyperoxic levels. This promotes angiogenesis, increased leukocyte killing, aminoglycoside transport across bacterial cell walls and osteoclast activity in removing necrotic bone.^{23,24}

Air or gas embolism (AGE)/Decompression sickness (DCS) : Air embolism can occur as a result of surgical procedures in a hospital setting. It can also occur in non-surgical patients due to over-expansion in a patient on respirator. Traumatic injuries such as penetrating injuries of the chest, blast injuries etc. can all lead to AGE. HBO is the primary treatment for AGE from any cause. DCS is caused by nitrogen bubble formation in the vascular system and in tissues sufficient to interfere with the function of an organ. The cause is rapid decompression during ascent from diving, flying or a hyperbaric/hypobaric chamber. HBO therapy should be begun during the acute episode and continued till symptoms clear.^{25,26}

Exceptional blood loss (Anaemia) : The patient has lost sufficient red cell mass to compromise respiratory requirements and will not receive transfusions because of medical or religious reasons. The intermittent use of hyperbaric oxygen therapy will supply enough oxygen to support the basic metabolic needs of the respective tissues of the body until red blood cells are restored.²⁷

Intracranial abscesses : HBO is recommended as an adjunctive therapy in abscesses in deep locations or multiple abscesses, in compromised hosts, in situations where surgery is contraindicated and in patients showing no response to conventional treatment. HBO therapy will be beneficial because of the anaerobic bacterial flora, reduction of edema, enhancement of host defence mechanism and the well known beneficial effect of HBO in concomitant skull osteomyelitis.³

Sudden deafness : It is well known that cochlear activity is very sensitive to constant supply of oxygen. Many studies have shown that the performance of the auditory system can

be improved by an intense application of oxygen during HBO therapy along with haemodilution and vasoactive drugs. Literature survey of 50 studies: 4109 patients treated within three months when conventional treatment failed concluded that HBO therapy is warranted within three months of above indications.²⁸

Post-anoxic encephalopathy : HBO increases oxygen supply to the ischemic neurons, reduces edemas and reverses the reduced flexibility of erythrocytes. HBO₂ should be administered as soon as possible and must be part of an intensive reanimation program.²⁹

Visual vascular pathology : HBO has been used in retinal arterial thrombosis (along with other measures) and has been shown to be effective if performed at the earliest in patients who can still tell the difference between light and dark. In retinal venous thrombosis it is beneficial in reducing vasogenic edema. It must be given as soon as possible and combined with other pharmacological measures.³⁰

INDICATIONS WITH PROMISE WHICH ARE PROMOTING RECENT INTEREST

Neurological indications : The rationale of use of hyperbaric oxygen in neurological indications is based on the finding in SPECT studies that around the central area of neuronal death is the penumbra: peri-infarct zone. This zone has hibernating/idling or sleeping neurons. Also what appears as gliosis (dead neurons) on CT scans may actually be viable tissue for years following the insult (confirmed with SPECT).²⁴ HBO delivers high oxygen to these "sleeping cells" and reactivates them. HBO increases oxygen supply to the ischemic neurons, reduces edema and reverses the reduced flexibility of erythrocytes. This is the basis of its use by some centres in acute stroke, post-traumatic brain injuries and cerebral palsy. These studies have shown improvement in these indications.³¹

Clinical trials and research areas : A number of areas are being explored to determine if hyperbaric oxygen might be of clinical benefit. Senility, stroke, and multiple sclerosis are all being investigated. Sports injuries, high altitude sickness, acute myocardial infarction, brain injury, malignancies, cognitive functions, migraine, glaucoma, fulminant hepatic failure are also being actively researched. Sickle cell crisis, spinal cord injury, closed head injury, purpura fulminans, actinomycosis, mesenteric thrombosis, central retinal artery occlusion, cystoid macular edema, Bell's palsy and leprosy are other areas being explored by workers in multicentric trials the world over. Other areas being addressed are designs of randomised clinical trials, placebo effect, Hawthorne effect, pharmacokinetics etc.^{3,32}

CONCLUSION

Hyperbaric medicine is poised at an exciting era of revival. The role of hyperbaric oxygen therapy is scientifically established in certain well defined conditions and the hyperbaric chamber is now an integral part of hospital

services. Doctors in all fields must familiarise themselves with recent evidence on this mode of therapy, so that their patients are not denied the gains of this modern treatment. Cost analysis have shown that the addition of hyperbaric oxygen to conventional treatment results in significant cost savings due to lesser stay in hospital and shorter course of illness.

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