Chronicles of Hyperbaric Oxygen Treatment

Where it stands today.

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Abstract

Hyperbaric oxygen therapy (HBOT) is a treatment procedure that involves breathing 100% O2 for a certain time and under a certain(high)pressure. HBOT is commonly administrated as a primary emergency treatment in certain acute pathologies or alternative therapy particularly in deep and chronic infections such as necrotizing fasciitis, osteomyelitis, chronic soft tissue infections, and infective endocarditis. for chronic long-term pathologies.The most important effects of hyperbaric oxygenation are the stimulation of fibroblast proliferation and differentiation, increased collagen formation and cross-linking, augmented neovascularization, and the stimulation of leukocyte microbial killing,induction of senolytic effects including increasing telomere length and clearance of senescent cells in the aging populations,stem cell mobilization,Stem Cell Proliferation,Neuroprotection,Assists tumor lytic effect by enhancing sensitivity of radio-chemotherapy by increasing oxygen tension within the hypoxic regions of the neoplastic tissue among multitudes of other health benefits, to name a few.

Keywords:hyperbaric, oxygen, wounds, infections,stem cells,tumor lysis.

1.INTRODUCTION

The Development of antibiotics has changed the landscape of many diseases since the more recent past times.Unfortunately, antibiotic efficacy is now largely being questioned due to the development of antibiotic resistant pathogens leading to diverse large scale mutations making an uprising of the superbugs,which are found to have been resistant to all of the available antibiotics today. (L.J. Piddock 2012). The ideation of bacteriophage therapy however is nor being practiced on a large clinical scale or is studied extensively.Bacterial infections play a critical role in the achievement of some advanced therapeutic procedures such as surgery, implant placement, transplantation and chemotherapy.Selection pressure from already restricted antimicrobial agents offers a competitive circumstance that results in a further increase of mutated resistant strains.So far antimicrobial-resistance challenge stands tall regardless of the chemical features or molecular mechanisms of the antibiotics.So as to manage the global antimicrobial resistance, on one hand it's advised to limit the usage and amounts of antibiotics,and on the other a robust strategy for reliable infection control policies is needed and the dire situation draws our attention more towards the alternative methods that can achieve at least some part of the need with clinical reliability and a reasonable side effect profile. Hyperbaric oxygen therapy (HBOT) is a treatment procedure that includes the breathing in of 100% pure O2 for a set period of time and under a certain high pressure for a number of

sessions particular to both the disease and the patient. Regarding the increase in antibiotic resistance frequency, the use of HBOT may be effective in the treatment of acute infections caused by antibiotic resistant pathogens as well as chronic wounds that present big clinical challenges over the burdenised immune system and repair mechanisms of the body especially in hospitalised clinical settings.

HBOT protocols and procedure:

Defined by the Undersea and Hyperbaric Medical Society (UHMS), HBOT is “an intervention in which an individual breathes near 100% oxygen intermittently while inside a hyperbaric chamber that is pressurised to greater than sea level pressure (1 atmosphere absolute, 1 ATA)”.As mentioned above,100% oxygen is given at a pressure higher than normal atmospheric pressure regarded as the 1 Atm, in a special monoplace or multiplace chamber with a minimum 1.4 atmosphere absolute (ATA) or higher so that the patient breathes in 100% pure oxygen in a pressurised environment either directly or by a head hood, mask or endotracheal tube depending upon the chamber settings. (Joe KS Leung, MHM (UNSW), FHKAM (Emergency Medicine)1; Rex PK Lam, MPH, FHKAM (Emergency Medicine)2018).

TABLE 1. Gas laws and their implications for hyperbaric oxygen therapy[3]

Gas law	Description	Implications
Boyle’s Law	At a constant temperature of a fixed mass of gas, the volume of a gas is inversely proportional to its absolute pressure.	It governs the change in the volume of gas bubbles and air space in the body during decompression and recompression, as well as air-filled components of therapeutic devices, such as endotracheal cuffs and pressure bag.
Gay-Lussac’s Law	At a constant volume, the absolute pressure of a given mass of gas is directly proportional to the absolute temperature.	In a fixed-volume chamber, the ambient temperature increases during compression and decreases during decompression.
Dalton’s Law	In a mixture of ideal gases, the total pressure is equal to the sum of the partial pressures of the component gases.	This is the basis for increased amount of dissolved gas in blood and tissue when the ambient pressure increases.
Henry’s Law	At a constant temperature, the amount of gas dissolved in a liquid is directly proportional to the partial pressure of that gas in equilibrium with that liquid.	—

BOX. Indications for hyperbaric oxygen therapy approved by the Undersea and Hyperbaric Medical Society[2]

1. Air or gas embolism
2. Arterial insufficiencies—central retinal artery occlusion and enhancement of healing of selected problem wounds
3. Carbon monoxide poisoning
4. Clostridial myonecrosis (gas gangrene)
5. Compromised grafts and flaps
6. Crush injuries and skeletal muscle compartment syndromes
7. Decompression sickness
8. Delayed radiation injuries
9. Idiopathic sudden sensorineural hearing loss
10. Intracranial abscess
11. Necrotising soft-tissue infections
12. Refractory osteomyelitis
13. Severe anaemia
14. Thermal burns

Indications for hyperbaric oxygen therapy approved by the Undersea and Hyperbaric Medical Society. (Neuman TS, Thom SR 2008)

2.Hyperbaric oxygen therapy: its use in medical emergencies

Decompression illness

Decompression illness is caused by an acute reduction in ambient pressure leading to formation of intravascular or extravascular gas bubbles. Gas embolism and decompression sickness (DCS) are the two major forms.Gas embolism occurs when gas enters the arterial (arterial gas embolism [AGE]) or venous (venous gas embolism [VGE]) circulation. (Moon RE, Gorman DF 2003).High-flow oxygen is used to correct hypoxia and to create a diffusion gradient from tissue to alveolar gas for the egress of nitrogen and other gases from the bubbles. For both AGE and DCS, recompression with HBOT is widely accepted as the definitive and potentially life-saving treatment despite a lack of randomised controlled trials (RCTs) in humans.The initial response to therapeutic pressurisation is in accordance with Boyle's Law—at 2.8 ATA pressure; bubble volume is immediately reduced by two-thirds.Hyperoxia corrects tissue hypoxia and, by

minimising blood nitrogen, maximises the diffusion gradient from the embolised gas to circulating plasma, thus optimising off-gassing.

Acute carbon monoxide poisoning

Hyperbaric oxygen therapy has been used in a variety of acute poisoning settings, including those caused by CO, methylene chloride, hydrogen sulphide, and carbon tetrachloride; gas embolism resulting from hydrogen peroxide ingestion; and methaemoglobinaemia.This article focuses on CO poisoning, as it remains a major cause of non-medicinal poisoning death and often results in persistent or delayed neurological sequelae.In brief, CO causes tissue hypoxia by forming carboxyhaemoglobin (COHb) and shifting the oxyhaemoglobin dissociation curve to the left. It also binds to various haem proteins, impairs mitochondrial function, causes release of nitric oxide and free radicals, and triggers inflammation through a myriad of mechanisms independent of hypoxia. (. Sircar K, Clower J, Shin MK, Bailey C, King M, Yip F.1999 to 2012)Oxygen therapy is the standard treatment. It works by reversing hypoxia, competing with CO for haemoglobin binding, and shortening the half-life of COHb (from 320 min in room air to about 70 min with 100% oxygen at 1 ATA); HBOT further reduces its half-life to 20 min (100% at 2.5 ATA), and increases the amount of dissolved oxygen in the plasma.

3.Clinical implications of HBOT:

3.1.Generalised infectious diseases:

At normal atmospheric pressure conditions, the levels of O2 concentration in blood is typically very low but is enough to provide the primary need for normal tissue.However,during the HBOT procedures, the O2 pressure in arterial blood can increase to 2000 mmHg, and the high blood-to-tissue oxygen pressure gradient increases the tissue O2 pressure to 500 mmHg and beyond.This is considered to be valuable for the healing of inflammatory and microcirculatory disorders in ischemic circumstances,infections and the compartment syndrome. HBOT also offers anti-edema effects by vasoconstriction, decreases leucocyte chemotaxis and adhesion, attenuates ischemic-reperfusion damage and suppresses the formation of inflammatory mediators along with wide variety of immune system responses in conditions such as for several skin soft tissue infection and osteomyelitis infections which are associated with hypoxia, caused by anaerobic and infections due antibiotic resistant bacteria and in the treatment of some deep and recalcitrant infections such as necrotizing fasciitis, (Shupak A, Shoshani O, Goldenberg I, Barzilai A, Moskuna R, Bursztein S 1995)osteomyelitis and chronic soft tissue

infections and infective endocarditis. The benefit of HBOT for sepsis, urinary tract infections and meningitis is relatively limited.

3.2.Surgical site infections

Surgical Site Infections (SSIs) are infections affecting either the incision or soft tissue at a surgical site in terms of anatomical location.Despite infectious control measures such as sterilization,usage of antimicrobial agents for prophylaxis and advancement of surgical techniques, SSIs have continued to be a postoperative problem increasing hospitalization costs and prolongation of hospital stay duration. Not only that SSIs are associated with increased morbidity and mortality of surgical patient reducing quality of life. SSIs have mono- or polymicrobial with either an anatomically superficial or deep etiology caused by both anaerobic and aerobic bacteria.Decreased local blood and O2 levels are the factors that stimulate the development of SSIs.Parts of the antimicrobial effects of HBOT are believed to be the result of formation of reactive oxygen species (ROS). HBOT also enhances the antimicrobial effects of the immune system and has an additive or synergistic effect with certain antimicrobial agents.HBOT has been recommended for the reduction of SSI incidence, particularly during clean-contaminated operations such as colorectal surgery. HBOT is being studied as a preventive measure for deep SSIs as in neuromuscular scoliosis.

3.3.Necrotizing soft tissue infections (NSTIs):

NSTIs are typically polymicrobial infections due to synergistic occurrence of different aerobic or anaerobic,mostly gas producing, bacterial pathogens. NSTI development although is uncommon,however often fulminant, and possesses a high mortality rate. (Q.A. Hussein, D.A. Anaya 2013).A Quick and apt diagnosis and treatment can possibly increase the chances of a favorable outcome.HBOT has been recommended as an adjunctive method in the treatment of NSTIs,as HBOT could be associated with increased survival and organ salvage and should be considered in the case of NSTIs,despite high Hospital costs and increased duration of stay,it may reduce mortality of the patients.

3.4. Diabetic foot infections:

Foot ulcers are one of the most frequent complications in diabetic individuals that commonly polymicrobial infections involving both the obligate and facultative anaerobic bacterial pathogens.Among several factors affecting wound healing in diabetic patients, deficiency of fibroblastic function, impaired collagen formation, cellular immune mechanisms, and phagocyte functions,Impairment in cutaneous oxygenation has been reported by many studies as being the strongest risk factor resulting in amputation of DFIs. (Health Quality Ontario

2017)Thus low O2 pressure and hypoxia have unfavorable effect on the innate function of leukocytes and fibroblasts during inflammatory response and healing. HBOT is reported to improve chronic skin damage healing by inducing angiogenesis due to beneficial effects of HBOT on vascular endothelium, the responsible tissue for angiogenesis.HBOT has been described to induce partial high tensions of O2 in circulating plasma. This stimulates O2 dependent collagen matrix formation, which is an essential phase in wound healing in DFIs decreasing the need of amputations and debridement that require surgical equipment.The low cost of HBOT compared to that of surgical procedures, commonly only accessible in a clinical setting, with limited complication and toxicity makes HBOT a favourable option.

3.5. Osteomyelitis

Osteomyelitis is the infection of the bone or marrow by bacterial pathogens with both acute and chronic severity and can be of refractory nature.Osteomyelitis is difficult to treat due to the relative paucity of blood vessels in bone and the fact that antibiotics often do not sufficiently penetrate bone.The chronic osteomyelitis is characterized by the persistent pathogens with mild inflammatory response,with incidence of necrosis and fistulous tracts in bone tissue. Refractory osteomyelitis is a chronic bone infection (Cooper PD, Smart DR. 2016) that persists or reappears after applicable mediations have been completed as a result of failure of antimicrobial and surgical interventions surpassing conventional management strategies.Increased O2 levels in the osteomyelitis lesion increases neutrophil activity, inhibition of bacterial pathogens, enhancing antibiotic effects, decreasing inflammation and enhancing healing mechanism thus resolving even chronic infections.

3.6. HBOT for fungal infections

World widely, more than 3 million people have chronic or invasive fungal infections, causing more than 600,000 deaths every year,in accordance with recent estimates,with Aspergillus fumigatus causing invasive pulmonary aspergillosis (IPA) in patients with compromised immune systems and is a primary contributor to increases in human fungal infections,with several factors such as hypoxic conditions in the course of fungal infections (Sourabh Dhingra 1 , Jay C Buckey 2 , Robert A Cramer 3 2018) with fungal adaptation to low levels of O2 for host adaptation and virulence, unfavorably affecting antifungal drug delivery to sites of infection and their usefulness,contributing to poor outcomes in the treatment with antifungal drugs making HBOT an attractive noninvasive procedure.HBOT is effective as an antifungal approach against Aspergillosis and Zygomycosis by reducing Aspergillus fumigatus colonies in vitro effect on biofilm through HBOT along with lack of fungal superoxide dismutase (SOD) genes

increasing the effect of HBOT on fungal growth inhibition.The effects of O2 on fungal-host interactions is complex and handling of O2 concentrations and/or O2 induced signaling pathways in vivo may have both helpful and harmful effects on the outcome of fungal infections.

4.Skin flaps,grafts,thermal burns

HBOT inhibits the immune reaction in antigens, decreases circulating lymphocytes and leukocytes and adjusts immunology to maintain the durability of an allograft, good flap takes and improved graft prognosis.HBOT is reported to improve chronic skin damage healing by inducing angiogenesis,O2 dependent collagen matrix. Severe burns are associated with high rate morbidity and mortality in patients.The use of HBOT in conjunction with comprehensive burn management led to the significant control of sepsis in burn patients, in many reported studies.

4. Antimicrobial effects of HBOT

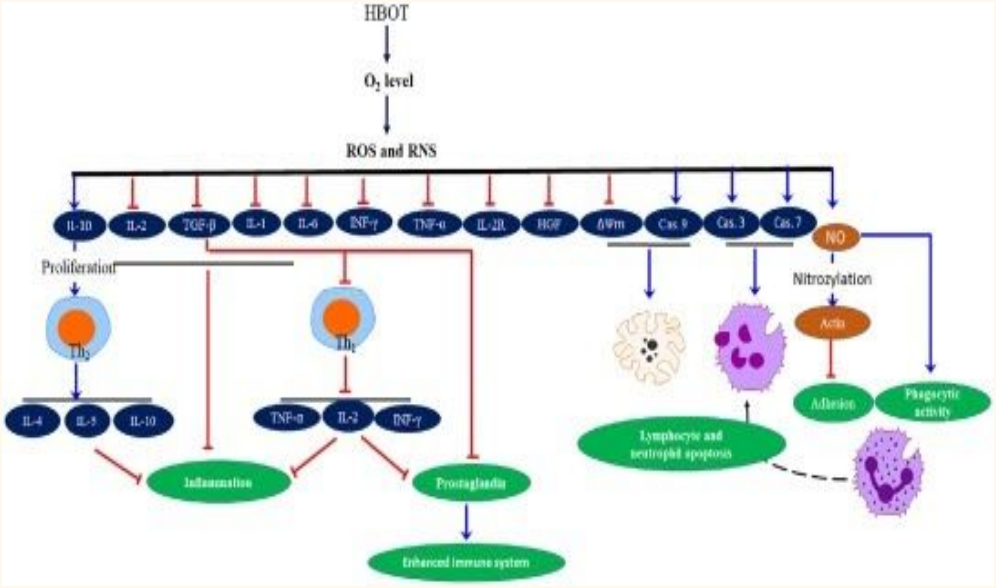
Due to the hyperoxic conditions induced by HBOT ,it promotes the healing of infections by three main mechanisms including direct bacteriostatic or bactericidal effects, enhancement of the immune systems antimicrobial effects, and additive or synergistic effects with certain antimicrobial agents and has bactericidal/bacteriostatic effects against both aerobic, and principally anaerobic, bacteria.

4.1.Augumentation of the antimicrobial effects of the immune system

There are many effects of HBOT on mechanisms of the immune system. The anti-inflammatory effects of HBOT, the expression of cytokines and other regulators of the inflammatory process,the overexpression and down-expression growth factors, (Qixu Zhang, Lisa J. Gould 2014) cellular effects such as the suppression of interferon- γ ,proinflammatory cytokines such as IL-1, IL-6, and TNF- α , a transient decrease in the CD4:CD8 T cell ratio ,the reduction of serum soluble IL- 2 receptor (sIL-2R) levels, enhancement of plasma fibronectin (Fn),significant elevation of IL-10,inhibition of the TGF β -pathway and induction of lymphocyte apoptosis by a mitochondrial pathway,Decreased zymosan-induced expression of toll-like receptor NF-jB signaling pathway,the O2 for antibacterial activity of neutrophils,have been reported to play an important role in reducing tissue damage and infection development. The bactericidal mechanism promotes potential respiratory bursts achieved via the production of superoxide radicals needing large amounts of O2 in infectious tissues with induction of ROS formation dependent on the local O2 partial pressure. A single 90 min pre-treatment with HBOT induces

the respiratory burst activity of neutrophil-like cells and increases phagocytosis of Staphylococcus aureus, with pro-apoptotic effect on neutrophils which is necessary for resolution of inflammation.The adhesion of neutrophil is mediated by beta-integrin interaction with intercellular adhesion molecules (ICAM) on the endothelial surface. HBOT suppresses neutrophil beta-2 integrin (Mac-1 (CD11b/CD18)) activity by a nitric oxide (NO) mediated process and neutrophil counter ligand ICAM-1 on vascular endothelium.This may be helpful in permitting neutrophil migration to the site of infections.

Inhibition of neutrophil beta-2 integrin is mediated via nitrosylation of actin,which is associated with increased NO formation. Phagocytosis of pathogens by neutrophils neesd a precise rearrangement of the actin cytoskeleton. The nitrosylation of actin was shown to stimulate the polymerization of acti and thus the phagocytotic action of neutrophils.



4.2. Direct antimicrobial effect of HBOT

Direct antimicrobial effects of HBOT are believed to be the result of formation of reactive oxygen species ‘ROS’ referring to reactive radicals, including superoxide anion (O2−), peroxide (O2−2), hydrogen peroxide (H2O2), hydroxyl radicals (OHradical dot), and hydroxyl (OH−) ions that are produced continually as alternative metabolites of several cell biological pathways.

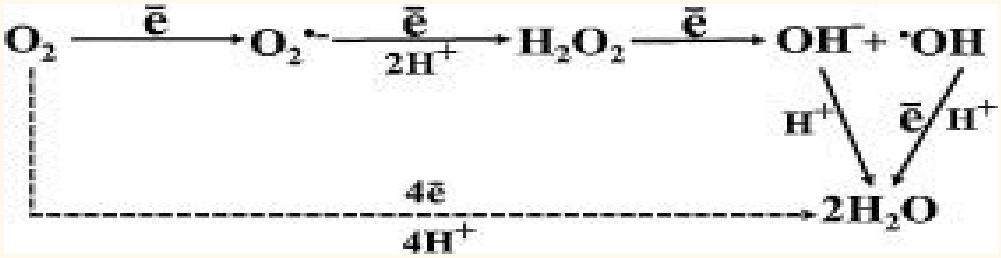


Fig. 1. ROS formation: the consecutive addition of an ē to O2 is association with ROS formation.

ROS,electron transport chain and mitochondria:

The interactions between O2 and cellular contents, mainly respiratory flavoenzymes, occur in association with ROS formation.In oxidative stress,the levels of ROS increase in cells due to a disturbed balance of ROS formation and its degradation.HBOT induces oxidative stress and eliminates the desired condition for bacteria that lack antioxidant defense pathways.During oxidative stress, generated O2 Radical dot− is catalyzed by superoxide dismutase to H2O2 and reduces Fe3+ via the Haber-Weiss reaction. H2O2 can then oxidize Fe2+ by the Fenton reaction to produce OHradical dot and Fe3+, thus it may start a deleterious redox sequence of ROS generation and damage.

DNA,RNA,nuclear components:

Since Fe2+ is capable of binding to cellular structures, OHradical dot can produce in the vicinity of DNA, proteins, and lipids and as a result, induces its destructive effect.Fe2+ has a sequence-specific affinity for interacting with DNA and contributing to the Fenton reaction. The cellular targets for ROS toxic effects are DNA, RNA, proteins and lipids. ROS induces antimicrobial activity via a dose-dependent mode of effect DNA is the main target in H2O2-depended cytotoxicity over an interaction that damages bases by breaking up the deoxyribose construction. ROS induces physical damage in incorporated or free nucleotides. Additionally, it breaks single or double-stranded DNA in the double helix, which can also be broken by by-products of induced lipid peroxidation by ROS.

Lipid structures:

The damaging OH• can trigger peroxidation of lipids and could stimulate the oxidation of poly unsaturated phospholipids in cell membranes, and thus cause a failure in its function.ROS can disrupt the lipid bilayer organization of the cell membrane that may disable membrane-located

receptors and proteins and can finally lead to cell fluidity, efflux of cytosolic contents and losing of enzyme function.

Protein structures:

Proteins are also a molecular target of ROS. Which can cause damage such as, oxidation of sulfhydryl groups, reduction of disulfides, oxidative adduction of amino acid residues near metal-binding locations through metal-depended oxidation, interaction with aldehydes, modification of prosthetic or metal groups, protein-protein cross-linking and peptide destruction [63]. Proteins can subject different specific oxidative changes at cysteine, methionine, tyrosine, phenylalanine and tryptophan residues. H2O2 can induce an oxidative alteration in proteins such as elongation factor G, DnaK, alcohol dehydrogenase E, enolase, OppA, OmpA and the F0F1-ATPase of E. coli.

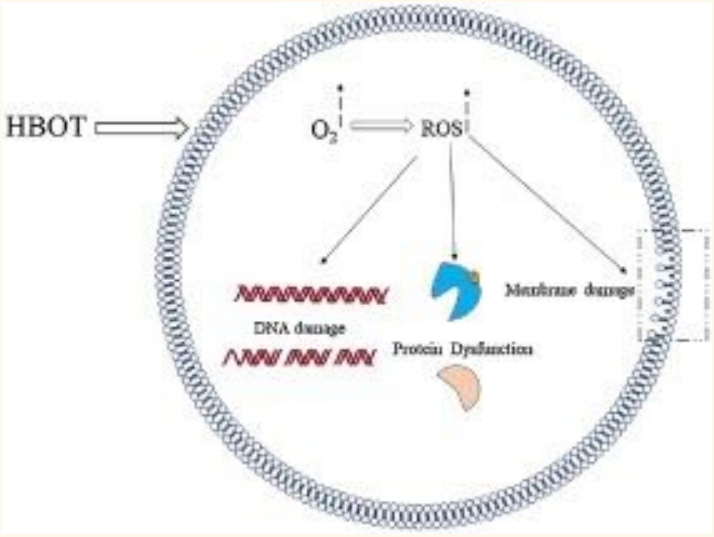


Fig. 2. The inhabitation of microbial growth by ROS formation and biological targets.

4.3. Synergism with certain antimicrobial agents

In the clinical setting, HBOT is commonly administered in combination with antibiotic therapy in the treatment of an infection.It has been revealed that some bactericidal agents such as β -lactams, quinolones and aminoglycosides (“Reinforcement of the bactericidal effect of ciprofloxacin on Pseudomonas aeruginosa biofilm by hyperbaric oxygen treatment” 2016)partly depend on bacterial aerobic metabolism in addition to their target-specific effects.The potential in vivo O2 concentration in the infectious tissues and its effect on antibiotic sensitivity of the pathogens are the key factors when setting susceptibility cutoff points for assessing the therapeutic property of an antimicrobial agent.It has been reported that low levels of O2

increase the resistance of Pseudomonas aeruginosa strains to piperacillin/tazobactam and Klebsiella pneumoniae strains to azithromycin. By contrast, some bacteria become more susceptible to tetracycline agents in the presence of low levels of O2.The aim of HBOT, as an alternative treatment, is to induce the aerobic metabolism of bacteria and to reoxygenate the O2-depleted infectious tissues and therefore increase the microbial susceptibility to antibiotics.Bacteria exposed to HBOT and simultaneously treated with antimicrobial agents exhibited significant changes in the cytoplasmic structure morphology; such as deformation and disorganization promoting aerobic metabolism leading to enhanced induction of ROS production in bacteria.The administration of adjunctive HBOT twice a day with an 8 h' interval (280 kPa (2.8 bar) for 114 min) in combination with subcutaneous tobramycin (20 mg/kg/day) has shown a decrease in the bacterial load in Staphylococcus aureus infective endocarditis.The exposure to HBOT (for 90 min at 2ATM) remarkably decreased the growth of MRSA.HBOT (under the pressure of 3 ATA at 37 °C for 5 h) increased the effects of imipenem on P. aeruginosa infections of macrophages.The combination of HBOT and cefazolin have shown to be more effective than cefazolin alone in the treatment of osteomyelitis caused by S. aureus in animal models.HBOT, by re-oxygenation of biofilm, can considerably increase the bactericidal effect of ciprofloxacin on P. aeruginosa after 90 min of exposure. The combination of ciprofloxacin and HBOT therefore may potentially improve the eradication of P. aeruginosa biofilm in infectious tissue by endogenous ROS formation as indicated by the higher susceptibility of a catalase-deficient mutant.HBOT Significantly increases effects of vancomycin, teicoplanin, and linezolid in combination with HBOT have been reported against methicillin-resistant Staphylococcus aureus (MRSA) in an animal model mediastinitis.Metronidazole is effectively used for anaerobic and polymicrobial infection such as diabetic foot infections (DFIs) and surgical site infections (SSIs) and more so in conjunction with HBOT.An obvious effective treatment of OXA-48 type carbapenemase-producing K. pneumonia osteomyelitis has been reported using HBOT without any concomitant antibiotics.The effect of HBOT in combination with antimicrobials should be studied in the future through in vitro and in vivo studies.Antimicrobial drugs tend to lose their effect over time due to the development and spreading of antibiotic resistant bacterial pathogens . HBOT may be suitable for the treatment and prevention of multi-drug resistant pathogens and could be considered in cases of antibiotic therapy failure

5. HBOT for antibiotic resistant isolates

Antimicrobial drugs tend to lose their effect over time due to the development of antibiotic (Mohammad Yousef Memar)resistant bacterial pathogens. HBOT may be suitable for the

treatment and prevention of multi-drug resistant MDR pathogens and could be considered in cases of antibiotic therapy failure.

6. The complications and side effects of HBOT

The risks of O2 toxicity, barotrauma,tension pneumothorax are among the documented complications of HBOT that can develop as a result of prolonged sessions of HBOT.

TABLE 2. Adverse effects of hyperbaric oxygen therapy

Type of effects	Adverse effects
Effects caused by barometric pressure change	1. Middle-ear barotrauma (myringotomy may be needed) 2. Sinus barotrauma 3. Lung barotrauma—haemoptysis, pneumothorax, pneumomediastinum, subcutaneous emphysema, or arterial gas embolism 4. Gas leakage or rupture of air-containing cavity in the body
Effects caused by oxygen toxicity	1. Neurological—muscle twitching, dysphoria, nausea and vomiting, convulsion 2. Pulmonary—increase in the work of breathing due to increase in gas density, tracheobronchitis (cough, dyspnoea, and chest tightness), deterioration in lung function 3. Ocular—reversible tunnel vision, temporary myopia, cataract after prolonged treatment

6.1.O2 toxicity

The risks of O2 toxicity depends on the level and intracellular localization of induced ROS. Due to the fact that exposure to hyperoxia in clinical HBOT procedures is rather brief, studies show that antioxidant responses are sufficient so that biological stresses induced by high levels of ROS are reversible.Induced damage of DNA by ROS appears to play a significant role in the stimulation of mutations and cancer.Under HBOT, the dissolved O2 in the blood and also the generation of ROS are significant elevated which is associated with toxicity.The stimulation of oxidative DNA base injury by HBOT is well known. DNA strand damage and oxidative base damage can be detected in peripheral blood, immediately, after a single session of HBOT, which in part demonstrates an increase in antioxidant defenses. DNA damage is not initiated when HBOT begins but is increases slowly and more so with increased exposure time.The transcriptional response patterns to certain ROS are influenced on a cellular level, and ‘classical’ antioxidant responses that are promoted by high levels of ROS can be suppressed when cells adapt to low levels of ROS.Activities of superoxide dismutase and glutathione peroxidase have been suggested as an indicator of a strong protective mechanism against the

hyperoxic condition, which is an adaptive reply for effective repair mechanisms.HBOT- exposed lymphocytes indicate a small but reproducible increase in cellular ferritin, which might suggest that the underlying protective response is established based on the stimulation of ferritin, which may act as antioxidant by inhibiting the formation of the DNA-damaging hydroxyl radical via the Fenton pathway. HBOT often include so-called air breaks, where a patient respires only air for 5 min intervals once or twice throughout the course of the treatment which may have some health concerns.HBOT is safe if it does not exceed 2 h and the pressure does not exceed 3 ATM.

6.2.Barotrauma

At 4 ATA,barotraumatic lesions in middle ear and lungs, confinement anxiety and visual effects.However these things can be prevented by careful pre-examination and monitoring.

7.Contraindications to HBOT

Absolute contraindications to HBOT include untreated pneumothorax (risk of becoming a tension pneumothorax), restrictive airway disorders (air becomes trapped with decompression and can lead to alveolar rupture with gas expansion), and simultaneous chemotherapy (has associated morbidity). (Mathieu D 2008).

TABLE 3. Contra-indications to hyperbaric oxygen therapy

Type	Conditions
Absolute	1. Untreated pneumothorax 2. Acute severe bronchospasm 3. Concomitant treatment with doxorubicin 4. Concomitant or recent treatment with bleomycin
Relative	1. Upper respiratory tract infection 2. Allergic rhinitis 3. Chronic sinusitis and otitis 4. Chronic obstructive pulmonary disease with emphysema 5. History of pneumothorax or thoracic surgery 6. History of ear, nose, and throat surgery 7. Epilepsy 8. Optic neuritis 9. Uncontrolled hypertension 10. Uncontrolled heart failure 11. Claustrophobia 12. Dangerous behaviour

If safety guidelines are strictly followed, HBOT is an effective modality with an acceptable rate of side effects.

8.Conclusion

HBOT is a primary emergency or alternative option for the treatment of infections. Regarding an increased frequency of antibiotic resistant pathogens, HBOT can be effective in the treatment of acute infections. HBOT promotes the healing of infections by direct bacteriostatic or bactericidal effects, enhancement of immune system antimicrobial effects, and additive or synergistic effects with certain antimicrobial agents. If safety guidelines are strictly followed, HBOT is an effective procedure with an acceptable rate of side effects.

Conflict of interest

There is no conflict of interest.

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