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The Inspiring Journey of Hyperbaric Oxygen Therapy, from the Controversy to the Acceptance by the Scientific Community

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Abstract

Background: Hyperbaric Oxygen Therapy (HBOT) is achieved when the patient is breathing 100% O_2 intermittently in a closed chamber (hyperbaric chamber), while the chamber pressure is greater than 1 atm. For the standards of contemporary medicine science, the HBOT is a relatively new treatment, as it struggles to be supported scientifically over the last 50 years. The objective of this literature review is to highlight the importance of the use of hyperbaric oxygen (HBO). Initially by presenting the continuous efforts made for hundreds of years, for safer and more effective use as therapy. Focusing on the history, clinical use, and finally understanding the effect of air under increased atmospheric pressure.

Methods: Bibliographic research in the following databases: Medline, Cochrane Database of Systematic Reviews, Cinahl, and Iatrotek on-line. Furthermore, relevant articles and books were also manually searched in the Library of the Health Sciences of the University of Athens.

Results: The use of HBO as an adjunctive therapy according to the internationally recognized indications, has become widely accepted, mainly due to the specification of the physiological effects of HBO in various systems and its mechanisms. Further research is necessary, in order to ensure the best possible therapeutic effect.

Conclusion: As medical thought and technology has matured, it appears that is the proper time for the complete clarification of the potential uses of HBO. Supported methods and advanced technological equipment are necessary in order to develop medical and nursing practice, as well as research documentation.

Keywords: Hyperbaric oxygen; History; Indications; Side-effects; Nursing

Introduction

Hyperbaric Oxygen Therapy (HBOT)

Hyperbaric Oxygen Therapy (HBOT) is achieved when the patient is breathing 100% O_2 intermittently, in a closed chamber (hyperbaric chamber), while being inside a chamber at a pressure higher than the pressure of the sea level (more than 1 atm). Exposing some parts of the body to 100% oxygen or breathing 100% O_2 at 1 atm of pressure does not constitute HBOT [1].

The Historical Evolution of HBOT

The use of air and oxygen under increased atmospheric pressure is distinguished in time “pre-scientific” and “scientific period”.

Pre-scientific period

Aristotle in 300 BC, described the ruptured eardrum as a complication of undersea diving [2]. During the 17^{th} century in England, metallic vessels strong enough to hold air under pressure, combined with the production of pumps capable of compressing air. Resulted in the treatment of patients with a variety of medical problems with hyperbaric air treatments [2].

In the 19^{th} century, in various European countries hyperbaric chambers, were initially created for exposing patients to ambient air under modest pressure and eventually became health spa

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accoutrements and were used empirically to treat a variety of maladies [3].

During the construction of the bridge of St. Louis in early 1870 in the U.S., out of the 600 workers who worked in underground tunnels, 119 showed severe neurological disease from a lack of decompression, while 14 of them finally died. In the following years**,** working in underground tunnels in the U.S., France and Great Britain resulted in similar morbidity and mortality [4].

Also, among the first scientists who studied the diver's disease, was the Greek professor Michael Katsaras (1888), who after many clinical and experimental studies, described in detail the pathogenesis and clinical types of the disease. He suggested the slow emergence of the diver and stopping at regular time intervals as a prevention method [5].

In 1899, Moir, an engineer in the bridge construction of Hudson River, recorded a 25% incidence of death as a result to decompression illness. Then, after installing a decompression chamber, only two deaths in 120 workers occurred over the period of 15 months. The recompression appeared to be effective and was considered that the improvement was due to the reduction of the size of the bubbles [2]. In the next years, a new technological equipment and data from experimental and clinical studies, led to successful treatments of recompression and reduced morbidity and mortality of the decompression sickness [6].

Since the beginning of the 20th century Hyperbaric Medicine enters a period of doubt. In Kansas City in 1921, Dr. Orville J. Cunningham built a multiplace hyperbaric compressed air chamber to treat patients with a wide variety of ailments. Supported by a wealthy industrialist, Cunningham later constructed the biggest hyperbaric chamber in the world (a five storey, 20 meter diameter, hyperbaric building, on the top floor of which, there was a smoking room), which had the potential to reach up to 3 atm pressure. This facility was used to treat a diverse collection of ailments, Cunningham's theory being that a cryptic anaerobic organism was responsible for a wide range of human diseases, such as hypertension, uremia and cancer. Finally, Cunningham was censored by the American Medical Association, and his building was broken up for scrap metal. Since that era, compressed ambient air has not been systematically used to treat disease [3].

Scientific period

The scientific period of HBOT actually begins in the late '50s. When in Amsterdam in 1956, the professor of surgery Boerema (1902-1978), having studied experimentally the effects of hyperbaric oxygen (HBO), used HBOT to extend the duration of disruption of cardiac function in cardiac surgery (before application of extracorporeal circulation) [7]. He observed that when the temperature drops into the core of an animal, the chances of survival from cardiac arrest are doubled. The hunt of this goal, led him to research in HBOT. The experiments were conducted in a hyperbaric tank, used for training submarine crews in the Royal Naval Academy of the Netherlands. The results of this experimental study were published in the article "Life without blood" [7]. With this experimental study, he showed that the oxygen supply is possible without blood cells, which led to a rapid increase of the experimental and clinical studies. By installing a hyperbaric chamber at the hospital in Amsterdam, many new cardiac methods were possible. Additionally, chambers were constructed at many major medical centers worldwide, including the USA, Europe, Russia, China and Japan [8].

Brummelkamp in the Netherlands demonstrated the therapeutic effect of HBO in anaerobic infections in general, however, perhaps the greatest achievement of HBOT was the treatment of gas gangrene. Before the use of HBOT, gas gangrene was treated with extensive debridement of damaged tissue or amputation. HBO was presented in 1960 as a possible treatment for gas gangrene and it was observed that the mortality rate sharply declined from 66% to 23%, as well as there were significant reductions in morbidity and disability resulting in the saving of life and limbs of patients.

Elements of physiology

HBO induces high oxygen partial pressure in all tissues; it causes activation of fibroblasts and macrophages, it stimulates angioneogenesis and it has bacteriostatic and bacteriocidic effect. In particular, during HBOT, 10-15 times increase of the concentration of O_2 is achieved in the plasma. This implies a partial pressure of oxygen as 1500 mmHg to 2000 mmHg (at sea-level the air pressure is 760 mmHg), creating four times increase of the distance of diffusion of oxygen from the capillaries. HBO exposure transiently suppresses stimulus-induced pro-inflammatory cytokine production. HBO can help preserve ischemic tissues and promotes healing in challenging wounds, [11] by the principle of Dalton's Law: an increase in environmental pressure increases the "driving force" behind the oxygen in the plasma, thus improving tissue oxygenation to the hypoxic tissue beds [12]. There has been quite reliable experimental data, for the action of hyperbaric oxygen in situations characterized as reperfusion injury. It has been established that HBO inhibits the adhesion of leukocytes to the endothelium of vessels and is likely to have a beneficial effect on reperfusion injury syndromes (myocardial infarction, ischemic stroke) [9,10].

HBOT induces haemodynamic changes such as: i) bradycardia **-** decrease in cardiac output , ii) peripheral vasoconstriction, the hyperoxia causes vasoconstriction and peripheral hyperoxia (Oxygen Paradox) reducing edema iii) decrease in Cerebral Blood Flow (CBF), iv**)** Suppression of chemoreceptors by decreasing ventilation, v) Affecting of enzymes and functions at the cellular level [12].

Indications for HBOT

In 2010, the Greek Ministry of Health and Social Solidarity promoted an initiative at the Greek hospitals and Hyperbaric & Diving Medicine Centers in Greece entitled "Establishment of approved indications for HBOT", which follows the guidelines of the scientific community [13].

Accepted indications of hyperbaric oxygen therapy according to the Undersea and Hyperbaric Medicine Society (UHMS) [1] are presented in the **Table 1**.

Table 1 Accepted indications of hyperbaric oxygen therapy [1].

Indications
Air or Gas embolism
Carbon monoxide (CO) poisoning complicated by cyanide poisoning
Clostridial myositis and myonecrosis (gas gangrene), anaerobic cellulitis and necrotizing fasciitis
Crush injury, compartment syndrome and other acute traumatic ischemias
Decompression Sickness (DCS)
Arterial Insufficiencies: i) central retinal artery occlusion ii) the enhancement healing of selected problem wounds (chronic ischemic ulcers)
Severe anemia
Adjunctive therapy in intracranial abscess (ICA)
Necrotizing soft tissue infections
Refractory osteomyelitis
Delayed radiation injuries (soft tissue and bony necrosis)
Compromised grafts and flaps
Acute thermal burn injury
Idiopathic Sudden Sensorineural Hearing Loss (ISSHL)

Air or Gas embolism is the most common and dangerous condition that can occur after compressed gas diving and characterized by the presence of air bubbles within the blood vessels. It can occur at shallow depth up to 2 meters. This involves the rapid increase in the volume of air into the lungs, causing the rupture of the alveoli. The air released from such rupture can cause pneumothorax, pneumomediastinum and air embolism. Moreover, the brain and spinal marrow are affected, by requiring a constant oxygen supply.

The main symptoms of air embolism can be the presence of mottled reddish skin blemishes, foam (rosacea or bloody) in nose and mouth, severe pain in muscles, joints and abdomen, dyspnoea and or chest pain, dizziness, nausea and vomiting, dysphasia (difficulty in speaking), difficulty in vision, paralysis and or coma, cardiac arrhythmias or ischemia pulse and even cardiac arrest [14].

In Europe, Carbon monoxide (CO) poisoning complicated by cyanide poisoning is the most common poisoning [4]. Pregnant women and children are most at risk of carbon monoxide poisoning because they have faster metabolic rates. The symptoms of poisoning by CO include loss of consciousness, confusion, headache, malaise, fatigue, forgetfulness, visual disturbances, nausea, vomiting, dizziness, cardiac ischemia, or metabolic acidosis, neurological or cognitive impairment (often permanent) [16].

Severe poisoning with carbon monoxide, can be satisfactorily treated by administering pure oxygen, because oxygen, when present in high concentrations in alveolar air, displaces carbon monoxide from its association with haemoglobin at a faster rate than at low partial oxygen pressure (PO_2) of ambient air [15]. HBO provides an alternative source of tissue oxygenation, by increasing the dissolved oxygen in the plasma and facilitates the separation of CO from haemoglobin. The half-life of the carboxyhaemoglobin (COHb) is 240-320 minutes in the air, 80-100 minutes in 100% oxygen inhalation and about 20 minutes in HBO. In addition, it separates the CO by cytochrome c oxidase improving electron transport and the cellular energy state [16].

Clostridial myositis and myonecrosis (gas gangrene), anaerobic cellulitis and necrotizing fasciitis, due to anaerobic bacteria (clostridia), lacking antioxidant defence mechanisms. The effectiveness of HBO is focusing on the inhibition of tissue necrosis, since the infections usually cause a decrease in tissue oxygen resulting in diminished ability of leukocytes to fight infection. Adding the fact that free-circulating toxins are rapidly detoxified. The use of HBO, surgical intervention and antibiotic medication, has contributed to the reduction in mortality and to the prevention of major amputations or excisions [4]. The combined debridement with antibiotics and HBOT, increase life expectancy by 5%. In clostridial myonecrosis, survival rates are increased from 70% to 95% if HBO is used.

Crush injury, compartment syndrome and other acute traumatic ischemias, are results of acute traumatic ischemia with clinical image of edema, tissue hypoxia and finally necrosis. Hyperbaric hyperoxia contributes to increased tissue oxygenation despite reduced blood supply from the circulatory traumatic injuries, the vascular compression and edema [4]. Reducing the edema by providing oxygen to the tissues, HBO interrupts the edema-ischemia "vicious circle" cycle to prevent progression of the injury. HBO acts on the endothelium and inhibits leukocyte accumulation, resulting in mitigation of the reperfusion injury [9,10].

The critical pathological event in Decompression Sickness (DCS also known as Diver's Disease) is the creation of inert gas bubbles in the blood or tissue, due to supersaturation [17]. It represents a complex clinical condition characterized by temporary or permanent dysfunction of one or more systems of the human organism when it is exposed to changes in atmospheric pressure. The symptoms of divers can occur 15 minutes after the end of the dive, up to 36 hours later. Most cases occur within 6 hours. DCS can be caused by a reduction in ambient pressure during ascent from a dive and less commonly, by rapid ascent at an altitude of 5,500 meters [5].

Type I of DCS is reported in mild forms including the myoskeletal pain in a limb (arm or leg), which is the most common form of the disease and occurs in 90% of cases. It varies in intensity and can come with an edema around the damaged joint. The key feature is that the pain is independent of the movements of the affected limb [5]. Manifestations of the lymphatic system, result from lymphatics occlusion due to nitrogen bubbles. There is swelling of the lymph node group and is frequently accompanied by pain and swelling of the surrounding tissues. The cutaneous manifestations of the disease can be pruritus with or without exfoliated rash and marbled rash (marbling or cutis marmorata) a maculopapular rash from venous occlusion of vessels in the skin, due to nitrogen bubbles. During the decompression, the erythema recedes [5,18].

The type II disease includes manifestations from the Central Nervous System, is a severe form of the disease and needs

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emergency treatment. The pulmonary form (Chokes) is characterized by retrosternal pain, caustic character and progressively increasing intensity, neurological dysfunction (peripheral or central nervous system bends), cardiorespiratory symptoms and pulmonary edema (chokes), shock and death. The neurological form, also includes the disease of the inner ear (Acoustic-Vestibular, Staggers) [5,14].

The HBO and the simultaneous compression of bubbles contributes to oxygenation of hypoxic tissues and has significantly improved the outcome of DCS (80%-85%) [4].

Arterial Insufficiencies including central retinal artery occlusion and the enhancement healing of selected problem wounds such as chronic ischemic ulcers might benefit by the use of HBO. If conditions are suitable for intervention with HBO as adjunctive therapy in the affected areas (elementary existence blood flow) HBO is possible to improve local host immune response and increase oxygenation of ischemic tissues by promoting the activity of neutrophils, granulocytes and fibroblasts and neovascularisation [4,19,20].

Goldman's systematic review in 2009, found that in patients with diabetic foot complications and surgical infection, HBOT reduces the likelihood of amputation (it is referred to 7 studies) and improves the chances of healing (it is referred to 6 studies) [21]. The results of research on the correlation of smoking with the healing of diabetic ulcers and the corresponding effect of HBO, of Oubre et al in 2007, showed that the clinician should assess the medical and social history of the patient to decide whether the patient is likely to benefit from HBOT [22].

The use of HBO is also suggested in cases of severe anemia, where there is difficulty in crossmatching the blood, e.g. due to rare blood group, or where due to religious beliefs the blood transfusion is forbidden [23].

HBO can be used as an adjunctive therapy in intracranial abscess (ICA) too [1].

Other indications for HBO are necrotizing soft tissue infections like anaerobic cellulitis, which usually occurs after trauma or vascular disease of lower limbs. Another necrotizing soft tissue infection is the progressive bacterial gangrene which is manifested by the hypoxia chronic dermal ulceration, throughout the thickness of the skin, but not in the fascia. The extensive necrosis of the superficial and deep fascia, which leads to destruction of adjacent tissues and generalized systemic toxicity is necrotizing fasciitis. The presence of muscle tissue involvement of the scrotal and perineal area in Fournier's gangrene, is defined as necrotic fasciitis or non clostridial myonecrosis [4].

Refractory osteomyelitis is an infection of bone or bone marrow, associated with hypoxia and dysfunction of defense and recovery mechanism [1,2]. When hyperbaric oxygen and antibiotics are combined with antibiotics and surgery, success rates of as high as 85% have been reported, but controlled trials are required [23].

Delayed radiation injuries (soft tissue and bony necrosis) are created, due to direct and near immediate toxicity of the cells caused by free radical-mediated damage to cellular DNA, leading to cell damage and vascular changes characterized by obliterative endarteritis. Chronic tissue hypoxia leads to the inability of collagen synthesis, lack of angiogenesis and fibrosis [4].

Soft tissue radionecrosis and osteonecrosis after surgery on irradiated mandibles are reduced by HBO. HBO is more effective in the irradiated tissue than Normobaric oxygen, oxygenating the tissue and promoting angioneogenesis and healing of wounds. Osteoradionecrosis was compared in a period of 6 months postoperatively during a controlled study, where the incidence was 5% in patients who received 30 preoperative HBOT in comparison with 30% in patients who received only preoperative antibiotics. The results showed a similar improvement in wound healing in both group of patients. HBO through achieving higher partial pressures, may stimulate neovascularization and wound healing in damaged tissue which has lost the capacity for restorative cellular proliferation [23].

The proposed use of HBO as supplementary therapeutic intervention in the management of compromised flaps or grafts that do not improve with standard wound therapy was based on the acquired experience of wound healing enhancement after HBO application in wounds and injuries of hypoxic soft tissues. Compromised tissues are usually hypoxic thus the necessity for improved oxygenation. HBO has been shown experimentally and clinically, able to support and restore healing mechanisms in hypoxic cellular environment of hypoperfusion [24,25].

Experimental and clinical studies have demonstrated effective intervention in addressing extensive burns, especially those in which there was an inhalation injury. If it is possible to combine the main treatment with the addition of HBO, the use of HBO is recommended, particularly in extensive burns (20%) or in smoke inhalation with concomitant carbon monoxide poisoning [2,26].

Idiopathic Sudden Sensorineural Hearing Loss (ISSHL) is the newest indication approved on October 8, 2011 by the UHMS Board of Directors. Hypoxia in the perilymph, the scala tympani and the organ of Corti seems to be the main characteristic [27]. ISSHL, mainly associated with acute circulatory failure and the treatment interventions, aim to better cochlear oxygenation. The functional activity of the inner ear requires the continuous presence of increased partial pressure O_2. HBOT participates in the therapeutic approach due to the significant increase in the arterial-perilymphatic oxygen concentration, despite the reduction of blood supply to the cochlea. The early intervention is associated with improved outcomes, when is initiated within two weeks of symptom onset and combined with corticosteroid treatment mainly in the group of patients with a high degree of hearing loss [2,27].

Indications under investigation

Further clinical research is needed in syndromes with satisfactory results from the adjunctive therapy with HBO, such as retinal ischemia, restoration of complicated fractures. Up to 10% of fractures occur annually in the U.S.A. result in non-union or delayed bone healing. The classic treatment with osteosynthesis and bone transplants are not always successful. The uses of HBO have positive indications in complicated fractures [28].

Other indications under investigation are perinatal asphyxia, anoxic encephalopathy (acute-chronic), CNS injuries, myocardial ischemia and Miscellaneous Sports Injuries [4].

For conditions where its use remains unproved, for example, gastro duodenal ulcer, cirrhosis and rheumatoid arthritis, HBO should be used only in the context of well controlled clinical trials [23].

Contraindications of HBOT

Table 2 presents the contraindications of HBOT including the absolute contraindication and the relative contraindications.

Absolute contraindication

The presence of untreated pneumothorax is generally accepted as an absolute contraindication to the use HBOT [26,29-32], since during HBOT compression and decompression is highly possible to develop tension pneumothorax and gas emboli [26]. More specifically, tension pneumothorax can be induced by the increasing in gas volume in relation to the decrease in the pressure in the hyperbaric chamber during the decompression period. Pleural cavities should be drained before the session of HBO in order to minimize the risk [29].

The use of certain drugs before or during the HBO therapy sessions is also an absolute contraindication. Doxorubicin (Adriamycin) and Cisplatin are both chemotherapeutics drugs, while Disulfiram (Antabuse) used in the treatment of alcoholism and Mafenide acetate (Sulfamylon) used to treat bacterial infections in burn wounds. During HBOT it has been observed that these drugs become toxic [30-32].

Relative contraindications

Claustrophobia [31] should be regarded as a contraindication for HBO, though sometimes occurs during treatment and it is considered as a side effect. It happens frequently in the treatment done in the monoplace chamber than in multiplace chamber and the appearance often leads the patient to panic attacks.

Chronic obstructive pulmonary disease (COPD), pulmonary emphysema with retention of CO_2, considered as a group possible to the occurrence of pneumothorax. In patients with COPD, prolonged exposure to hyperoxia leads to further burden of respiratory function, mainly through the mechanism of venous bubbles in the circulation during decompression and previous disturbance of gas exchange, low presence of antioxidant enzymes in patients with documented oxidative stress.[16]

Upper respiratory infections (Otitis and Sinusitis) [31], are contraindications as they can lead to ear barotrauma and increased pressure in the paranasal sinuses.

The appearance of non-reasoning pulmonary opacities on the chest radiograph (possible indication of serious illness or cancer) is also a contraindication [32].

Studies in animals have shown that HBOT can lead to congenital abnormalities, especially in the first trimester of pregnancy [32]. However, in situations threatening the life of the mother, like in poisoning by CO, HBOT should be applied with short treatment duration.

A history of optic neuritis constitutes a contraindication, because there is a possibility of blindness with the application of HBOT.

In cases of previous thoracic surgery or ear surgery, HBO should be avoided and uncontrolled high fever should be reduced with antipyretics before placing the patient in the chamber.

Epileptic seizures [16] are rare and usually cause no permanent damage. More integrated into the side effects because it can occur in toxic effects of hyperoxia in Central Nervous System [4].

Congenital spherocytosis and the presence of cardiac pacemaker are considered as contraindications for HBO [26].

Table 2 Contraindications of hyperbaric oxygen therapy.

Contraindications	
Absolute contraindications	**Relative contraindications**
Untreated pneumothorax	Claustrophobia
The use of Doxorubicin (Adriamycin), Cisplatin, Disulfiram (Antabuse), Mafenide acetate (Sulfamylon)	Chronic obstructive pulmonary disease (COPD)
	Upper respiratory infections (Otitis and Sinusitis)
	Non-reasoning pulmonary opacities on chest radiograph
	Pregnancy
	History of optic neuritis
	Previous thoracic surgery or ear surgery
	Uncontrolled high fever
	Epileptic seizures
	Congenital spherocytosis
	Cardiac pacemaker

HBO and Cancer

Through a number of studies published from 1960 to today, it has been shown that exposure to HBO neither promotes tumor growth, nor to enhance its recurrence [33]. The findings of Schönmeyr et al. in 2008, conclude that HBO does not interfere with the conversion of growth and proliferation of cancer cells *in vitro* and *in vivo*. Furthermore, they showed that HBO may be a transient reduction of tumor hypoxia [34]. Moen's and Stuhr's systematic review on HBO and cancer during 2004–2012 demonstrated that HBOT is considered safe in patients with cancer. Furthermore, it was found that HBO might have tumor-inhibitory effects in specific types of cancer ie in breast cancer subtypes. Certainly, further research is needed to inquire into the impact and the mechanisms of tumor oxygenation [33].

Side Effects of HBOT

When HBOT is based on specific protocols, i.e. generally, if O_2 pressure dosn't exceed 3 atm, the treatment time is not longer than 120 minutes, and sessions do not exceed 30, is considered absolutely safe with side effects rate below 1%. The side effects are the result of changes in pressure and the toxicity of O_2 (**Table 3**).

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Table 3 Side effects of hyperbaric oxygen therapy.

Side Effects
Middle ear barotrauma, Pulmonary barotrauma
Claustrophobia
Fatigue
Vomiting
Reversible myopia
Cataract
Oxygen toxicity: i) on the central nervous system, seizures rarely occur and usually do not cause permanent damage ii) pulmonary toxicity
Headache
Hypoglycemia
Thrombocytopenia
Disease due to rapid decompression
Respiratory failure (in cases of pulmonary fibrosis may be irreversible)
Attention to the patient's cardiac history in vasoconstriction and sugar levels in diabetes
Fire hazard

In a study of Karahatay et al. in patients treated with HBO for acute deafness, complications in wound healing and complications from diabetes (diabetic ulcers), concluded that even small abnormalities of otoscopy are at increased risk of developing middle ear barotrauma, if HBOT continues without any precautions [35]. On the other hand, pulmonary barotrauma can be a very serious side effect too [31].

Most patients do not have a particular problem in the chamber's limited space. Some patients need a little time to get used to it, while only few patients find it impossible to continue treatment due to claustrophobia [4]. Fatigue and vomiting might be a result of the use of HBO. Although, reversible myopia, [31] is the commonest side effect due to oxygen toxicity on the lens and can last for weeks or months [23]. Cataract can be another side effect.

Oxygen toxicity in the central nervous system, can rarely cause seizures [12,16], with no permanent damage. Pulmonary toxicity can also be induced. Additionally, the toxicity of O_2 in most tissues of the body can be prevented by 10 minutes periods intervals of air every 30 minutes, [12] since it allows the antioxidant to be unified with the oxygen radicals produced during the hyperoxic period [23].

Headache, hypoglycemia, thrombocytopenia, disease due to rapid decompression [4,23] and respiratory failure (in cases of pulmonary fibrosis may be irreversible) can be presented in some patients. Furthermore, particular attention should be paid to the patient's cardiac history in vasoconstriction and sugar levels in diabetes [19].

The HBO is safe as long as all participants, staff and patients to be aware of the proper procedures - protocols and applied them strictly. Moreover, there is always a possibility for fire hazard, [23] so extensive fire precautions are important to prevent the catastrophe of fire in a hyperbaric environment. The precautions routinely taken contribute to the rare manifestation of this event [3].

Perspectives for Hyperbaric Oxygen Therapy

Future applications of HBOT, include the study of the pathogenesis of septic shock and multiple organ dysfunction syndrome (MODS). In an experimental study of Rinaldi et al in rats, shock and MODS were induced by the substance zymosan (it causes similar clinical picture of septic shock) and 2 of the 4 groups were then exposed to HBO. The development of intestine, liver and lung injury was reduced considerably by the HBO exposure. The zymosan-induced expression of Toll-like receptors TLR2 and TLR4, cytokine production and Nuclear Factor-κB (NF-κB) activation were also remarkably reduced [36]. Based on the assumption that the exact mechanism of action of hyperbaric oxygen has not yet been established, this study lays the foundations for continued experimental studies and the beginning of clinical trials, even in patients with septic shock [4].

Gottlieb and Neubauer have extended their interest in other fields, such as chronic disorders such as cerebral palsy [37]. In the scientific laboratories oriented at diving, a very useful research on the toxicity of O_2 continues. Hyperbaric environment presents an opportunity to study the physiological systems under extreme environmental pressure by an introspection within the limits of physiological tolerance [38].

New applications of HBO include migraine, chronic fatigue syndrome, posttraumatic treatment and rehabilitation, peripheral vascular disease, peripheral neuropathy, treatment after stroke, multiple sclerosis, myocardial infarction, paralysis of the facial nerve and cerebral palsy [11].

In Greece, there is a significant number of doctors who are trained in diving - hyperbaric medicine and there is enough experience in the treatment of patients with chronic osteomyelitis, diabetic foot, ischemic wounds and grafts etc. The presence of HBO centres in large general hospitals, proper education and updating of the health professionals, an adequate legislative framework and regulations for safe operation and use of international and Greek experience, are crucial preconditions for the proper development of HBO [11].

Conclusion

For the standards of contemporary medicine, the HBOT is a relatively new treatment, as it has struggled to be supported scientifically over the last 50 years. HBOT should not be addressed as an almost "magic" treatment for any disease since there are specific indications and therefore it should be treated with caution.

The use of HBOT as an adjunctive therapy according to the internationally recognized indications has become widely accepted, mainly due to the clarification of the physiological effects of hyperbaric oxygen in various systems and its mechanisms. A further investigation is required, in order to ensure the best possible both clinical and therapeutic effect.

It appears that in the treatment of decompression sickness and other diseases HBOT is the treatment of choice. However, the lack of randomized, controlled trials makes it difficult to assess the effectiveness of HBO in many diseases.

As medical thought and technology has matured, it appears that is the proper time for the complete clarification of the potential uses of HBO. Supported methods and advanced technological equipment are necessary in order to develop medical and nursing practice, as well as research documentation.

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