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REVIEW ARTICLE

Hyperbaric Oxygen as a Therapeutic Approach in Periodontitis

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***ABSTRACT*:**
Periodontitis is an infectious disease caused primarily by pathogenic bacteria. Hyperbaric oxygen therapy (HBOT) includes therapeutic administration of 100% oxygen under pressure, which has a deleterious effect on anaerobic microorganisms responsible for periodontal diseases. This review explains on the role of HBOT as a therapeutic measure for individual with periodontal diseases.
Key words: Hyperbaric Oxygen, Periodontitis.

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INTRODUCTION

Periodontitis is an infectious disease caused primarily by pathogenic bacteria. Host factors and environmental factors are equally important determinants of disease occurrence and severity of outcome. The interaction of these factors is well-demonstrated by recent research findings that demonstrate the complexity of the interactions in multifactorial diseases and include roles for specific bacteria and genetic and environmental modifying and risk factors. However, the mere presence of putative periodontal pathogens in the gingival crevice is not sufficient to initiate the inflammation process. Elevation of the relative proportions of these bacteria play a crucial role in causing tissue-damage. In general, treatment of periodontitis is multifaceted and vigorous, including mechanical, antibiotic and antiseptic therapy, and the various treatment approaches should be employed within a short time period. Now a day various novel therapeutic approaches are tried as an alternative to conventional therapy or in combination with conventional therapy to reduce load of periodontopathic pathogens**.** One of the effective therapeutic measures can be use of hyperbaric oxygen (HBO2).

HYPERBARIC OXYGEN

Hyper "is simply an increase," while "baric" refers to the pressure. As a procedure or therapy, hyperbaric is simply the process of increasing the atmospheric pressure around the body. HBO therapy (HBOT) has been described as "a therapy in search of diseases." The pressure is usually about 2-4 absolute atmospheres or ATA; it is essentially the therapeutic use of oxygen as a drug. When oxygen is used as a drug, the dose is controlled by the technology of a HBO2 chamber, which sets the dosage at 100% oxygen. Molecular oxygen is one of the crucial nutrients of the wound and has a central role in the reparative cases. Collagen synthesis, matrix formation, angiogenesis, epithelialization, and bacterial killing require molecular oxygen during the reparative process.

HISTORICAL BACKGROUND

The concept of using respirable gases at raised ambient pressures in the treatment of illnesses dates back to 1662 when hyperbaric air was used by Henshaw for the treatment of "affections of the lung." In 1834 Junod, in France, built a chamber to treat pulmonary conditions at pressures between 2 and 4 atmospheres absolute (ATA). Hyperbaric air was used to treat a wide variety of ailments, including lung infections, cardiac disease, carcinomas, diabetes, and dementia.

Orville J Cunningham is regarded as being the last exponent of compressed air therapy. His observations that people with heart disease and other circulatory disorders did poorly at altitude and improved at sea level formed the basis for his use of hyperbaric air. In 1918, he successfully treated sufferers of the Spanish flu epidemic with hyperbaric air.

Oxygen, which was discovered in 1775 by Joseph Priestley was first used successfully by Behnke and Shaw in 1937 for the treatment of decompression illness. The application of hyperbaric oxygen (HBO2) in clinical medicine really began with separate work done by Churchill–Davidson and Boerema in 1955 and 1956. Churchill-Davidson used it to enhance the radiosensitivity of tumors, while Boerema successfully used it in cardiac surgery to prolong the time allowed for crossclamping of the major vessels.

In 1900's: Hyperbaric spas flourished in the North American continent and Europe. Lack of a firm physiological basis and poor choice of indications caused scientific stasis in this field for many subsequent years

In 1930's: HBO was first used in decompression sickness suffered by deep sea divers to recompress by Behnke
In 1950's: The modern clinical application of HBO began, in parallel with an increased understanding of blood gas analysis and gas exchange physiology
In 1960's two institutions preeminently pursued the clinical aspects of high pressure oxygenation. Dr. Bakers from the University of Amsterdam developed the use of intermittent HBO, for the treatment of gas-gangrene. Second major focus of interest in this area was Royal Infirmary of Glassgow, where various anesthetic and surgical aspects of HBO were applied and discussed. Among these were treatment of necrotizing infections and anesthesia under hyperbaric conditions. In 1965: It was first used to assist wound healing when it was noted that burns of the victims of coalmine explosions treated with HBO2 healed faster.
In 1968: Duke University in North Carolina expanded a long-standing program of environmental physiology with the construction of inter-connected multiplace hyperbaric chambers
Since 1970: Most of the instructional courses, research work and guidance have been provided by Under seas and Hyperbaric Medical Society (Headquarters in Kensington, Maryland). This medical organization publishes guidelines for hyperbaric oxygenation every 2-3 years.

HBO2 CHAMBERS
HBO2 chambers, the main equipment of HBOT, can basically be divided into two types: Monoplace chambers or multiplace chambers.

TYPES OF CHAMBERS
These include:

Multiplace chambers
These units can accommodate between 2 and 18 or more patients and commonly incorporate a minimum pressure capability of 6.0 ATA.

Advantages
1. Constant patient attendance and evaluation (particularly useful in treating evolving neurological diseases such as decompression sickness and cerebral arterial gas embolism).
2. Multiple patients treated per session.
3. Greater working pressure.

Disadvantages
1. Higher capitalization requirements.
2. Major space requirements; basement and/or ground floor level limitations.
3. Higher operating costs.

Monoplace chambers
They were designed for single occupancy and usually constructed of acrylic, having a pressure capability of 3.0 ATA, and compressed with 100% oxygen. The high flow oxygen requirement is ideally supplied via a hospital's existing liquid oxygen system.

Advantages
1. Cost efficient delivery of HBO2.
2. No risk of decompression sickness.
3. Portable, less space, less equipments, no hood or mask.
4. No risk of iatrogenic decompression sickness in patient or staff.

Disadvantages
1. Relative patient isolation.
2. Associated fire hazard.
3. Inability to use certain diagnostic and/or therapeutic equipment.

How does it work?
The earth's atmosphere normally exerts 14.7 pounds per square inch of pressure at sea level. That is equivalent to one atmosphere absolute (abbreviated as 1 ATA). In this atmosphere we breathe approximately 20 percent oxygen and 80 percent nitrogen. During HBOT, the pressure is increased up to two times the normal and the patient breathes 100 percent oxygen while the entire body is totally immersed in 100 percent oxygen. Increased pressure combined with the increase in oxygen content dissolves oxygen into the blood and all other body tissues and fluid at up to 20 times the normal concentration—high enough to sustain life with no blood at all and even with the heart stopped.

Does the increased pressure cause discomfort?
Hyperbaric treatments are painless, but the patient may experience a sensation of "fullness" in the ears, similar to driving down a mountain, flying, or scuba diving. The "full" feeling occurs as the eardrums respond to the change in pressure. The HBOT technician demonstrates how to relieve this fullness before treatment.

What does it feel like?
Once a patient is in the chamber and the door is closed, the oxygen begins to circulate. This starts a gradual increase in pressure—called compression. There may be some slight warmth, but that is temporary. The HBOT technician remains by the chamber throughout the treatment to adjust the rate of compression according to patient tolerance and to coach the patient on relieving the "full" sensation in the ears. Compression generally lasts 10-15 minutes depending on how effective one is at clearing their ears.
When the interior of the chamber reaches the prescribed pressure, the sensation of "fullness" in the ears will cease and the patient is free to rest or sleep. The temperature in the chamber remains at room temperature. The patient may also watch TV, listen to music, or chat with family over the intercom during the treatment, which usually lasts one hour.
Near to the end of the treatment, the HBO technician will gradually decrease pressure that was added at the beginning. This is decompression, which generally lasts 10 to 15 minutes. During decompression, there may be a slight "popping" sensation in the ears as a result of the changing (decreasing) pressure. This "popping" is a normal adjustment, similar to what happens when driving up a mountain or ascending in an airplane. It is usually much easier to equalize ear pressure during decompression than during the compression phase.

Are there any negative after effects?

Generally patients experience no negative after effects from HBOT. However, some patients report a "cracking" sensation in their ears between treatments as oxygen behind the eardrums is absorbed into the blood stream. This can be relieved in the same manner as clearing the ears during compression and decompression. Also, some patients report feeling light headed for a few minutes immediately following a treatment, but this is brief, and they are quickly able to continue with their normal daily activities such as working or driving.

MECHANISM OF ACTION

Hyperbaric oxygen therapy has two primary mechanisms of action: Hyper-oxygenation and a decrease in bubble size. Hyper-oxygenation results from an increase in dissolved oxygen in plasma as a result of increased partial pressure of arterial oxygen. A pressure of three ATA results in 6 ml of O2 being dissolved per 100 ml of plasma, thus rendering as much O2 delivery as by hemoglobin bound O2. It is useful in management of crush injury, compartment syndrome, flap salvage and acute blood loss anemia. High air pressure decreases the volume of gas bubbles in the blood 2-3 times that of normal air pressure. High oxygen (100%) intake saturates the blood plasma with oxygen. It is the primary mechanism at work in management of decompression sickness and arterial gas embolism.

Hyperbaric oxygen therapy exerts both direct and indirect effects against bacteria. Direct bactericidal and bacteriostatic effects occur through the generation of oxygen free radicals.

This free radical oxidizes proteins and membrane lipids, damages DNA, and inhibits metabolic functions essential for the growth of organisms.

Indirect effect of HBO2 in bacterial killing is through improving leukocytes function and is regarded as being more significant than the direct bactericidal and bacteriostatic effects. Neutrophils require oxygen as a substrate for microbial killing, after phagocytosis occurs.

Hypoxia reduces this function. Significant reductions in the killing capacity of leukocytes occur when tissue pO2 falls below 30 mmHg. Infected and traumatized tissues often have a partial pressure of oxygen below this, making them much more susceptible to infection due to decrease in neutrophil activity.

Hyperoxia and HBO2 influence the activity of some antibiotics, enhancing the effectiveness of some and inhibiting others.

PHYSIOLOGICAL BASIS

When we normally breathe air (with 21% O2) at sea level pressure, most tissues need of oxygen are met from the oxygen combined to hemoglobin, which is 95% saturated. 100 ml blood carries 19 ml O2 combined with hemoglobin and 0.32 ml dissolved in plasma. At the same pressure if 100% O2 (oxygen) is inspired, O2 combined with hemoglobin increases to a maximum of 20 ml and that dissolved in plasma to 2.09 ml. The higher pressure during HBO treatment pushes more oxygen into solution. The amount of O2 dissolved in plasma increases to 4.4 ml/dL at a pressure of 2 ATA and to 6.8 ml/dL at 3 ATA. This additional O2 in solution is almost sufficient to meet tissue needs without contribution from O2 bound to hemoglobin and is responsible for most of the beneficial effects of this therapy.

The principal rationale of HBO therapy is to decrease tissue O2 tension. Hence, it is reasonable that primary indications are conditions that include either regional or global hypoxia.

Another group of indications take advantage of the fact that specific micro-organisms are oxygen intolerant. The increase in hydrostatic pressure inherent in HBO therapy provides an important part of the rationale for use in gas lesion diseases such as gas embolism, etc.

TOPICAL HYPERBARIC OXYGENATION

The rationale for the topical approach is that when topical oxygen dissolves in sufficient quantity, it exert bactericidal and angiogenic effects.

The devices employed in the topical application of oxygen typically consist of a compartment to encase the affected portion of the body. The compartments that enclose the wound may be box-like or function as disposable plastic bags.

INDICATIONS

1. Air or gas embolism.
2. Carbon monoxide poisoning or carbon monoxide poisoning complicated by cyanide poisoning.
3. Clostridal myositis and myonecrosis (gas gangrene).
4. Crush injury, compartment syndrome, and other acute traumatic ischemia.
5. Decompression sickness.
6. Enhancement of healing in selected problem wounds;

a. Diabetically derived illness, such as diabetic foot, diabetic retinopathy, diabetic nephropathy.

7. Exceptional blood loss (anemia).
8. Intracranial abscess.
9. Necrotizing soft tissue infections (necrotizing fasciitis).
10. Osteomyelitis (refractory).
11. Delayed radiation injury (soft tissue and bony necrosis).
12. Skin grafts and flaps (compromised).
13. Thermal burns.

CONTRAINDICATIONS

Absolute

a. Untreated tension pneumothorax.

b. Concurrent administration of certain medications like.

1. Bleomycin - Causes interstitial pneumonia.
2. Cisplatin - Causes impaired wound healing.
3. Doxorubicin - Causes cardiotoxicity.
4. Disulfiram - Blocks superoxide dismutase, which is protective against oxygen toxicity.
5. Sulfamylon - Causes impaired wound healing.

Relative

a. Upper respiratory tract infection.

b. Chronic pulmonary obstructive disease.

c. Congenital spherocytosis.

d. Eustachian tube dysfunction.

e. Asthma.
f. Pregnancy.
g. Claustrophobia.
h. Seizure disorder.
i. Hyperthermia.

PREPARATIONS BEFORE HYPERBARIC OXYGEN THERAPY

Medication

The HBO2 technician will obtain a complete drug history before treatment since some medications are not compatible with HBOT. These include: High doses of prednisolone (or similar cortisone type drugs), and morphine, or alcohol, insulin within 8 h of treatment. Such drugs should be substituted for another drug. Patients will be instructed to take a regimen of high potency nutritional supplements containing vitamin E and other antioxidants during a course of HBOT.

Cold and other symptoms

Patients with the symptoms of a cold or the flu, fever, cough, sore throat, runny nose, cold sore, nausea, vomiting or diarrhoea are not helped by oxygen. HBO2 treatments may need to be postponed until symptoms have subsided.

Smoking

Hyperbaric oxygen therapy will not be effective in patients who use tobacco in any form like cigarettes, pipe tobacco, and cigars, as well as chewing tobacco and snuff.

Cosmetics

Cosmetics, hair spray, nail polish, perfume, or shaving lotion containing petroleum, alcohol or oil base are not allowed while in the HBO2 chamber. It is important to discuss all skin care products with the HBO2 technician, so they may assure safety.

Clothing

Patients are provided with 100% cotton gowns to wear during treatment. No articles containing nylon or polyester can be worn in the chamber.

CELLULAR AND BIOCHEMICAL BENEFITS OF HYPERBARIC OXYGEN

• Promotes angiogenesis and wound healing
• Kills certain anaerobes
• Prevents growth of species such as Pseudomonas
• Prevents production of clostridial alpha-toxin
• Restores neutrophil mediated bacterial killing in previously hypoxic tissues
• Reduces leucocyte adhesion in reperfusion injury preventing the release of proteases and free radicals which cause vasoconstriction and cellular damage.

MEDICAL USES OF HYPERBARIC OXYGEN

Regional hypoxia (compromised graft flap, osteoradionecrosis (ORN), wounds and ulcers), crush injuries, thermal burns, global hypoxia (CO, CN intoxication, and severe anemia), infections (clostridial myonecrosis, necrotizing fasciitis, refractory osteomyelitis, and rhinocerebral mucormycosis), gas lesion conditions (gas embolism and decompression sickness).

THERAPEUTIC EFFECTS OF HYPERBARIC OXYGEN

Hyperoxygenation causes (i) immune stimulation by restoring white blood cell (WBC) function and enhancing their phagocytic capabilities and (ii) neovascularisation in hypoxic areas by augmenting fibroblastic activity and capillary growth. This is useful in radiation tissue damage and other problem wounds. Vasoconstriction reduces edema and tissue swelling, while ensuring adequate oxygen delivery and is thus useful in acute trauma wounds and burns.

Bactericidal for anaerobic organisms and inhibits the growth of aerobic bacteria at pressures >1.3 ATA. It inhibits the production of alpha-toxin by Clostridium welchii and is synergistic with aminoglycosides and quinolones. Thus, it is lifesaving in gas-gangrene and severe necrotizing infections.

Reactivates “sleeping cells” in the penumbra region around central dead neuronal tissue. This is the basis of its use in neurological conditions.

Reduces adherence of WBC’s to capillary walls and may be useful in acute brain and spinal cord injury.

BENEFICIAL EFFECTS OF HYPERBARIC OXYGEN

• Safe therapy with very few and minor side-effects
• Addition of HBO obviates the need for frequent surgical procedures, promotes healing and early mobilization of the patient
• Reduces length of hospitalization and thereby overall treatment and rehabilitation costs
• Emerging role in indications which have lifetime disabilities.

CONTRAINDICATIONS OF HYPERBARIC OXYGEN

Absolute contraindication in patients with untreated pneumothorax and relative contraindications are in patients with optic neuritis, acute viral infection, congenital spherocytosis, uncontrolled acute seizures disorders, uncontrolled high fever, upper respiratory tract infections, pregnancy (if required), psychiatric problems, history of prior thoracic or ear surgery, which would make it impossible to equalize middle ear pressure or pulmonary pressure.

EFFECT OF HYPERBARIC OXYGEN THERAPY ON OSTEORADIONECROSIS

Osteoradionecrosis of the mandible is a significant complication of radiation therapy for head and neck cancer.

In this condition, bone within the radiation field becomes devitalized and exposed through the overlying skin or mucosa, persisting as a nonhealing wound for 3 months or more. In 1926, Ewing first recognized the bone changes associated with radiation therapy and described them as “radiation osteitis.” **In 1983, Marx** proposed the first staging system for ORN that also served as a

treatment protocol. This protocol advocated that patients whose disease progressed following conservative therapy (HBO, local wound care, and debridement) were advanced to a radical resection with a staged reconstruction utilizing a nonvascularized bone graft.

The basis for applying HBO to ORN is an extension of Marx's theory that ORN is the result of tissue hypoxia, hypocellularity and hypovascularity. The purpose of HBO is to increase the blood-tissue oxygen gradient, which enhances the diffusion of oxygen into hypoxic tissues. The increased oxygen supply stimulates fibroblast proliferation, angiogenesis, and collagen formation. In addition, the increased oxygen tension is bactericidal and bacteriostatic.

After evaluating the literature, it appears clear that advanced ORN requires aggressive surgical therapy, and it has become increasingly evident that HBO alone has minimal if any benefit in the treatment of advanced ORN. In addition, as some recent publications have suggested, HBO may not have a clear role in the treatment of advanced ORN when a vascularized reconstruction is used. The use of HBO in early and intermediate ORN remains important because the benefit seems clear based on numerous retrospective studies. The morbidity of HBO is minimal including transient myopia, middle ear barotrauma and seizures. Absolute contraindications for HBO include optic neuritis, history of chronic obstructive pulmonary disease or congenital pulmonary blebs.

Reduces half-life of carboxy hemoglobin from 4 to 5 h to 20 min or less and is the treatment of choice for carbon monoxide poisoning in fire victims. **Mechanical effects**: Direct benefit of increased pressure helps reduces bubble size in air embolism and decompression illnesses.

HYPERBARIC OXYGEN AND PERIODONTITIS

Mechanism

Hyperbaric oxygen therapy showed to increase oxygen distribution at the base of the pocket which is deleterious to periodontal pathogens, particularly to the anaerobic microorganisms. Cultivation of plaque microorganisms from sites of chronic periodontitis reveals high percentages of anaerobic (90%) bacterial species. HBO2 increases generation of oxygen free radicals, which oxidize proteins and membrane lipids, damage deoxyribonucleic acid and inhibit bacterial metabolic functions. It also facilitates the oxygen-dependent peroxidase system by which leukocytes kill bacteria. HBO2 also improves the oxygen-dependent transport of certain antibiotics across bacterial cell walls.

In this way HBOT results in inhibition of bacterial growth. While on the other hand, HBOT would also allow the ischemic tissues to receive an adequate intake of oxygen sufficient for a rapid recovery of cell metabolism. Oxygen tension in periodontal pockets is very low (pO2 5-27 mmHg) when compared with atmospheric pO2 (155 mmHg), the arterial blood pO2 (95 mmHg), and the venous blood pO2 (20-40 mmHg). Fibroblast and leukocyte function are severely compromised when pO2 is ≤30 mmHg. HBO2 increases collagen formation for capillary growth. HBO2 also promotes fibroblast replication and collagen formation, while the patient is in the hyperbaric chamber. It also increases bactericidal function of leukocytes. HBOT also improve gingival microcirculation and increase gingival blood flow.

Thus in periodontal tissues, HBOT showed to have a deleterious effect on periodontal microorganisms as well as beneficial effects on periodontal healing by raising oxygen tension in pocket.

Evidence

Manhold et al in 1974 showed through an experiment that some commercially available oxygenating agents demonstrated shorter healing times when applied on inflamed gingiva.

Hirsch et al in 1994 studied the effect of locally released oxygen on the development of plaque and gingivitis in man and concluded that there was no significant effect of oxygen on plaque formation, crevicular fluid flow, or the number of gingival bleeding sites.

Schlagenhauf et al in 1994 used repeated subgingival oxygen irrigations in previously untreated periodontal patients. They concluded that repeated oxygen insufflations resulted in a significant clinical improvement of the periodontal baseline conditions superior to the one found in the control.

Gaggl et al in 2006 applied localized oxygenation in contrast to systemic oxygen therapy, to help treat acute necrotizing periodontal diseases. In both groups of patients, colonization with ***Prevotella intermedia*****,** ***Tannerella forsythia*****, and** ***Treponema denticola*** was initially positive. None of these microorganisms were completely eradicated in any of the patients in the group without oxygen therapy within the first 10 days.

Signoretto et al in 2007 evaluated the effects of HBO2 on patients suffering from adult chronic periodontitis in comparison with surgical intervention (scaling and root planning [SRP]),as well as the effects of a combination of both therapies on the evolution over time of the microflora of the periodontal pockets and found that the combination of HBO2 and SRP substantially reduced (by up to 99.9%) the Gram-negative anaerobe loads of the subgingival microflora. The low values of pathogens persisted for at least 2 months after the therapy.HBO2 or SRP alone produced a temporarily more limited effect on periodontal anaerobes. In addition, molecular detection of the main periodontopathogenic bacteria significantly reduced in the number of dental sites, which harbored them.

Nogueira-Filho et al in 2010 evaluated the effect of HBOT as an adjunct to SRP on the treatment of severe cases of periodontitis. They concluded that HBOT had a shortterm beneficial effect on pocket reduction and bacterial elimination, and may be considered potential adjunct therapeutic option to improve the clinical outcomes of scaling in severe cases of chronic periodontitis.

Chen et al in 2012 investigated the effects of HBO2 on aggressive periodontitis (AgP), and subgingival obligate anaerobes in Chinese patients and concluded that HBO2 inhibits the growth of subgingival obligate anaerobes and facultative anaerobes and *Bacteroides melaninogenicus* thus promoting healing of peridontium, which will be of help in the treatment of AgP. HBO2 therapy combined with SRP appears to be even better for synergistic treatment of AgP. The effects can last >2 years.

Shannon et al in 1988 tested oxygen effects on healing gingival wedge excisions using Sprague-Dawley rats operated controls were maintained at normal pressure in room air experimental groups of 40 rats each were exposed for 90 min daily to one of the following: (1) 20.8% oxygen at 2.4 atmospheres pressure, (2) 100% oxygen at 1 atmosphere pressure, and (3) 100% oxygen at 2.4 atmosphere pressure. Histometric analysis was performed using light microscopy. The controls failed to show healing comparable to experimental animals until the end of 2 weeks. Enhanced connective tissue healing was most significant in the 2.4 atmospheres pressure groups at 3 and 6 weeks when compared with controls.
However, by 12 weeks, no significant differences could be detected. Early connective tissue adaptation does not imply eventual attachment as epithelial down growth progressively displaced the connective adjacent to the root in both experimental and control groups. Oxygen can also be applied locally when the oral mucous membrane is diseased, such that the resorption barrier is reduced, and there is only a short distance of diffusion. In addition, gingival and periodontal infections can also be caused or even dominated by anaerobic microorganisms, making it desirable to impair the milieu to reduce the growth of anaerobic microorganisms.
Several studies have described the beneficial role of HBO in the treatment of various human pathologies either alone or in combination with other therapies. Very few studies have been conducted to analyze the effects of HBO therapy on periodontal disease.

Chen et al in 2002 showed that HBO increases local oxygen distribution, especially at the base of the periodontal pocket. This could inhibit the growth of anaerobe bacteria, and also on the other hand, would allow the ischemic tissues to receive an adequate intake of oxygen sufficient for a rapid recovery of cell metabolism.
A combination of both HBO and SRP substantially reduces (by up to 99.9%) the Gram-negative anaerobe loads of the subgingival microflora. HBO or SRP alone produces a temporarily more limited effect on the periodontal anaerobe load, which later reverts to the pretreatment values. HBO exerts its killing action specifically against those micro-organisms which, via the production of sophisticated virulence determinants, are responsible for direct tissue damage. The presence of high counts of periodonto pathogenic bacteria enhances the inflammation response which, in turn, is mainly responsible for the clinical signs of periodontal diseases such as gingival edema, bleeding and migration of the gingival crevice with eventual formation of a periodontal pocket. These pathological effects can be measured by means of specific parameters. One of these is the gingival index, which is a reliable parameter for evaluating the degree of inflammation at the gingival level.

Chen et al. in 2003, have reported the effects of HBO in a controlled study of periodontitis in 24 patients. The study teeth were divided into four groups based on treatment: (1) HBO therapy, (2) HBO therapy + scaling, (3) scaling, and (4) control. Highly significant differences in gingival indices (GI), sulcus bleeding indices (SBI), probing depth (PD), attachment loss (AL), plaque index (PLI), and gingival blood flow (GBF) were seen in the HBO, the HBO + scaling and the scaling groups compared to the control group. The numbers of subgingival anaerobes as well as the numbers of rods, fusi and spiro were reduced markedly in these three treatment groups. Statistically greater differences in clinical indices, GBF, subgingival anaerobes number and number of rods were found. Fusi and spiro were found by comparison of HBO + scaling and HBO groups, as well as between the HBO + scaling and scaling groups, but no significant differences were observed in GI, SBI, PD,or AL between the HBO and scaling groups. Results of this study confirmed that HBO therapy combined with scaling and root planning was the most beneficial in the treatment of periodontitis and treatment effect would last >1-year.

Chen et al. in 2003 studied the therapeutic effects and holding time of HBO on severe periodontitis patients. 30 cases with periodontitis were selected and randomly divided into two groups, that is, the HBO group was exposed to a pressure of 0.25 MPa and control group were rinsed. GI, SBI, PLI, PD, AL and gingival crevicular fluid (GCF) were measured during the first and last clinical visits and 1-year after HBO therapy. The GBF was measured by laser Doppler flow meter. HBO can decrease GI of patients with periodontitis by 1.1, SBI by 1.2, PD and AL by 0.7 mm, volume of GCF by 2.0, and significant differences could be seen in the above indices between pre- and post-HBO therapy. The GBF had a 1.8-fold increase after HBO exposure. GI and SBI 1-year after HBO therapy were larger than that of time after HBO therapy. There were no significant differences in the PLI, PD, AL, GCF, and GBF between post HBO therapy and 1-year after HBO therapy. It was concluded that HBO had good therapeutic effect on severe periodontitis, and this effect lasted for >1-year.

Coulthard et al in 2003 investigated the effectiveness of HBO therapy for irradiated patients who required dental implants using data from randomized control clinical trials (RCT's). There was no RCT's comparing with and without HBO for implants treatment in irradiated patients.

Chen et al in 2012 investigation conducted by chen et al provided good evidence that HBO2 inhibits the growth of subgingival obligate anaerobes and facultative anaerobes and Bacteroides melaninogenicus thus promoting healing of periodontium, which will be of help in the treatment of aggressive periodontitis (AgP). HBO2 therapy combined

with scaling and root planning appears to be even better for synergistic treatment of AgP. The effects can last >2 years. The mechanism of HBO2 therapy on AgP is not clear. However, following might be involved in the mechanism of action of HBO2: An inhibition of growth and reproduction of subgingival plaque and anaerobes, and in particular the growth of obligate and facultative anaerobes and B. melaninogenicus at the base of the pockets. Collectively, these results indicated a therapeutic benefit of HBO2 for the treatment of patients with AgP.
Microorganisms can secrete different enzymes that can destroy collagen and growth factors. When the oxygen concentration in gingival tissue is low, amount of bacteria in the periodontal pockets increases. HBO2 seems to effectively decrease the amount of bacteria and simultaneously inhibit collagenase secretion. A study by **Rabkin and Hunt in 1987** showed that oxygen at 2.0 ATA could inhibit the growth of certain pathogens related to periodontitis. HBO2 has also shown bactericidal/ bacteriostatic effects on Actinomyces, Bacteroides, and Streptococcus.

Hyperbaric Oxygen and Flaps

The role of the elective hyperbaric oxygen protocol when either muocutaneous or free vascularized soft tissue or bone transfers are employed in radiated tissue is to develop a vascular and cellular tissue bed into which these flaps can heal. If such flaps are required as part of elective construction efforts the patient undergoes 20 sessions of hyperbaric oxygen first, followed by the planned surgery. The patient returns to the hyperbaric oxygen chamber for the remaining 10 sessions when he or she has sufficiently recovered from the surgery (usually within a week or two). Because the hyperbaric oxygen angiogenic effects are permanent, a delay between the first 20 sessions and the surgery is not critical. In the same manner, should the patient require additional elective surgery later, a second protocol of hyperbaric oxygen is not necessary. However, it is important that the initial hyperbaric oxygen protocol of 20 sessions prior to surgery followed by 10 sessions after surgery be complete with no interruptions of more than 3 days. An interrupted or incomplete oxygen protocol doesn't develop its maximal angiogenic benefit and therefore place the patient at greater risk for wound dehiscence, wound infection and delayed wound healing. Related to wound infections the pattern of results was similar. The hyperbaric oxygen group showed an infection rate of 6% of which only 2.5% required reoperation, while the non-hyperbaric oxygen group showed an infection rate of 24% of which 16% were major infections requiring prolonged treatment and additional surgery. No doubt the use of this elective surgery protocol of hyperbaric oxygen has a proven outcome efficiency in both scientific studies and clinical experience.

Chronic periodontitis

Animal study

Robert H. Guenthcrman et al (1972) Studied the effect of increased blood oxygen tensions on artificially induced Periodontal disease.
Periodontal pathology induced in dogs, a process thought to be caused primarily by anaerobic bacteria, was treated with hyperoxygenation.
Blood oxygen tensions were elevated to at least 1900 mm Hg, by means of a hyperbaric oxygen chamber for two hours twice a day, two days a week for four weeks. Clinical appearance and loss of alveolar bone was recorded in treated and untreated animals.
The animals receiving hyperbaric oxygen had gingival tissues that appeared clinically healthy and were found to have modest bone loss at the end of eight weeks. On the other hand the control animals often had grossly inflamed gingiva and marked loss of bone at the end of eight week period.

Chen T, Lin S, Liu J, Xu B, Hai J, Tang D IN 2002 Studied the effects and the therapeutic mechanism of hyperbaric oxygen (HBO) on prostaglandin E(2) (PGE(2)) in alveolar bone and gingiva of experimental periodontitis in animal. Experimental periodontitis was produced by silk thread sutures combined with high content sugar diet. For HBO therapy, they were exposed to a pressure of 0.25 MPa (2.5ATA), breathing pure oxygen one session a day for 60 min. The treatment course was 2 weeks. The value of PGE(2) in gingiva and alveolar bone was analyzed by enzyme immunoassay (EIA). The value of PGE(2) in gingiva of control group was 3.21 ng/g, and that of PGE(2) in alveolar bone was 3.22 ng/g. The contents of PGE (2) in gingiva (13.96 ng/g) and alveolar bone (13.32 ng/g) of periodontitis group increased markedly than control group ($P < 0.01$). The contents of PGE(2) in gingiva (5.21 ng/g) of HBO group were 62.7% which was lower than that of periodontitis group, and the value of PGE(2) in alveolar bone (4.05 ng/g) were 69.6% lower than that of periodontitis group. The difference of PGE(2) in gingiva or alveolar bone was significant for the HBO group and periodontitis group ($P < 0.01$). CThe authors concluded that, the contents of PGE(2) in alveolar bone and gingiva increased markedly when experimental periodontitis has formed. The value of PGE(2) in alveolar bone and gingiva reduce markedly after HBO exposure, and the decreased rate of PGE(2) in alveolar bone is more evident than that of PGE(2) in gingiva after HBO therapy.

Chen T, Zhou Y, Liu J, Xu B, Wu Z , Li D., 2002 , studied the effects of Hyperbaric Oxygen (HBO[2]) in a controlled study of periodontitis in 24 patients. The patients received either HBO[2] or no HBO[2], and study teeth were divided into 4 groups based on treatment: 1- HBO[2] therapy, 2- HBO[2] + scaling, 3-scaling, 4- control. The indices of periodontal disease and gingival blood flow (GBF) were measured . The microorganisms in a periodontal pocket were stained and the percentage of straight rods (Rods), curved rods (Cur), fusiforms (Fusi) and spirochetes (Spiro) were observed. The numbers of anaerobic organisms were measured by routine anaerobic culture. Highly significant differences in Gingival Indices (GI), Sulcus Bleeding Indices (SBI), Probing Depth (PD), Attachment Loss (AL), Plaque Index (PLI), and GBF were seen in the HBO[2], the

HBO[2] + Scaling and the Scaling Groups compared to the Control Group (P<0.01). The number of subgingival anaerobes as well as the number of Rods, Cur, Fusi, and Spiro were reduced markedly in these three treatment groups. Statistically greater differences in clinical indices, GBF, subgingival anaerobe number and number of Rods, Cur, Fusi and Spiro were found by comparison of HBO[2] [+] Scaling and HBO[2] Groups, as well as between the HBO[2] [+] Scaling and Scaling Groups, but no significant differences were observed in GI, SBI, PD, or AL between the HBO[2] and Scaling Groups. The authors conclude that, HBO[2] had beneficial therapeutic effects on severe periodontitis. HBO[2]therapy combined with scaling and root planing was the most beneficial in the treatment of periodontitis. Clinical follow-up suggests that this treatment effect could last more than 1 year.

HYPERBARIC OXYGEN AND IMPLANT

Dental implants offer a way to replace missing teeth. Patients who have undergone radiotherapy or surgery may benefit from reconstruction with implants.

Mechanism

Hyperbaric oxygen has been shown to affect angiogenesis, bone metabolism bone turnover. In relation to radiotherapy, HBO2 can thus counteract some of the negative effects from irradiation and actually act as a stimulator of osseointegration. The exact mechanisms at the cellular level where HBO2 act remain obscure. It has been recently shown that HBO2 and basic fibroblast growth factor (bFGF) acts synergistically in irradiated bone. Factors that could be involved in bone protection by bFGF and HBO2 are bone marrow radioprotection, induction of oxygen radical scavengers and production of different cytokines.

Hyperbaric oxygen and bFGF can also enhance the level of insulin-growth factor, which is known to promote proliferation and differentiation of bone. They could also affect bone progenitor cells by promoting DNA synthesis, stimulating enzymes involved in bone formation or affect membrane receptors. HBO2 has furthermore been shown to affect the interface between the titanium implant and bone, which could be different from cellular effect.

Oxygen under hyperbaric conditions could thus play a role in osseointegration by affecting bone cell metabolism, implant interface and capillary network in the implant bed.

Evidence

Taylor and Worthington in 1993 reported that when implants were placed in conjunction with HBOT healing was more reliable, although still slow. They recommended HBO2 for patients treated with >50 Gy.

Marx and Morales in 1998 reported a 5-year survival in 622 out of 748 osseointegrated implants after HBO2 treatment.

Granström et al in 1999 in a case-controlled study found that about 53.7% implants failed in the irradiated group compared to 13.5% in nonirradiated group and 8.1% for irradiated HBO2-treated group.

Esposito et al in 2008 in a systematic review found only one andomized controlled trials (RCTs) comparing HBO2 with no HBO2 for implant treatment in irradiated patients and they concluded that HBOT in irradiated patients requiring dental implants may not offer any appreciable clinical benefits. There is a definite need for more RCTs to ascertain the effectiveness of HBO2 in irradiated patients requiring dental implants.

SAFETY OF HBOT

HBOT is a relatively safe treatment, but does carry some risks, due to the increased pressure and hyperoxia. In general possible complications of HBOT are:

Ocular effects: The most common effect of oxygen toxicity is a progressive, reversible myopia, thought to be due to physical lens deformation. There is no evidence for other optical side-effects such as cataracts.

Barotraumatic lesions of middle ear, inner ear, nasal sinus, lungs and teeth, are caused by compression or expansion of enclosed gas volume.

Oxygen toxicity in central nervous system causing generalized convulsion (Paul Bert effect) and in lung causes (Lorraine Smith effect) occasional dry cough and burning substernal sensations. Prolonged hyperoxygenation causes alveolar exudation and edema.

Confinement anxiety

The only absolute contraindication to HBO2 is an untreated tension pneumothorax, and this must be excluded before treatment. Relative contraindications include impaired pressure equalization, pregnancy and cardiac disease.

CURRENT EVIDENCE

Microbiological effect

Microbiological data indicate that the combination of HBO2 and scaling and root planning (SRP) substantially reduced (by up to 99.9%) the Gram-negative anaerobe loads of the subgingival microflora. The low values of pathogens persisted for at least 2 months after the therapy. In addition, molecular detection of the main periodontopathogenic bacteria significantly reduced in the number of dental sites which harbored them. HBOT combined with SRP was the most beneficial in the treatment of aggressive periodontitis when compared with SRP and HBOT alone. The therapeutic effect of HBOT is mostly through inhibition of the growth of subgingival anaerobes. Clinical follow-ups suggest that the effect could last more than 2 years.

Biological effect on periodontal tissue

Animal studies showed that HBO2 can increase the amounts of opened blood vessels, and increase the gingival blood flow and blood current velocity, decrease the blood concentration.

HBO2 may regulate the microcirculation by changing the opened blood vessels and endoepithelial cell metabolism.

Periodontal clinical indices and gingival blood flow markedly decreased after HBOT, and the therapeutic effects could last more than 1 month. Contents of prostaglandin E2 (PGE2) in alveolar bone and gingiva increased markedly when experimental periodontitis has

formed. The value of PGE2 in alveolar bone and gingiva reduce markedly after HBO2 exposure.

Some evidences available showing beneficial therapeutic effect of HBOT in cases of periodontitis. **Chen et al in 2002** showed that HBO2 combined with SRP was more beneficial than SRP or HBOT alone in the treatment of periodontitis. Furthermore, HBOT may be considered as potential adjunct therapeutic option to SRP to improve clinical outcome even in severe cases of periodontitis and its effect could last more than 1 year. HBOT is also effective on the aged with periodontitis it may be an important technique of non-operative treatment. HBO2 is effective in treating periodontitis after periodontal flap surgery.

FDA-Approved Conditions for Hyperbaric Oxygen Therapy Treatments

HBOT Provides Healing to All Types of Health Concerns

Hyperbaric oxygen therapy is FDA-approved for multiple conditions. By exposing the patient to 100% oxygen and higher atmospheric pressure, HBOT provides many benefits, including:

- Increasing the amount of oxygen intake to cells
- Aiding in circulation
- Increasing the diameter of blood vessels
- Assisting in cleansing the patient's body of toxins
- Enhancing white blood cell action
- Rejuvenating skin cells
- Increasing energy
- Increasing endurance

Treatment Indications for HBOT (FDA Approved)

- Air or gas embolism
- Carbon monoxide poisoning and carbon monoxide poisoning complicated by cyanide poisoning
- Clostridial myositis and myonecrosis (gas gangrene)
- Crush injury, compartment syndrome, and other acute traumatic ischemias
- Decompression sickness
- Enhanced healing of selected problem wounds
- Exceptional blood loss anemia
- Necrotizing soft tissue infections
- Osteomyelitis (refractory)
- Delayed radiation injury (soft tissue and bony necrosis)
- Skin grafts and flaps (compromised)
- Thermal burns
- Intracranial abscess

CONCLUSION

Hyperbaric oxygen has been successfully used in several medical applications. The therapeutic effect is related to elevated partial oxygen pressure in the tissues. Dental patients too could be benefited with this treatment approach along with the advancement in the medicines and technical equipment's used in the patient care.

Although available evidences are few, HBOT was shown to improve gingival blood flow and microcirculation, inhibit the growth of periodontal pathogens in periodontal pocket when used alone or in combination with conventional periodontal therapy. In future, further research will required to be conducted to prove potential benefits of HBOT.

Although HBOT is not without side-effects, most specialists in the field consider the risk profile for patients acceptable when treating the conditions for which HBO2 is clearly indicated.

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