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The Potential of Hyperbaric Oxygen Therapy

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"A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather its opponents eventually die, and a new generation grows up that is familiar with it."

Max Planck

INTRODUCTION

The use of compressed air as a therapeutic treatment has been around since the 1660's. With the discovery of oxygen in 1775, the development of better pumping systems and a better understanding of the role of oxygen in human and animal biology have expanded oxygen's medical use. Since the early 1900s an observational approach to using hyperbaric oxygen has resulted in its application to a number of different diseases with improvements in clinical outcome. Recently, through applications in veterinary and human medicine, hyperbaric oxygen therapy (HBOT) is set to expand in clinical application in areas that were unheard of twenty years ago.

The State of HBOT

In the last 40 years, through careful observation, application and experimentation, HBOT has shown remarkable promise to treat a number of different diseases, either as a direct therapy, as in the case of stroke (1-5) and heart attacks (6-10) , or as an adjunct therapy to improve outcome or reduce side-effects in cancer chemo- or radiotherapy (11). Yet due to the lack of hyperbaric fellowships, which has a direct impact on the number of current practicing physicians in the use of hyperbaric medicine, high initial up-front costs for hyperbaric chambers and poorly understood mechanisms of action on the body, this technology has lagged in its medical application by US physicians. HBOT is mostly used in the US to treat decompression sickness (the bends), bacterial infections that are not affected by standard antibiotic treatment and as a adjunctive therapy for standard treatments in wound healing, skin grafts and severe cases of blood loss or anemia (12).

The applications approved for reimbursement by the Centers for Medicare and Medicaid Services (CMS) are fewer that what are approved in the medical communities of Europe, Russia, Japan and China (12). In Europe, over 30 applications are recommended and experimental approaches for treatments are less restricted. The two major impediments to expansion of HBOT use in the United States are: 1- The dearth of clinical and basic research funding for HBOT; 2- Current insurance-based reimbursement system. Since only 14 reimbursable indications exist for HBOT in the Unites States, applications are tightly limited to "best practices". The only way to receive approval via CMS or other insurance agencies is to prove that a treatment is not experimental and provides a real and reproducible benefit to patients. The gold standard for proving a beneficial effect in medicine in the United States is the clinical trial.

Clinical trials are normally randomized, double-blind, placebo-control studies: the patient receiving the treatment (as well as the doctor administering the treatment) does not know if they are receiving the actual treatment or a sham treatment. This arrangement ensures that patients are not "fooling" themselves, ensuring that the study measures a real change and not a psychological one. The costs in doing these types of studies are substantial, but the major limitation remains one of long-term support: oxygen cannot be patented (unlike pharmaceuticals),

it is considered a drug, it remains poorly understood, there is very little training in its use to physicians and insurance companies will pay for very few indications. Yet, it is due to the limited number of hyperbaric trained physicians and researchers that we currently have the knowledge and ability to continue its use.

HBOT in Medicine

HBOT has been safely treating a variety of medical conditions for over 100 years [13-15]. HBOT is a treatment in which the entire body is exposed to 100 % oxygen under increased pressure. By augmenting total gas pressure, oxygen levels in all body organs can be increased dramatically [13, 15] sparing and maintaining organs that are oxygen deprived, removing obstructions in blood flow caused by gas bubbles, and inhibiting certain types of bacteria [16-18].

Recent studies reveal that HBOT has other beneficial effects. In traumatic brain injury (TBI) studies of rats and mice treated with HBOT, behavioral and neurological damage is spared or reversed [19-26]. In humans, clinical reports show similar effects. Armed service personnel that were diagnosed with mild-to-moderate TBI shows that repeated HBOT exposures produce beneficial effects in terms of brain function [27, 28]. Recent studies reveal that HBOT has other beneficial effects that can treat stroke and in some cases prevent its reoccurrence. HBOT has been studied in animal models of stroke [2, 29-35], clearly demonstrating a protective effect with single exposures. In humans, several thousand case studies [12] reveal a therapeutic and brain sparing effect when HBOT is applied in the first few hours of stroke. What is most interesting is that the protective effect for stroke is seen with a single treatment of hyperbaric oxygen in the immediate time after a stroke [36, 37]. HBOT appears to hold an even greater potential as a post-stroke recovery therapy [38, 39] with multiple exposures.

How is it that a single therapy can produce such remarkable changes? Given the role that oxygen plays in the cellular function of the brain, it should not be surprising that HBOT provides healing and protection. HBOT probably produces all these beneficial effects though multiple, parallel pathways. In rats, data demonstrates that HBOT promotes new neuron [40] and blood vessel regrowth [41-43]. Cellular metabolism and cell survival is improved [44-46] and cellular death [22, 45] is inhibited. Inflammation of the brain after TBI is a common response to damage (47), but inflammation is reduced [48] by HBOT, as well as brain bleeding [49, 50] and brain swelling [51, 52]. It is still not known if these are all the benefits that HBOT provides or just the most obvious that have been observed to date. It seems apparent that the synergistic effect that HBOT has with other treatments [53, 54], strongly suggests that combining therapies with HBOT could yield better results than either alone. Further development of HBOT will require a new openness by researchers, hospitals and clinics to participate in studies that develop this field.

HBOT in Neurological Diseases

Current and past research on HBOT reveals that this technology still has room for growth. Brain trauma and stroke are only two areas in the field of neurology that HBOT has shown excellent clinical outcome. Disorders like autism [55, 56], cerebral palsy [57] and multiple sclerosis [58] have shown positive outcomes for patients undergoing HBOT. This suggests that other diseases of the brain, like Alzheimer's (AD) and Parkinson's (PD), may be treatable with HBOT.

In reports of omental transplantation into the brains of AD patients [59-62], symptoms of AD are reversed and reduction in a key determinant of AD (senile plaques) was observed [63]. The omentum is a tissue that can induce the regrowth of blood vessels, when transplanted into the brain. In HBOT the induction of blood vessel regrowth is observed in the brain [43], as well.

In Parkinson's disease, transplantation of dopamine neurons is considered the most promising strategy for reversing the disease. Yet, the most important factor in determining success is the regrowth of blood vessels to support the new transplant. In rat models of PD,

transplants [64, 65] show long-term survival only when there is robust new growth in local blood vessels. Again, HBOT has shown the ability to stimulate new blood vessel growth in areas of implanted tissue.

As a better understanding of the dose, duration and frequency of treatment with HBOT is established, new avenues for treatment of diseases of the brain will be opened. The addition of surgical and/or pharmaceutical adjunct treatments with HBOT should help accelerate the investigational and clinical application in the near future.

HBOT in Cancer Treatment

Currently, 1 in 4 deaths is due to cancer in the United States [66]. It is a continuing public health problem that strikes across gender and racial lines. HBOT is used in conjunction in chemotherapy and radiotherapy for cancer treatment to offset side effects. It appears that HBOT may have anti-tumor abilities in and of itself. Recent studies demonstrate that in implanted tumors of rats, HBOT can reduce their size and induce apoptosis (programmed cell death) [67]. One objection regarding HBOT in cancer therapy was the promotion of cell division and blood vessel growth, which was hypothesized to stimulate tumor and cancer metastases. Recent studies reveal that [68-70] no such cancer growth promoting events have been observed. At the same time, coupling the known anti-tumor properties of HBOT with anti-cancer therapies, improves outcomes in a variety of experimental cancers [71-76].

In the near future, HBOT should be made standard clinical practice as a main therapy to treat cancer, especially in photodynamic therapy [77, 78]. In the next few years, as HBOT is recognized as a vastly underutilized medical tool, more clinical research will be devoted to studying the most effective way to treat cancer with HBOT, especially with the standard therapies that are used with chemotherapy, radiotherapy and surgery.

HBOT in the Future

Hyperbaric oxygen therapy in the last 100 years has gone from being ignored by most physicians, to being recognized as an important tool in the medical arsenal. It is still highly underutilized by hospitals and physicians, but as it gains acceptance in terms of effectiveness and cost savings [79], the benefits to patients and to the economy will be enormous. Given that TBI, stroke and heart attack account for an aggregate cost to society of ~$200 billion dollars annually, any improvement in survival and quality of life will be an enormous plus to the citizens of this country.

This small review only provides a glimpse at the promise of HBOT. In other medical areas, including gerontology, ophthalmology, immunology, gastroenterology and pediatrics the field of HBOT remains untapped or underutilized. With so much work to be done and many benefits uncovered to date, HBOT may prove to be an indispensable tool in a short amount of time. In the near future, as more research uncovers the benefits of oxygen therapy at the cellular and molecular level, it may open up an entire sub-discipline in medicine for gas therapies that will include carbon monoxide, hydrogen sulfide and nitric oxide [80]. These preliminary steps may be essential in life extending therapies as well, as more understanding is reached with these mitochondrial regulating gases.

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