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Hyperbaric Oxygen Therapy in the Treatment of Stroke

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"Each year in the United States, there are more than 700,000 [cases of people suffering] strokes. Stroke is the third leading cause of death in the country. And stroke causes more serious long-term disabilities than any other disease. Nearly three-quarters of all strokes occur in people over the age of 65 and the risk of having a stroke more than doubles each decade after the age of 55." (National Institutes of Neurological Disorders and Stroke, NIH, Centers for Disease Control and Prevention, 2004)

INTRODUCTION

In the U.S. it is estimated that 6.4 million adults have suffered a stroke and another 13 million may have experienced a "silent stroke", loss of brain cells without visible symptoms. The financial burdens associated with stroke treatment and recovery (both direct and indirect) is estimated to be $73 billion dollars for 2010. In spite of modest declining rates of strokes for the last 7 years, the prevalence of this disease continues to constitute a major source of long-term disabilities for the American public, as well as an expanding cost in health care and household budgets.
Drug treatments for brain strokes are only available for patients diagnosed 1-3 hours after the onset of a clot induced stroke. With more than 90% of stroke patients falling outside of this treatment group, new treatments must be developed. Therapies that focus on salvaging and protection of brain tissue in this large group of stroke sufferers is a major focus for the medical and scientific community. One treatment that has the proven ability to salvage oxygen starved tissue is hyperbaric oxygen therapy (HBOT).

HBOT has been used for more than a 100 years to increase oxygen intake in damaged or oxygen-starved tissues. By increasing atmospheric pressure around the damaged tissue and applying 100% oxygen, the total amount of oxygen in the blood and organs increases, ensuring that all cells are supplied with this life sustaining gas.

Evidence of the benefits of HBOT in the treatment of stroke has been accumulating this past decade. With the improvement of imaging technology and better clinical assessment a positive effect of HBOT for stroke patients has been established. Clinical studies and reports in animal models of stroke clearly show a protective effect, as well as a strong therapeutic potential for alleviating neurological symptoms and restoring functionality, even in patients that have suffered a stroke weeks or months earlier.

What Is A Stroke?

A stroke occurs when the blood supply to part of the brain is suddenly blocked (ischemic) or when a blood vessel in the brain bursts (hemorrhage), producing a loss of nutrients and oxygen in brain cells. In the same way that a person suffering a loss of blood flow to the heart is said to be having a heart attack, a person with a loss of blood flow to the brain or sudden bleeding in the brain is having a "brain attack."

Brain cells die when they no longer receive oxygen and nutrients from the blood or when they are damaged by sudden bleeding into or around the brain. A stroke ultimately leads to infarction, the death of brain cells which are eventually replaced by a fluid-filled cavity (or infarct) in the injured brain. Although a stroke might affect a small area of the brain directly, it is the tissue that surrounds the core of a stroke that is at risk of dying if not treated effectively [(1)]. Defined as a "penumbra", this region surrounding the core (a doughnut shaped region) has brain tissue that is compromised, but can still be rescued [(1)]. Re-establishing blood supply to the deprived brain region(s) is the major priority for doctors when a stroke is diagnosed. Surgical intervention to reestablish blood flow or stop bleeding is the most common treatment for the majority of strokes.

Ischemic strokes are classified into focal ischemia (loss of blood supply to a small region of the brain) and global ischemia (loss of blood supply to the entire brain). Both types of stroke can be transient (loss of blood supply is reversed in a few minutes or hours) or permanent ischemia (the blood vessels are completely blocked and cannot be cleared spontaneously).

The high prevalence of strokes among the U.S population has resulted in ever increasing amounts of research to protect against and to recover from the ravages of stroke. Currently, tissue plasminogen activator (tPA; a clot dissolving protein), is the only approved drug to treat blockage that results in a stroke [(2)]. Although tPA is effective, it is only recommended for patients that have been diagnosed in the first 3 hours of stroke symptoms, which accounts for ~5% of stroke patients [(3)]. Patients that have had one stroke are 20-30% more likely to have a second or third stroke, even with drug treatment aimed at preventing another blockage [(4)].

The severity of the stroke and the time delay between stroke diagnosis and symptoms, will determine the amount of damage that a person will sustain to their brain, but apart from supporting physical functions and trying to prevent another stroke, little in the way of therapy exists to treat stroke damage directly. Physical and functional therapies are the only approved methods for recovery or salvaging lost motor and cognitive skills [(5, 6)].

Why Use Hyperbaric Oxygen Therapy?

Hyperbaric oxygen therapy (HBOT) has been in use for over 100 years, safely treating a variety of medical condition [(7-9)]. 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 [(7, 9)] sparing and maintaining organs that are oxygen deprived, removing obstructions in blood flow caused by gas bubbles, and inhibiting certain types of bacteria [(10-12)].

Recent studies reveal that HBOT has other beneficial effects that can treat stroke and in some cases prevent its reoccurrence. For many decades, HBOT has been studied in animal models of stroke [(2, 13-19)], clearly demonstrating a protective effect with single exposures. Swelling due to edema (water that accumulates and causes swelling), hemorrhage (blood pooling that increases pressure on the brain), and neuron death from lack of oxygen is decreased and recovery of brain function are all improved by HBOT. In humans, several thousand case studies [(1)] 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 [(20, 21)]. HBOT appears to hold an even greater potential as a post-stroke recovery therapy [(22, 23)].

Animal models and clinical reports clearly show that multiple HBOT treatments provide a better outcome than single HBO treatments [(20, 24)]. The sustained exposure of oxygen to tissues that cannot receive blood is an important feature, especially when trying to rescue brain tissue in stroke patients. In cases where a stroke patient is over the critical three hour window of treatment with tPA, HBOT can potentially extend the treatment window that will help break the clot in the

blood vessel [20]. In recent years, the idea of using HBOT in combination with other therapies has gained support based on animal studies [25, 26]. Administration of tPA with HBOT in animals shows a faster recovery and better outcome [25]. As well as increasing the survival time of cells after stroke, HBOT can protect against a second stroke [27] and increases survival in cases of open heart surgery and brain surgery [13, 28-30].

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 through multiple, parallel pathways. In rats, data demonstrates that HBOT promotes new neuron [31] and blood vessel regrowth [32-34]. Also, cellular metabolism and cell survival is improved [35-37] and cellular death [36, 38] is inhibited. Inflammation is reduced [39] by HBOT, as well as brain bleeding [40, 41] and brain swelling [42, 43]. 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 [25, 44], strongly suggests that combining therapies with HBOT could yield better results than either alone.

Stroke treatment with HBOT

Patients who survive a stroke have few options for rehabilitation. Eighty percent of stroke survivors are affected by brain function loss. In almost all cases mental and physical rehabilitation, learning how to walk, talk and eat, are the only treatments available. Doctors are slowly becoming aware that HBOT can provide an increased margin of safety, an extension in treatment time and surgical intervention and offers a potential to alleviate symptoms and reverse damage with minimal risk. Recent advances in diagnostic tests and brain imaging are allowing for a better and faster diagnosis, allowing doctors to identify patients that will benefit from HBOT treatment. In the near future, as advances in drug therapy come into play, the integration of HBOT and drug, physical or behavioral treatments could provide improved protection of brain tissue during the early phases of stroke and rehabilitation of brain function in the post-stroke period.

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