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Hyperbaric Oxygen: A Critical Treatment for Carbon Monoxide Intoxication

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ABSTRACT

Hyperbaric Oxygen Therapy (HBOT) is a medical intervention that involves administering pure oxygen at high pressure for various conditions like decompression sickness, severe anemia and including carbon monoxide (CO) poisoning. This literature review aims to evaluate the effectiveness of HBOT in reducing neurocognitive symptoms caused by CO poisoning, as well as to review the mechanisms, indications, contraindications, and application of Hyperbaric Oxygen Therapy in Carbon Monoxide Poisoning. The review findings indicate that HBOT significantly enhances tissue oxygenation and accelerates the healing process, which can reduce the risk of neurocognitive damage. Hyperbaric Oxygen Therapy has also been found to modulate inflammatory responses, which play a crucial role in the recovery of patients with CO poisoning. However, some studies show variations in the long-term effectiveness of HBOT on neurocognitive symptoms, highlighting the need for further research. This literature review concludes that HBOT offers significant benefits in the treatment of CO poisoning; however, further research is needed to optimize clinical use and ensure its long-term effectiveness.

INTRODUCTION

Hyperbaric oxygen therapy is the use of 100% oxygen at a higher pressure than atmospheric pressure. Patients gradually inhale 100% oxygen concurrently with an increase in the therapy chamber's pressure to more than 1 absolute atmosphere (ATA). The foundation of hyperbaric therapy is rooted in physics principles. The Torricelli theory, which underpins this therapy, is utilized to determine that the air pressure at 1 atm is 760 mmHg. This air pressure, comprising 79% nitrogen (N2) and 21% oxygen (O2), contains the elements of air. Hyperbaric therapy is also based on fundamental physics theories such as Dalton's, Boyle's, Charles', and Henry's laws.[1]

Hyperbaric oxygen therapy was initially used by Behnke in 1930 to alleviate symptoms of Caisson's disease, a form of decompression sickness occurring after diving. The use of hyperbaric oxygen was further developed as a complement to radiation effects in cancer treatment by Churchill Davidson in the 1950s, in addition to supporting care during cardiac surgery, treating clostridial gas gangrene, and addressing carbon monoxide poisoning.[1] Hyperbaric therapy leverages the response to high-pressure oxygen, increasing oxygen concentrations in hemoglobin and plasma. Based on its solubility under pressure, it enhances the diffusion gradient for deeper delivery into tissues, which is the primary mechanism of Hyperbaric Oxygen Therapy (HBOT). The increased dissolved oxygen from hyperbaric therapy has several physiological effects that can alter tissue responses to various physiological changes.[2]

Carbon monoxide (CO) is a colorless, odorless, and tasteless gas, making it challenging to detect upon exposure. CO gas at concentrations higher than 35 ppm is toxic to humans. It is a leading cause of poisoning-related deaths globally and may be responsible for more than half of fatal poisonings worldwide. About 50% of deaths from burns are related to inhalation trauma, with early hypoxia being the cause of death in over 50% of inhalation trauma cases. CO gas intoxication is a serious consequence of smoke inhalation cases, accounting for over 80% of inhalation trauma-related fatalities.[3]

Carbon monoxide (CO) has become a leading cause of poisoning-related deaths in many countries, and hyperbaric oxygen is widely accepted as a treatment for carbon monoxide poisoning. Some individuals with CO poisoning may still experience

residual neurocognitive symptoms despite hyperbaric oxygen therapy. Hyperbaric oxygen has been used in preventing and treating residual neurocognitive symptoms after carbon monoxide poisoning. Various mechanisms have also been proposed for the potential neuroprotective effects of hyperbaric oxygen on neurocognitive disorders after carbon monoxide poisoning, but there is still controversy regarding the effectiveness of hyperbaric oxygen on residual neurocognitive symptoms after carbon monoxide poisoning.[3] Previous studies have reported that 68.6% of patients experience intellectual impairment and 48.7% experience neurological symptoms after CO poisoning. A study involving 25,912 CO poisoning patients found that the prevalence rate of residual neurological symptoms after CO poisoning was 9.1%.[3]

METHOD

This article used a narrative literature review approach to synthesize published evidence on the mechanisms, indications, contraindications, adverse effects, and clinical application of hyperbaric oxygen therapy in carbon monoxide poisoning, with particular attention to neurocognitive outcomes.

RESULT AND DISCUSSION

Hyperbaric Oxygen Therapy

The prefix "hyper" means increased, while "baric" refers to pressure. In Hyperbaric Oxygen Therapy (HBOT), patients breathe 100% pure oxygen at pressures greater than normal atmospheric pressure inside a high-pressure chamber. The oxygen pressure is typically 1.5-3 times higher than at sea level. The procedure follows guidelines from the Undersea and Hyperbaric Medical Society (UHMS).[2] Hyperbaric oxygen therapy involves placing the patient in a sealed high-pressure chamber called a hyperbaric chamber. The pressure in the chamber is controlled from a panel and can be increased from 1 atmosphere absolute (ATA) up to 4 ATA to enhance oxygenation.[4]

Hyperbaric Oxygen Therapy works on the principle of oxygen distribution in arterial and venous blood, influenced by hemoglobin's affinity for oxygen (Hb-O2) and oxygen's solubility in plasma. According to Henry's law, oxygen solubility increases with partial pressure. In anemia, oxygen delivery continues through plasma diffusion aided by increased partial pressure from HBOT. Normal atmospheric pressure is 1 ATA, equivalent to 760 mmHg. An increase of 1 ATA elevates oxygen solubility by 1.8 ml/dl. At 3 ATA with 100% oxygen, plasma oxygen solubility increases to 4.6 ml/dl, enhancing alveolar oxygen concentration.[5]

This therapy also activates nitric oxide (NO) through reactive nitrogen species (RNS), promoting vasodilation and reducing pro-inflammatory mediators. Reactive oxygen species (ROS) aid cell and tissue repair by mediating vasoconstriction, platelet aggregation, and thrombus formation, along with recruiting lymphocytes and migrating neutrophils. ROS activation also triggers epithelial and vascular endothelial growth factors (EGF and VEGF), essential for angiogenesis and tissue repair. HBOT increases oxygen transport via hemoglobin binding and plasma solubility.[6,7] At ambient pressure (1 ATM), 19 ml of oxygen per 100 ml of blood is transported, with hemoglobin carrying 18.7 ml and plasma 0.3 ml. With 100% oxygen, hemoglobin is fully saturated, and excess oxygen dissolves in plasma, increasing with each ATA increment. According to Boyle's law, increasing pressure reduces gas volume, aiding in treating conditions with gas bubbles in the body, such as decompression sickness or gas embolism.[8]

To prevent oxygen toxicity during extended HBOT sessions, short breaks with normal air are provided to reduce excess oxygen intake by tissues. Dosage varies by age, pathology, and disease location to minimize toxicity and complications. Common reversible symptoms include mild headaches and fatigue, which subside when exiting the hyperbaric chamber.[2] Side effects of HBOT are minimal for sessions under 2 hours and pressures below 300 kPa compared to normal atmospheric pressure. Though generally mild, side effects can be serious if untreated, including nausea, vomiting, myopia, tightness, fatigue, and headaches.

Indications for Hyperbaric Oxygen Therapy (HBOT) are numerous and span across various medical conditions. HBOT is employed in the management of reflex osteomyelitis, which is a bone infection, and osteoradionecrosis, a severe complication from radiotherapy. It is also a crucial treatment for carbon monoxide poisoning and smoke inhalation, as well as cyanide poisoning. The therapy is effective for gas gangrene and decompression sickness, a risk for deep-sea divers. It aids in the recovery from crush injuries with sudden inadequate arterial blood flow and ischemic injuries, and supports the healing of delayed wounds, grafts, and flaps.

HBOT is used for severe soft tissue infections caused by necrotizing bacteria, gas embolism from air bubbles in blood vessels, and traumatic brain injuries, as well as chronic stroke and acute brain edema. It has been shown to facilitate delayed diabetic wound healing and serve as an adjunct treatment for anemia due to significant blood loss and hemorrhagic shock. Moreover, it treats radiation injuries and infections from clostridial myonecrosis and actinomycosis. Hyperbaric oxygen therapy is also indicated for stage IV neuroblastoma, post-anorexia encephalopathy, sudden hearing loss, and for enhancing the success of limb replantation, skin grafts, and flaps.

Additionally, it helps in the management of aggressive periodontitis and pneumatosis cystoides intestinalis, underscoring its wide-ranging applicability in both acute and chronic conditions.[2] Absolute contraindications include untreated pneumothorax and severe acute bronchospasm. Relative contraindications involve conditions affecting pressure equalization in sinuses, ears, or lungs, such as upper respiratory infections, sinusitis, COPD, and claustrophobia. Potential HBOT side effects include severe lung damage, ear barotrauma, sinus pathology, vision changes, dental pain, pulmonary fluid accumulation, and seizures.[9]

Lung damage is a potential side effect of HBOT. This occurs primarily due to increased pressure and high oxygen levels during treatment. The main mechanisms of lung damage include barotrauma and oxygen toxicity. Barotrauma happens when the lungs are damaged due to pressure changes. During HBOT, increased pressure can cause the lungs to over-expand if not properly managed, leading to alveolar rupture and pneumothorax (collapsed lung). Additionally, exposure to high concentrations of

oxygen over prolonged periods can lead to the formation of reactive oxygen species (ROS). These ROS can damage the alveolar-capillary membrane, causing pulmonary edema (fluid accumulation in the lungs) and acute respiratory distress syndrome (ARDS). Symptoms resulting from lung damage include shortness of breath, chest pain, coughing, fatigue, and in severe cases, respiratory failure. According to Thom (2011), in his review of the mechanisms and efficacy of HBOT, barotrauma and oxygen toxicity are two major factors causing lung damage during this therapy. Furthermore, clinical guidelines from the Hyperbaric Oxygen Therapy Committee (2019) provide detailed protocols to minimize the risks associated with HBOT, including lung damage.[10,11]

Hyperbaric oxygen therapy chambers, designed to NFPA safety standards, include monoplace, multiplace, and portable recompression chambers, each with distinct advantages and limitations. Monoplace chambers, accommodating one patient, are practical and affordable but carry a fire risk due to 100% oxygen use. Multiplace chambers, holding multiple patients and medical staff, allow intensive monitoring and treatment but pose decompression sickness risks to staff. Portable recompression chambers, used in emergencies, are lightweight and manually inflated, providing temporary relief until further evacuation.[12]

Carbon Monoxide (CO) Poisoning

Carbon monoxide (CO) is a colorless, odorless, and tasteless gas, making it extremely difficult to detect. CO concentrations above 35 ppm are toxic to humans. Known as the "silent killer," CO doesn't cause irritation and has a density of 0.97, making it slightly lighter than air. Carbon monoxide (CO) is produced from incomplete combustion of organic matter. Major sources of CO include vehicle exhaust, especially from vehicles using gasoline or diesel, household heating systems using fuels like gas, oil, or wood, and appliances such as water heaters, ovens, and clothes dryers, which can produce CO if they malfunction or lack adequate ventilation, stoves and fireplaces, cigarette smoke, fires, both indoors and outdoors, indoor combustion engines such as generators, lawnmowers, some industrial processes, such as metal smelting, chemical production, and fossil fuel combustion, methylene chloride, solvent used in paint strippers and some other industrial products can be broken down into CO in the body after being inhaled or swallowed.

In Japan, CO poisoning results in 2,000-5,000 deaths annually, being a leading cause of poisoning deaths. Global CO poisoning incidents have remained stable for 25 years. In Japan, CO poisoning deaths doubled in 2003 compared to 2001, partly due to increased suicides facilitated by online information.[13,14] Carbon monoxide is inhaled and enters the bloodstream from the lungs. It binds to hemoglobin (Hb) with an affinity 230-270 times greater than oxygen, forming carboxyhemoglobin (CO-Hb).

The formation of CO-Hb depends on inhaled CO concentration, exposure duration, lung ventilation, exercise, and health status. A small amount of CO is produced in vivo from heme protein degradation. Most inhaled CO remains unoxidized, with less than 0.1% converted to carbon dioxide, and is eventually exhaled. Carbon monoxide has a high affinity not only for hemoglobin but also for other heme proteins like myoglobin and cytochrome c oxidase. It binds to myoglobin in the myocardium and skeletal muscle, with 15% of total CO in the body taken up by tissues. Carbon monoxide can diffuse from organs back into the blood as CO-Hb saturation decreases.[13]

The following formula estimates CO-Hb saturation in the blood:

$$\text{CO-Hb (\%)} = \alpha \text{ x times CO in inhaled air (\%) x time (minutes)}$$

Where α is a constant with values of 3 at rest, 5 during light activity, 8 during light work, and 11 during heavy work. Respiratory minute volume (RMV) has standard values of 8.5 at rest, 25 during light exercise, and 50 during heavy exercise. CO-Hb saturation in healthy, non-smoking individuals is less than 2%, increasing to 4-6% in hemolytic anemia cases, and up to 10% depending on the disease. Methylene chloride, a solvent in paint strippers, metabolizes into CO, causing severe CO poisoning with CO-Hb saturation up to 50%. CO-Hb saturation decreases easily with oxygen administration. Carbon monoxide elimination half-life varies with factors like inhaled CO concentration, exposure duration, post-rescue oxygenation, and RMV. For a resting adult, the half-life is about 4-5 hours under room air at sea level, 80 minutes with 100% oxygen at normobaric pressure, and 23 minutes with oxygen at 3 ATA.[15]

Acute CO poisoning causes tissue hypoxia due to CO-Hb formation, reducing oxygen transport and resulting in inadequate tissue oxygenation. Carbon monoxide binding to hemoglobin shifts the oxygen-hemoglobin dissociation curve leftward, inhibiting oxygen release in low-oxygen areas, leading to tissue hypoxia. Carbon monoxide also binds to myocardial and skeletal muscle myoglobin, causing dysfunctional oxygen transport, leading to cardiac dysfunction and inhibiting enzyme activity like cytochrome c oxidase.

Carbon monoxide poisoning is associated with cardiac and neurological dysfunction, apoptosis in myocardial cells, and oxidative stress in neural cells. Tissue hypoxia from CO causes vascular permeability, increased interstitial fluid accumulation, and reduced circulating blood volume, affecting multiple organs. Carbon monoxide activates neutrophils, proliferates lymphocytes, causes mitochondrial dysfunction, and lipid peroxidation. Clinical symptoms of acute CO poisoning range from mild to severe and can vary based on the concentration of CO and the duration of exposure.

Initial symptoms may include headaches, often described as a dull, frontal headache; dizziness or feelings of lightheadedness or vertigo; weakness, characterized by general fatigue and muscle weakness; nausea and vomiting; shortness of breath or difficulty breathing; confusion and disorientation, leading to cognitive impairment and memory issues; chest pain and angina; visual disturbances, such as blurred or double vision; and tinnitus, or ringing in the ears.

In more severe cases, symptoms may escalate to loss of consciousness, seizures, arrhythmias, coma, respiratory arrest, and potentially death. Long-term neurological injuries can include ataxia, dementia, concentration deficits, or abnormal behavior.

Structural changes in the subcortical and pallidum areas, as well as hippocampal atrophy, have been observed. Long-term damage may manifest after symptom-free intervals of days to weeks post-poisoning, indicating many unreported cases.[15]

The Application of Hyperbaric Oxygen Therapy in Carbon Monoxide Poisoning

Carbon monoxide (CO) binds to hemoglobin in the blood with 200 times the affinity of oxygen, reducing oxygen availability and causing hypoxia. Hyperbaric Oxygen Therapy provides an alternative oxygen source by dissolving oxygen in the plasma, displacing CO from hemoglobin and myoglobin. Symptoms of CO poisoning include loss of consciousness, neurological abnormalities, myocardial ischemia, pulmonary edema, metabolic acidosis, headaches, and delayed neurological effects, which may become permanent if not treated early.

HBOT at 2-3 ATA for 60-90 minutes with 100% oxygen helps treat these conditions. High-flow oxygen through a non-rebreather mask is crucial for suspected or confirmed CO poisoning and removal from the CO source. If the patient is comatose or cannot protect their airway due to severe neurological impairment, intubation and administration of 100% oxygen are required. Close monitoring for cardiac arrhythmias and management of associated conditions are essential for optimal outcomes.[13]

Distinguishing between intentional and unintentional poisoning is important, but if the cause is unknown, consider the possibility of a suicide attempt. In conscious patients, assess for suicidal intent. Treatment decisions regarding HBO2 therapy can be controversial, but most experts agree that it is indicated for loss of consciousness at the scene or in the hospital, new neurological deficits, altered mental status, end-organ ischemia (EKG changes, pH less than 7.1), or pregnancy (especially if COHb is over 20%).

Most experts say COHb levels do not always correlate with clinical symptoms, but levels above 25% are considered severe poisoning and require immediate treatment. HBO2 reduces the risk of neurological deficits by mitigating central nervous system ischemia-reperfusion injury. It also reduces neutrophil adhesion to damaged brain endothelium, decreasing tissue edema and lipid peroxidation. Extra oxygen delivered to tissues helps displace CO from cytochrome proteins in cell mitochondria, aiding in the restoration of oxidative phosphorylation, crucial for neuron function and survival after ischemic injury.

The optimal number of HBO2 treatments and care protocols are debated. Most hyperbaric practitioners follow the Weaver protocol or its modifications. Regardless of the protocol, the goal is the same: to provide 100% oxygen at two to three atmospheres absolute (ATA) for 60 to 90 minutes to quickly clear CO and treat ischemia-reperfusion injury. Severe CO poisoning cases may require two to three treatments twice a day. For moderate cases with neurological deficits, a single treatment may suffice. HBOT is most beneficial within the first six hours after exposure. After adequate medical treatment, patient disposition depends on clinical status. Most patients with unintentional poisoning can be discharged with instructions to return if neurological deficits arise.[15,16]

CONCLUSION

Carbon monoxide (CO) poses a serious health threat due to its high affinity for hemoglobin, causing oxygen deprivation and various severe symptoms. Hyperbaric Oxygen Therapy is effective in displacing CO from hemoglobin and treating CO poisoning, especially when administered promptly after exposure. High-flow oxygen and close monitoring are crucial in managing suspected or confirmed cases, with the timing of HBOT within the first six hours post-exposure being critical for optimal outcomes.

AUTHOR CONTRIBUTIONS

All authors contributed to the conception of the review, literature interpretation, manuscript preparation, and critical revision, and approved the final manuscript.

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