Hyperbaric Oxygen Therapy in Bloodless Medicine and Surgery

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Red blood cells contain hemoglobin; hemoglobin is the major carrier of oxygen throughout the human body. When hemoglobin levels decrease, anemia results and patients may exhibit signs and symptoms of decreased oxygen delivery to tissues (also known as oxygen debt). The signs and symptoms of oxygen debt may include tachycardia, dyspnea, fatigue, chest pain, and altered mental status; laboratory findings may include metabolic acidosis, hyperlactatemia, and elevated cardiac enzymes. Transfusion of packed red blood cells is generally administered to anemic patients who are symptomatic, with the goal of relieving their signs and symptoms of oxygen debt.

The amount of oxygen delivered to the body (DO2) is dependent on the arterial oxygen content (CaO2) and cardiac index (CI). The equation representing this is as follows:

$$\text{DO2} = \text{CaO2} \times \text{CI}$$

The CaO2 is mostly dependent on hemoglobin concentration; each hemoglobin molecule can carry up to 1.38 ml of oxygen per gram of hemoglobin. A very small amount of the arterial oxygen supply is dissolved in the plasma and is dependent on the partial pressure of oxygen in the blood (PaO2). The CaO2 is determined by the following equation:

$$\text{CaO2} = (\text{Hemoglobin} \ [\text{g/dL}] \times 1.38 \ \text{ml O2} \times \% \text{oxygen saturation}) + (0.003 \times \text{PaO2})$$

Oxygen that is delivered to tissues is then extracted and used by the tissues. On average, the human body extracts 5-6 vol% of oxygen from the blood. As long as oxygen supply equals or exceeds the amount of extracted oxygen, symptoms of oxygen debt do not occur. In anemic patients, oxygen delivery via hemoglobin may not be sufficient to compensate for oxygen extraction. When hemoglobin concentrations drop below 6 g/dL, oxygen delivery and extraction become unequal, and when hemoglobin concentrations drop below 4 g/dL, tissue oxygenation delivery is significantly impaired. At hemoglobin concentrations less than 6 g/dL, impairments in memory and reaction time occur in humans.

Historically, indications for transfusion of red blood cells were based on hemoglobin concentrations. Prior to the 1980’s, the “10/30” rule was a commonly followed transfusion protocol; according to this rule, a patient’s hemoglobin and hematocrit should exceed 10 g/dL or 30%, respectively, prior to operative procedures. Modern recommendations for management of anemia include transfusion thresholds that are based on both laboratory values and patient-specific factors. Currently, a commonly utilized threshold for transfusion of packed red blood cells is a hemoglobin concentration of 7 g/dL in patients who exhibit signs or symptoms of anemia. This threshold is based on the disequilibrium of oxygen delivery and extraction as well as the clinical symptoms that occur at higher frequency below this hemoglobin concentration.

Blood transfusions are common in hospitalized patients; in 2013, over 13 million blood products were transfused to patients in the United States. Some patients, however, are unable to receive blood transfusions due to religious beliefs or other reasons. According to the Jehovah’s Witnesses religion, portions of the bible (including Genesis 9:4, Leviticus 17:12, Deuteronomy 12:23, and Acts 15:29) state that its followers must abstain from receiving blood. Jehovah’s Witnesses will...
not accept blood transfusions, and this religious belief has been upheld in the American legal system. Some patients are unable to accept blood products due to medical reasons. Examples of this include patients with hemolysis and antibody formation due to transfusion reactions, or those with crossmatch incompatibility. Patients who cannot accept blood transfusions for medical or religious purposes are at increased risk for morbidity and death after acute and unexpected blood loss from conditions including postpartum bleeding, trauma, and intraoperative hemorrhage. Many hospitals have established bloodless medicine programs which focus the diagnosis and treatment of anemia and the minimization of blood loss in the population of patients who cannot accept transfusions. Strategies included in bloodless medicine programs may include administration of iron and erythropoietin, use of pediatric phlebotomy tubes to limit iatrogenic blood loss, minimization of unnecessary blood draws, and administration of hyperbaric oxygen therapy.

Hyperbaric oxygen therapy (HBO) is a treatment in which patients breathe 100% oxygen while pressurized to a depth greater than sea level. The use of hyperbaric pressurization as a treatment for medical conditions dates back to the 1600’s, prior to the discovery of oxygen. Currently, HBO is used as a primary treatment for decompression sickness, air embolism, and carbon monoxide poisoning. It is also used as an adjunctive treatment for additional medical conditions including compromised grafts and flaps, chronic refractory osteomyelitis, and diabetic foot ulcerations (DFU). The Undersea and Hyperbaric Medical Society currently recommends the use of HBO as a treatment of the following conditions.

1. Air or gas embolism
2. Decompression sickness
3. Acute carbon monoxide poisoning
4. Arterial insufficiencies, including enhancement of healing in selected problem wounds
5. Radiation-induced soft tissue and bone necrosis
6. Intracranial abscess
7. Clostridial myonecrosis
8. Necrotizing soft tissue infections
9. Compromised grafts and flaps
10. Crush injuries and compartment syndromes
11. Chronic refractory osteomyelitis
12. Thermal burns
13. Severe anemia where transfusion is impossible due to religious or medical concerns
14. Idiopathic sudden sensorineural hearing loss

HBO is administered while a patient is enclosed within a hyperbaric chamber. These chambers, composed of steel and acrylic components, are commonly located within outpatient wound centers in the United States and are utilized as an adjunctive wound healing modality. Monoplace hyperbaric chambers can accommodate one patient; multiplace hyperbaric chambers can accommodate multiple patients. In the United States, monoplace chambers are the most commonly encountered hyperbaric treatment vessels in hospital settings. During hyperbaric treatments, patients sit or lie supine in the hyperbaric chamber and breathe 100% oxygen for the duration of the treatment. Hyperbaric treatments are generally scheduled on a daily basis; most hyperbaric chambers in the United States operate during weekday business hours only, but
some facilities may offer weekend or after-hours treatments for emergent conditions such as acute carbon monoxide poisoning. Each hyperbaric treatment is approximately two hours in duration; patients typically sleep or watch a movie during the treatment. The HBO treatment course is typically tailored to each individual patient; some patients may end their treatment course earlier than expected based on a more rapid course of healing or symptom resolution. Interestingly, despite the lengthy time commitment and need to present to the hospital for daily treatments, HBO has not been associated with decrements in patient quality of life.

The use of traditional medical equipment and implanted devices in the hyperbaric environment poses unique challenges related to the inability of many modern medical devices (including intravenous pumps and ventilators) to withstand the typical pressurization encountered in the hyperbaric chamber. Most monoplace chambers are designed to treat the outpatient population only, as they are unable to accommodate patients who are undergoing treatment with mechanical ventilation or continuous intravenous infusions. Some implanted medical devices are unsuitable for use in the hyperbaric environment, due to fire safety concerns. Fortunately, many pacemaker manufacturers have tested their devices under pressure, and thus permanent pacemakers are often not regarded as a contraindication to hyperbaric compression. Topical oxygen therapy involves administration of oxygen via a bag, boot, or other device to a specific area of the body, most commonly the lower extremity. Advantages of topical oxygen therapy include a lower cost than traditional HBO, and ease of use: topical oxygen can be administered in an out-of-hospital setting such as a private residence or nursing facility. Unlike HBO, topical oxygen therapy is not associated with the potential for systemic oxygen toxicity. However, topical oxygen delivery systems generally do not achieve the high pressures found in hyperbaric chamber environments, and at this time there is not sufficient high-quality evidence to support the use of topical oxygen therapy as a medical treatment. Because of this, the procedure is often not reimbursed by insurance carriers.

In 1959, the Dutch surgeon Boerema published “Life without blood”, a manuscript detailing the use of HBO for the treatment of anemia. Boerema exsanguinated healthy piglets, and replaced the blood volume with a plasma-like solution. The piglets’ resulting hemoglobin concentration was 0.4 g/dL, a hemoglobin concentration that is incompatible with life. The piglets were then pressurized in a hyperbaric chamber to 3 absolute atmospheres (ATA) for 45 minutes. The animals survived this exposure, despite having essentially no hemoglobin present, and recovered uneventfully after they were re-infused with normal blood. Boerema noted that under hyperbaric conditions, the amount of oxygen dissolved in the plasma can greatly exceed the amount present while breathing air under normobaric conditions. This phenomenon is due to Henry’s Law, which states that the amount of gas dissolved in a solution is directly proportional to the partial pressure of the gas. When partial pressures of a gas increase, such as under hyperbaric pressurization, more of that gas dissolves in solution. Breathing room air (21% oxygen) under normobaric conditions results in a PaO2 of approximately 100 mmHg; breathing 100% oxygen under hyperbaric conditions results in a PaO2 of greater than 1600 mmHg. Under hyperbaric conditions, oxygen dissolved in the plasma can approximate or meet the body’s metabolic demands of oxygen extraction. This is the basis for the use of HBO for patients with severe anemia who are unable to receive transfusion. Since Boerema’s initial publication on this subject, there have been multiple reported cases of the use of hyperbaric oxygen therapy for the treatment of acute blood loss anemia in patients who are unable to receive transfusion of blood products.
In these cases, patients received one to three HBO treatments daily; treatment frequency was based on the patient’s clinical presentation, and was titrated based on improvement or resolution of the signs and symptoms of oxygen debt. Currently, hyperbaric facilities across the United States continue to treat patients with acute blood loss anemia who are unable to receive blood transfusion due to religious or medical beliefs. A majority of insurance carriers, with the exception of the Centers for Medicare and Medicaid Services (CMS), consider hyperbaric oxygen therapy to be a medically necessary treatment for this patient population and will provide insurance reimbursement for this procedure.

The hormone erythropoietin (EPO) regulates red blood cell synthesis; the kidneys are the primary location of EPO release in adults. Intermittent hypoxia stimulates endogenous erythropoietin (EPO) synthesis, resulting in reticulocytosis and increased red blood cell production. Because of this mechanism, anemic bloodless medicine patients are often treated with exogenous EPO in an attempt to stimulate red blood cell production. Recently, intermittent normobaric hyperoxic exposures in healthy, non-anemic human subjects have been found to result in significant increases in endogenous EPO production and hemoglobin concentration. This phenomenon has been termed the “normobaric oxygen paradox.” It logically follows that patients who are exposed to intermittent hyperbaric oxygen may experience the same increases in reticulocytosis and hemoglobin concentration, but this has not been well studied. In one study, the administration of a single HBO treatment to healthy adult volunteers was found to decrease endogenous EPO production by 53%. However, the clinical implications of this study are unclear, as the majority of severely anemic bloodless medicine patients receive more than a single HBO treatment. The effect of serial HBO treatments on endogenous EPO production and subsequent reticulocytosis remains unclear at this time. At MedStar Georgetown University Hospital, preliminary data from bloodless medicine patients treated with HBO suggests that this treatment may actually stimulate erythropoiesis in patients with acute blood loss anemia, leading to faster resolution of anemia as well as potentially shorter hospital lengths of stay and decreased mortality.

Adverse effects of HBO are rare. Middle ear barotrauma is the most common complication of HBO; this is generally self-limited and can be prevented by carefully instructing patients on appropriate ear pressure equalization techniques. Central nervous system oxygen toxicity may result in seizures; however, seizures are rarely encountered in clinical hyperbaric practice. The risk of central nervous system oxygen toxicity may be reduced by the use of intermittent air breathing periods during each hyperbaric treatment. In diabetic patients, hyperbaric pressurization may result in hypoglycemia. Some patients may experience a temporary myopic shift during their hyperbaric treatment course, and patients with a history of anxiety or claustrophobia may exhibit confinement anxiety during hyperbaric treatments. Finally, as the hyperbaric environment is oxygen enriched by definition, fire safety is of paramount importance. Careful assessment and mitigation of any potential fire risk factors must be performed and maintained during each hyperbaric treatment. Fire-related fatalities have occurred in hyperbaric chambers due to the presence of static electricity, electrical shorts, and tobacco use within the hyperbaric environment. The National Fire Protection Association (NFPA) publishes standards for fire safety in health care facilities; hospital-based hyperbaric chambers must follow these standards. In accordance with NFPA regulations, patients may not wear garments of less than 50% cotton in monoplace hyperbaric chambers; in addition, patients may not bring cell phones, personal entertainment devices, personal warming devices, or any other items that may ignite or fuel a fire.
When administered correctly, HBO is a safe procedure with minimal adverse effects. In patients with acute blood loss anemia who are unable to receive transfusion of blood products due to religious beliefs, HBO administration may result in improvement and/or more rapid resolution of the signs and symptoms of anemia. In the bloodless medicine patient population, adjunctive use of hyperbaric oxygenation in addition to standard bloodless medicine interventions can result in enhanced patient outcomes.

References


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