CHAPTER 25

HBO AND EXCEPTIONAL BLOOD LOSS ANEMIA

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INTRODUCTION

Blood loss of sufficient magnitude is usually replaced in the emergency situation by blood that has been donated by others. Where blood loss is anticipated by the patient and the attending physician, blood may be drawn periodically, stored and returned to the patient as needed. Recently, erythropoietin has been administered to a patient with anemia from a chronic disease in order to enhance autologous blood donation prior to a difficult hip operation.\(^{(35)}\) Thus, the problems associated with replacing lost red cell mass will occur now in unplanned or emergent situations that were not anticipated. Further, these emergencies may take exception to receiving blood from others for one reason or another and may need a temporizing element such as HBO to support the patient until the red cell mass is replaced. For purposes of proposing this type of treatment it is appropriate to define exceptional blood loss anemia.

DEFINITION OF EXCEPTIONAL BLOOD LOSS ANEMIA

Exceptional blood loss anemia occurs when the patient has lost sufficient red cell mass to compromise respiratory requirements and cannot or will not receive red cell replacement because of medical or religious reasons.

Medical

There arise, from time to time, incompatibilities in typing and cross-matching wherein blood cannot be matched, at least for a time, to replace blood lost. Idiopathic autoimmune hemolytic anemia represents a rare problem where transfusions may be hazardous even with compatible blood\(^{(10)}\) and would therefore need some temporizing modality until replacement can be safely effected. Recently, patients have become concerned about the transmission of blood-borne viral infections (hepatitis and HIV infection), and this concern could be the cause of refusal in the future.

Religious

There is a religious sect whose members staunchly refuse blood transfusions to replace lost RBC’s even in the most life-threatening situations. Many states (such as Texas) allow the Justice of the Peace to give immediate, legally enforced, orders for blood replacement. However, in many states (as California) such a court order is only obtained when involving a minor or in the case of an adult, by a lengthy formal court hearing—after which time the need for blood replacement has long past.

RATIONALE

The brain requires a basic supply of six volumes percent oxygen to support its basic metabolic requirements in man.\(^{(20)}\) HBO at three atmospheres (3 ATA) will place six volumes per cent of dissolved molecular oxygen in the
intravascular acellular perfusate of man\(^{(22)}\) for direct use of tissue cells. The concept of supporting a severely anemic animal model with dissolved oxygen was tested by Boerema, et al.\(^{(8)}\) Otherwise normal piglets were exsanguinated and their blood was replaced with an acellular perfusate and survived with no apparent neurological deficit at 3 ATA oxygen.

Attar, et al.\(^{(8)}\) noted an improved survival over controls in animals in hemorrhagic shock treated with HBO. These animal studies have been replicated showing improved survival beyond controls and those breathing 100% oxygen at ambient pressure.\(^{(5,11,23,29)}\) The necessity of an appropriate pressure of oxygen above ambient to supply the cellular needs when the RBC's are lost is clearly revealed in the animal model by Norman.\(^{(30)}\) HBO protects the synthesis of RNA and DNA in rats after massive blood loss.\(^{(36)}\) HBO exerts a favorable stimulus on erythropoiesis following massive blood loss in rats by increasing circulating erythropoietins—causing an early replacement of the lost erythrocytes.\(^{(4)}\) When used early, HBO prevents the accumulation of anaerobic byproducts in the brains of cats in hemorrhagic shock.\(^{(24)}\)

Thus, the prime reason for using HBO intermittently is to dissolve enough oxygen in the severely anemic patient to support the basic metabolic needs of the body until sufficient RBC's are restored to the circulation to furnish the oxygen demand.

Successful human application was first reported by Amonic on a patient in chronic hemorrhagic shock. Limited experiences\(^{(16,27)}\) followed until Hart et al.'s\(^{(15)}\) report on a group of 26 patients in severe exceptional acute blood loss anemia. There was an overall survival of 70% in this group of patients who qualified as representatives of Class IV hemorrhage\(^{(9)}\)—i.e. a loss of 50% or greater of the circulating blood volume or more without RBC replacement. Remarkably, if one discards those who arrived late, namely patients without cerebral function, there was a mortality rate of one out of 19 patients (5%).

**TREATMENT ROUTINE**

1. Replacement of blood volume with crystalloids/plasma expanders as per American College of Surgeons' Committee on Trauma for hemorrhage.
2. Medical support for the severe anemia: Hemetemesis, antibiotics and cardiotoxins as needed.
3. Hyperbaric oxygen to be administered immediately and repetitively **POSTHEMORRHAGE** for Class IV Hemorrhage when the patient cannot accept blood replacement for medical or religious reasons. The following indications dictate the repetitive use of HBO:
   A. Shock, systolic blood pressures below 90 mmHg or pressures maintained by vasopressors.
   B. Disorientation to coma.
   C. Ischemic changes of the myocardium as demonstrated on the ECG.
   D. Ischemic gut as demonstrated by a sprue-like diarrhea.
The HBO is repeated as needed, at pressures which are appropriate to relieve the relative hypoxia, and discontinued when the RBC's have been replaced in numbers so as to alleviate the preceding symptoms and signs. This (as a rule of thumb) appears to occur at a hematocrit of 22.9% and a hemoglobin of 7.7 Gm% (approximate) based on our present data.

TREATMENT PROTOCOL

A. Multiplace:

1. HBO—first treatment: 2 to 3 ATA oxygen according to physiological response—i.e. blood pressure is elevated from shock levels, the pulse rate slows, while the sensorium clears. Generally, we proceed to 3 ATA for the first thirty minutes and reduce the pressure to 2.5 ATA, for an hour. We then give an air break of one hour and retreat for an hour at 2.5 ATA, if tolerated, with improvement over baseline. The duration of the air breaks is lengthened and oxygen pressures are reduced, but each HBO exposure is an hour in duration. When the air breaks reach two hours the patient may be removed from the chamber for diagnostic or other treatment impossible to perform at pressure. The exposures of HBO remain at one hour per exposure and the pressures are decreased as the patient becomes able to tolerate the ambient air environment, which may be assisted by oxygen by mask or cannula. Note: Pulmonary oxygen toxicity is avoided by intermittent exposure to air.

2. Volume replacement with Hestastarch and Ringers lactate with the early administration of intravenous hyperalimentation. Note, we avoid the use of lipids for intravenous hyperalimentation due to the possibility of accelerating pulmonary oxygen toxicity as demonstrated by Alam and Alam, Hageman & Hunt, and Kehrer and Autor. (1,14,19)

3. Antibiotics, analgesics and other interventions are rendered as indicated.

B. Monoplace: Treatment is the same as with the multiplace protocol with air breaks being given if an appropriate air supply is available; if not, the patient is decompressed for the ambient air breaks.

REPORT OF RECENT CASE

A previously healthy 20-year-old female (110 pounds and 61 inches in height) Jehovah's Witness was brought to Long Beach Memorial Medical Center as a trauma victim of a drive-by shooting in May 1991. She sustained a single penetrating gun shot wound (GSW) to the left chest. Preoperative hematocrit was 24%. She refused any blood transfusions due to her religious convictions.
Operative exploration revealed penetration of the left lung, left hemidiaphragm, spleen, left kidney and spinal cord. Volume replacement was accomplished with hetastarch solutions and Ringer's solutions.

Postoperatively, the patient was conscious with a complete paraplegia at the level of thoracic cord at T-6,7. Specifically, she had no lower extremity voluntary movement, no response to touch or pain in the lower extremities, and was areflexic in the lower extremities. Oncotic pressure and blood pressure were maintained with crystalloids and hetastarch. High dose steroids were given for acute spinal cord injury. The postoperative hematocrit was 18% and she was started on HBO receiving treatments of 2 ATA for periods of 90 minutes three times a day. The erythropoietin (EPO) levels on the first and second postoperative day were 5.8 and 10.3 MU/ML (normal range is 2.0-19.0 MU/ML).

The EPO level was 86.5 MU/ML on the eighth post-op day, and EPO 8,000 Units (8 KU) was started as a daily administration by subcutaneous injection. Nine days following the operation she had onset of high fever and became confused. Over a two-day period it was established that she had a perforation of an intestine. She was returned to the operating room and the perforation was repaired on the eleventh day following admission. Following the operation the erythropoietin was increased to 10 KU and administered intravenously as the reticulocyte count had fallen to 2.7% following the repair of the perforation. This dosage was continued for a period of 11 days. HBO was continued postoperatively on an approximately twice-a-day schedule and was discontinued on the 28th day. Iron dextran was given as calculated every other day for ten more days and discontinued. See Graph #1 for a display of the reticulocyte count compared with that of the hematocrit.

![Graph showing hematocrit and reticulocyte counts over days with labels for HBO, EPO, and perforated abdominal viscous.]

**TABLE 1** Acute blood loss anemia. 20 year female - Jehovah's Witness
Exogenous erythropoietin was started on the eighth hospital day, as the patient’s endogenous erythropoietin was elevated to only 86.5 MU/ML. Despite the elevated EPO and the administered EPO there was a remarkable depression of the bone marrow function coinciding with the perforated viscus and the resulting sepsis. It is difficult to assess the value of EPO in this patient due to the administration of the corticosteroids and the septic event. It, however, was not the response that was measured in healthy men where a maximum reticulocyte count occurred on the third to fourth day after EPO. She received a total of 138 hours of hyperbaric oxygen over 28 days to support the relative ischemia. It was stopped when the hematocrit had climbed to 22%.

The patient remains a complete paraplegic. She has otherwise been rehabilitated to the fullest of her neurologic capabilities.

**COSTS OF HYPERBARIC OXYGEN**

HBO compares favorably with blood transfusions in the following cost analysis using 1990 dollars:

1. The cost of four units of packed red cells over the first 24 hour period in a Southern California private, non-profit hospital is $1,040.00. Fresh frozen plasma, albumin, or other fractions if needed would add to this cost.
2. HBO for 5 treatments of 66 minutes each (treatment protocol per the author) in the first 24 hours at $84.00 per half hour would cost $924.00. There may be additional costs for intensive care, monitoring, and/or use of a respirator, but these are usually facts of life for those receiving transfusions as well for these seriously ill patients.

**COMPLICATIONS**

The major complication of HBO therapy is barotrauma resulting in middle ear effusions, which are easily relieved by nasal decongestants or may require PE tube insertion in the most severe cases. No instance of pulmonary or CNS oxygen toxicity occurred in Hart’s 1987 series.

**ALTERNATIVES**

There is presently no satisfactory blood substitute available to use in exceptional blood loss anemia. The fluorocarbons may unfavorably alter the reticuloendothelial system by long term retention and lower the immunity of the subject. The linear oxygen dissociation curve with the fluorocarbons dictates that a high inspired oxygen level must be maintained in order to achieve useful oxygen exchange. Gould found that perfluorocarbons are unnecessary in moderate anemia and ineffective in severe anemia.
Stroma free hemoglobin solutions have a limited half-life of a few hours,26,32 and have a limited storage life due to a high hemoglobin formation-plus an undesirably high affinity for oxygen. There is further concern about these solutions impairing the immune systems.17

There are reports of success utilizing EPO in treating blood loss in Jehovah’s Witness patients who have suffered a moderate to severe acute blood loss.18,21,31 The lowest hematocrit declared in those five patients was 13.5%, and it appears that there was a lag time of about 5 days for the EPO to show the desired reticulocyte increase. It therefore appears that HBO complements the use of EPO and supports the hypoxic patient until a satisfactory EPO response has occurred.

CONCLUSIONS

HBO is a valuable adjunct when used early in treating acute blood loss anemia in those who cannot receive blood replacement for medical or religious reasons. In those who are not considered the best candidates for transfusion, HBO can enhance the hematocrit and can fulfill the patient’s request for no blood products.

REFERENCES

11. Elliott DP and Paton BC. “Effect of 100 percent oxygen at 1 and 3 atmospheres on dogs subjected to hemorrhagic hypotension.” Surgery. 1965;57:401-408.


