Facilitation of Recovery From Acute Blood Loss With Hyperbaric Oxygen

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Background: Hyperbaric oxygen (HBO) has been used for more than 25 years as therapy for extreme blood loss in cases where transfusion has been unavailable. The use of HBO for lesser amounts of blood loss to avoid the transfusion of blood products has not been investigated.

Hypothesis: Hyperbaric oxygen up-regulates hemoglobin synthesis after acute blood loss in an animal model of moderate (30%) blood loss.

Design: Twenty-four New Zealand white rabbits were bled to a calculated loss of 30% of the circulating blood volume. The rabbits received Ringer lactate infusions to correct hypovolemia and were divided into 2 groups: a control group and a treatment group receiving HBO.

Intervention: One group of 12 animals received no treatment other than Ringer lactate resuscitation, whereas the other group of 12 received 5 HBO treatments in the 4 days immediately following blood loss. Hemoglobin levels and reticulocyte counts were monitored for 14 days after the bleeding episode.

Results: The control group was more affected by the blood withdrawal than the HBO group, reaching a low of 37% hemoglobin loss compared with 29% hemoglobin loss at 48 hours ($P<.001$). The HBO group recovered faster, reaching the baseline level of hemoglobin in 11 days as opposed to 14 days for the control group ($P<.001$). Reticulocyte counts were not significantly affected by HBO treatment.

Conclusions: Treatment with HBO favorably affected recovery from moderate (30%) acute blood loss, resulting in lessened effects at 48 hours and hastening recovery to baseline hemoglobin levels. Our results support the data gained from clinical experience treating extreme blood loss with HBO.

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The treatment of acute hemorrhage remains a challenge in trauma surgery. With the possibility of disease transmission through blood products and the increasing scarcity of blood, the development of other treatments for blood loss is increasingly important. More than 25 years ago, Hart1 was able to demonstrate that hyperbaric oxygen (HBO) is an effective and lifesaving treatment for patients with anemia due to extreme blood loss. Hyperbaric oxygen has also been used as a temporizing lifesaving measure to oxygenate ischemic tissues when blood transfusion was not available or was refused by the patient. In recent years, it has become clear that HBO can induce actions other than tissue oxygenation. These mechanisms of action include vasoconstriction, interference with neutrophil activation in ischemia-reperfusion injury, down-regulation of inflammatory cytokines, up-regulation of growth factors, enhancement of neutrophil activity against bacteria, and direct bactericidal and bacteriostatic effects.2-16 Because HBO has been shown to help ameliorate the effects of hypoxia in hypovolemic shock and to enhance or speed up wound healing in a variety of conditions, we postulated that HBO would also facilitate recovery from acute blood loss.

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MATERIALS AND METHODS

GENERAL EXPERIMENTAL DESIGN

Twenty-four New Zealand white rabbits (Oryctolagus cuniculus) were used. The protocol was approved by the Wilford Hall Medical Center Institutional Animal Care and Use Committee (Lackland Air Force Base, Tex). At the beginning of the study, the animals underwent blood withdrawal from the femoral vein to simulate acute blood loss, and blood samples were obtained from an ear 6 additional times during the 2-week study period. The rabbits were randomized into 2 groups. One group received HBO as a treatment following bleeding, and the other was a control group.

ACUTE BLOOD LOSS AND SAMPLING

The animals were preoxygenated for 2 to 3 minutes via face mask with 100% ambient oxygen. Anesthesia was induced via face mask with 4.5% isoflurane 3 in an air-oxygen mixture (40%-60%) and maintained for the duration of the venous blood withdrawal from the femoral vein. Using a cut-down procedure, the femoral vein was cannulated with a 22-gauge catheter, and 21 mL/kg of venous blood was obtained during a 10-minute period. Intravenous Ringer lactate was administered through an ear vein in the amount of 47 mL/kg (2.25 mL of Ringer lactate per milliliter of blood obtained). The animals were recovered for 1.5 hours and were returned to their cages when awake. Food and water were available ad libitum.

HBO TREATMENT

The animals were put in a multiplace hyperbaric chamber in individual plastic cages. The chamber was pressurized with 100% oxygen, and the oxygen concentration of the chamber was maintained at 100%. The treatment dive profile was 45 ft of seawater (2.38 atmospheres absolute, or 241 kilopascals) for 90 minutes with a 5-minute descent and 10-minute ascent, for a total bottom time of 95 minutes. The total time of each dive was 105 minutes. Hyperbaric oxygen treatment was administered 5 times during the first 4 days: at 2, 8, 24, 48, and 72 hours after bleeding for the HBO group.

BLOOD SAMPLING

Venous blood samples were obtained at 7 intervals during the study: at the initiation of bleeding, at 4 hours, and at 2, 4, 8, 11, and 14 days following the bleeding episode. After the initial bleeding, 2 mL of blood was obtained from an ear vein for each sample. The samples were analyzed in an automated Coulter counter for hemoglobin levels, hematocrit levels, and reticulocyte counts.

STATISTICS

Statistical multivariate repeated-measures analysis of variance was performed with group (control vs HBO) as the independent factor and time (day 1, 2, 4, 8, 11, or 14) as the dependent factor.

There were 12.4 million units of blood transfused in 1999, an increase of 7.6% compared with 1997. Despite recent well-publicized national blood shortages, the ratio of blood transfused to recipients in 1999 was 2.8 units per transfusion. Many of this blood may have been unnecessary because a transfusion of less than 2 units in an adult is not thought to provide a significant clinical benefit. If alternative treatments for blood loss such as HBO were available, many unnecessary transfusions could be avoided. Recent terrorist and mass casualty events have emphasized the difficulty of obtaining adequate blood supplies in these situations. If viable alternatives to blood transfusion were readily available, transfusion might be delayed while alternate treatments were pursued, and blood use might be reduced.

Hyperbaric oxygen therapy is an intriguing alternative to blood transfusion, not only because of the increased oxygen delivery to tissues but also because of several other beneficial actions of oxygen when delivered in pharmacologic doses for relatively short periods. Patients with crush injury who were given HBO had an in-

**COMMENT**

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increased incidence of primary healing, less need for secondary surgery, and lowered amputation rates. Wound edema is reduced in burns, resulting in shorter healing times, less time in the hospital, and less need for adjunctive surgery. The healing rate and time for chronic wounds is shortened, resulting in fewer amputations in patients with leg ulcers. Flaps and grafts used to reconstruct wounds may benefit from HBO through edema reduction, reduction of ischemia-reperfusion injury, oxygenation of hypoxic tissue, and ultimately enhanced flap or graft survival.

In this study, we were unable to investigate the mechanism of HBO that facilitates recovery from blood loss. A previously published report indicated that HBO was deleterious to erythropoiesis when given prior to bleeding and for 6 to 7 hours after bleeding. However, this treatment schedule is not analogous to current treatment regimens because of the excessive dose of oxygen. Too much oxygen is likely to inhibit wound healing and erythropoiesis. When applied judiciously, HBO has been shown to up-regulate vascular endothelial growth factor and enhance the effect of exogenously applied growth factor. In this study, it is possible that the HBO up-regulated erythropoietin release or synthesis or that it modulated the effect of erythropoietin, resulting in the formation of more hemoglobin. We did not measure a statistically significant increase in the reticulocyte count in the HBO group. An increase in the number of reticulocytes does not seem to account for the elevated level of hemoglobin in the HBO-treated animals. The increased hemoglobin level may come from an acceleration of hemoglobin synthesis and/or erythrocyte formation.

Of note was the lessening of the effect of acute blood loss at 48 hours by HBO. The HBO-treated animals reached a low of 29% blood loss compared with 37% in the control group. We did not investigate the mechanism of this effect, although it may be due to cytokine suppression after acute blood loss or to the vasoconstrictive hemodynamic effects of HBO. This effect clearly needs to be investigated further.

Hyperbaric oxygen probably would not be a replacement for blood transfusion in large numbers of casualties because of the logistics of placing patients in the chamber and the time required for treatment. However, in selected cases, HBO may eliminate the need for transfusion or reduce the requirement while conferring the additional benefits of enhanced wound healing. As part of a concerted effort using plasma expanders, erythropoietin, oxygen delivered by face mask, and drugs such as free radical scavengers and clotting enhancers, HBO can be a valuable asset to a bloodless surgery program.

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REFERENCES


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Adverse Events Associated With Methicillin-Resistant Staphylococcus aureus in a Nursing Home

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Background: Methicillin-resistant Staphylococcus aureus (MRSA) generates concern in nursing homes. Restrictive isolation precautions may be applied for indefinite periods. Adverse events driving these concerns include transmission and infection.

Methods: The 721-bed Wisconsin Veterans Home in King performs approximately 645 cultures annually. The site, severity, and number of MRSA infections were determined for 69 months. Pulsed-field gel electrophoresis was performed on all initial isolates, followed by a statistical cluster analysis looking for evidence of transmission.

Results: Sixty-seven MRSA infections were identified (1.6 per 100 residents per year); many were polymicrobial, and it was difficult to determine the proportionate role of MRSA in morbidity or mortality. There was an episode of rapidly fatal MRSA septicemia in which empiric antibiotic therapy was ineffective. Twenty-one genetic strains were encountered. Statistical analysis identified 13 clusters of genetically identical strains clustered in time and space (P<.05).

Conclusions: Infections with MRSA were identified at relatively low rates; however, the etiology of many serious nursing home infections is not determined, especially pneumonia. Statistical analysis revealed clustering and evidence of transmission. Nursing home practitioners should consider MRSA when applying empiric treatment to serious infections. We recommend a program including (1) judicious use of antibiotics, including topical agents, to reduce selection of resistant organisms; (2) obtaining and tracking cultures of infectious secretions to diagnose MRSA infections and focus antibiotic therapy; (3) universal standard secretion precautions because any resident could be a carrier; and (4) a detailed assessment and care plan for the carrier that maximizes containment of secretions and independence in activities. However, basic hygiene cannot be maintained in communal areas by some residents without restriction of activities of daily living. (2001;161:2371-2377)

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**Correction**

Error in Figure Positions. In the Original Article titled “Facilitation of Recovery From Acute Blood Loss With Hyperbaric Oxygen,” published in the July issue of the *ARCHIVES* (2002;137:850-853), the positions of Figure 1 and Figure 2 were reversed. Figures 1 and 2 are reprinted correctly as follows.

**Figure 1.** Curves depicting mean percent blood loss for the control and hyperbaric oxygen (HBO) groups. Baseline hemoglobin at the start of the study = 0.

**Figure 2.** Effect of hyperbaric oxygen (HBO) on reticulocyte counts after blood loss. Day 0 = initial time of blood loss.