Acute Normovolemic Hemodilution in a Jehovah’s Witness Patient: A Case Report

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Patients who are Jehovah’s Witnesses refuse blood transfusions and blood products as a matter of faith. For surgical procedures during which substantial blood loss is possible, their refusal presents a challenge. Anesthetists must generally respect the requests of adults not to receive blood and thus should have a clear understanding of how they will respond in the event of bleeding. Several blood conservation techniques are available for consideration, including acute normovolemic hemodilution. This technique entails the preoperative phlebotomy of whole blood that contains a high concentration of red blood cells and coagulation factors, while replacing the lost volume with a crystalloid and/or colloid infusion. The procured whole blood can then be transfused back during or after the procedure as a treatment of hypovolemia. Leaving the procured blood continuously attached to the patient through the collection tubing makes the procedure acceptable to most Jehovah’s Witness patients. Current literature is unclear when this technique should be used. In this particular case, acute normovolemic hemodilution contributed to the successful outcome of an anemic Jehovah’s Witness who was undergoing major surgery.

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Patients of the Jehovah’s Witness faith present unique anesthetic challenges. While requiring the same surgical procedures as other patients, they generally will not accept either allogeneic or autologous blood transfusions based on Bible passages that prohibit eating blood (e.g., Genesis 9:3,4). The Watch Tower Bible and Tract Society, which publishes the interpretive guidelines that Jehovah’s Witnesses follow, has defined blood as containing red blood cells, white blood cells, platelets, and plasma, and advises that transfusions of any of these are prohibited.1,2

However, some blood fractionations and volume management techniques commonly used during anesthesia are acceptable to many Jehovah’s Witness patients. This means that anesthesia providers and a Jehovah’s Witness patient must discuss and agree preoperatively what will, and will not, be done in the event of blood loss during surgery. Acute normovolemic hemodilution (ANH) is one blood conservation technique that generally does not conflict with the Jehovah’s Witness faith and helps conserve existing red blood cells and coagulation factors. Acute normovolemic hemodilution can be safely and quickly set up in both routine and emergent settings.

We present a case in which ANH worked well to treat intraoperative bleeding and prevent a potentially catastrophic outcome.

Case Report
A 22-year-old man presented to the preoperative holding area for a retroperitoneal lymph node dissection. His past surgical history included an orchiopexy at age 6 months and an orchiectomy, for testicular cancer, 6 months before our introduction to the patient. Following his orchiectomy the patient received 4 rounds of chemotherapy with bleomycin, etoposide, and platinum. While undergoing chemotherapy the patient suffered a pulmonary embolism and was started on a warfarin regimen. A recent computed tomography scan showed a 2-cm mass in the aortocaval region at the level of the renal arteries. The patient had no other pertinent medical history. Current medications included warfarin, 12 mg/d (stopped 7 days before surgery); magnesium; and famotidine, 30 mg twice daily, as prophylaxis against radiation esophagitis and gastritis. The patient had a known allergy to heparin.

During our initial interview, the patient stated that he would accept neither blood nor blood products because of his religious beliefs as a Jehovah’s Witness. With further discussion he agreed to receive synthetic colloids and as a last resort albumin. His preoperative hemoglobin was 11.4 g/dL and hematocrit was 33%. The surgery and anesthesia teams jointly advised the patient that the risk of extensive bleeding during this surgery was high, and that his anemia could be improved by delaying the procedure for 2 weeks while taking erythropoietin and iron. The risks and benefits of delaying and proceeding with the surgery were reviewed with the patient and his family. After deliberation, the patient requested that his surgery be performed that day. This decision was based on a potentially cancerous mass that needed to be removed, his
emotional preparation for surgery, and the long distance he had traveled to the hospital.

We then reviewed the benefits and risks of several blood conservation techniques with the patient including ANH and the infusion of antifibrinolytic drugs such as aminocaproic acid. A complete description of ANH was given to the patient and family to ensure it would not conflict with their beliefs. Antifibrinolytic drugs were rejected due to the recent diagnosis of pulmonary embolism. We set postphlebotomy targets for ANH therapy at a hemoglobin concentration of 8.0 g/dL and a hematocrit of 25%.

The patient was premedicated with 2 mg of midazolam intravenously and taken to the operating room. Standard intravenous induction was accomplished with 100 µg of fentanyl, 200 mg of propofol, 100 mg of lidocaine, and 50 mg of rocuronium. His trachea was intubated, and sevoflurane was administered, with fractional inspired oxygen maintained at 0.40 because of the recent exposure to bleomycin. Postinduction remifentanil and vecuronium infusions were initiated. A 20-gauge right radial arterial catheter and an 8.5F 4-lumen right subclavian central venous catheter were placed.

At this time 2 citrate phosphate dextrose adenine (CPDA-1) blood collection bags were simultaneously attached to a 14-gauge central line port for phlebotomy, as shown in Figure 1. Each collection bag was then spiked with a 60-drip intravenous line that had been primed with normal saline solution. These intravenous lines were then connected to an 18-gauge port on the central line via 2 Luer-Lok stopcocks (BD, Franklin Lakes, NJ). This method allowed for a continuous column of fluid from each port of the central line, establishing a closed-circuit system and thus complying with the patient’s wishes. Prephlebotomy hemoglobin and hematocrit measurements were 10.3 g/dL and 29%, respectively. Approximately 600 mL of whole blood was withdrawn from the patient while 500 mL of 6% hetastarch was concurrently infused via peripheral access over a period of approximately 30 minutes. The blood bag was periodically agitated to facilitate the mixture of blood with the CPDA anticoagulant and was stored in a cooler while remaining attached to the 18-gauge infusion port. Upon completion, the phlebotomy lines were tied off and disconnected and a blood specimen was obtained. The hemoglobin and hematocrit values were 8.6 g/dL and 25%.

Approximately 3 hours into the procedure the hematocrit was found to be 27%. At that time the surgeons notified the anesthesia team of ensuing blood loss. To maintain hemodynamic stability, 750 mL of 6% hetastarch and 1,000 mL Plasma-Lyte A (multiple electrolytes injection, type 1, US Pharmacopeia) were administered. Concern at this time that the patient would continue to require aggressive resuscitation with crystalloid is why the normal saline solution was replaced with multiple electrolytes, which minimizes electrolyte imbalances while being compatible with a blood transfusion. The inferior aorta was clamped for 2 to 3 minutes below the renal artery to control bleeding, during which approximately 1,000 mL of blood was lost. A calculated base deficit of 2.1 mEq/L and a hematocrit of 20% were noted after the loss. The patient was transfused 300 mL of the blood obtained through the ANH technique.

No further periods of rapid blood loss occurred during the case. The remaining 300 mL of ANH-acquired blood was transfused before the end of the case. After neuromuscular blockade reversal with neostigmine and glycopyrrolate, a smooth emergence from general anesthesia followed. The patient was extubated without difficulty and was transferred to the intensive care unit for continuous monitoring.

The surgical procedure lasted 4.9 hours. The patient received 600 mL of autologous ANH blood, 1,500 mL of hetastarch, 2,000 mL of lactated Ringer’s solution, 2,250 mL of normal saline, and 1,200 mL of multiple electrolytes. The estimated blood loss was 1,150 mL, and urine output was 695 mL.

A blood specimen obtained shortly after surgery showed a hemoglobin concentration of 9.1 g/dL and a hematocrit of 26%. All electrolytes were within normal limits and the cre-
Preoperative considerations

- Complete history and physical to determine incidence of abnormal bleeding, anemia, coexisting disease, current medications (eg, nonsteroidal anti-inflammatory drugs, acetylsalicylic acid, anticoagulants, platelet aggregation inhibitors)
- Patient-specific beliefs related to blood products and blood fractionations
- If necessary, complete assessment of anemia, including serum ferritin, vitamin B₁₂, folate, and complete blood count
- Careful management of anticoagulation medications
- Restrict diagnostic phlebotomy or consider the use of pediatric collection tubes
- Use of recombinant human erythropoietin
- Iron replacement therapy
- Conjugated estrogens
- Vitamin K
- Discuss minimally invasive surgical techniques

Intraoperative considerations

- Optimize cardiac output and volume status using crystalloids or synthetic colloids
- Optimize ventilation and oxygenation
- Minimize oxygen demand (controlled hypothermia, sedation, muscle relaxation, adequate analgesia)
- Pharmacologic hemostatic agents (eg, tranexamic acid, vasopressin, octreotide, ε-aminocaproic acid)
- Controlled hypotension
- Closed-circuit cell salvage
- Closed-circuit acute normovolemic hemodilution
- Closed-circuit component sequestration (eg, plateletpheresis)
- Use of blood fractionations
- Recombinant activated factor VIIa
- Clotting factor replacement therapy (factors, VIIa, VIII, IX)
- Prothrombin complex concentrate
- Cryoprecipitate

Discussion

Jehovah’s Witnesses interpret biblical passages forbidding the “eating of blood” as prohibiting any consumption of blood, including transfusion. As a core belief, its violation would result in being cut off from eternal life after death.³ Case law strongly supports the right of an adult patient, who is of sound mind, to refuse transfusion. A medical practitioner who violates this refusal can be guilty of assault. Case law is less clear in transfusion refusals by a pregnant woman or by parents for a child. This discrepancy in law relates to the inability of a child or fetus to give meaningful consent.⁴ In our case the patient could make a well-informed decision about his care, so we agreed to proceed, administering blood only through ANH.

Surgery and anesthesia in Jehovah’s Witness patients should include the use of techniques that minimize blood loss.⁵ This should include careful attention to hemostasis, and where appropriate, the use of minimally invasive surgical techniques, prophylactic angiographic embolization, the use of tourniquets or a closed-circuit autologous blood recovery system (eg, Cell Saver). Anesthetically this may entail maximizing the red blood cell count preoperatively, administering antifibrinolytics, minimizing blood loss through hypotensive anesthetic techniques, and preventing coagulopathies.⁶,⁷ Table 1 provides a detailed list of perioperative techniques for consideration.⁸⁻¹¹ The Watch Tower Society of Pennsylvania offers 24-hour service for both medical professionals and patients who may have questions regarding what is and is not acceptable, and Table 2 lists unacceptable transfusion therapies. The Hospital Information Services for Jehovah’s Witnesses can be reached by email at his@jw.org or by telephone at (718) 560-4300.³

Acute normovolemic hemodilution is based on the concepts that blood removed and stored at the beginning of a case will contain the highest concentrations of red blood cells and clotting factors, that blood lost during the case will contain less, and that the blood removed initially can be rein infused at the end of surgery to help restore an adequate blood cell count and coagulability. The infusion of crystalloids or colloids during initial phlebotomy allows the maintenance of an adequate cardiac output and hemodynamic stability while decreasing the viscosity of the blood and therefore resistance to blood flow. During periods of bleeding, fewer red blood cells are lost,
and at the end of surgery the collected blood with its greater red blood cell concentration is reinfused.\textsuperscript{12,13}

Some controversy over whether to use ANH results from the 1997 meta-analysis of Bryson et al.\textsuperscript{12} These investigators examined 24 prospective randomized trials of ANH that included 1,218 patients. Although they noted that many studies reported impressive reductions in blood transfusions and that ANH overall reduced both the likelihood of exposure to allogeneic blood and the total units of allogeneic blood transfused, their results were statistically inconclusive. When all of the reviewed ANH trials were combined, a large amount of unexplained heterogeneity suggested that the benefit of ANH may be inconsistent.\textsuperscript{12}

Around the same time as the release of the meta-analysis by Bryson et al, Monk et al\textsuperscript{13} published a study on ANH during radical prostatectomy. Their results indicated that the technique may be less costly and as effective as preoperative autologous blood donation, therefore making it a preferred method of blood conservation. In a case report, Grubbs et al\textsuperscript{14} recognized ANH as effective and a blood conservation technique that most Jehovah's Witness patients would accept.

Recent studies have shown that ANH is quite effective for major surgery. A prospective randomized trial that enlisted 155 patients undergoing elective hip surgery found ANH effective in reducing the total number of units transfused, postoperative complications, and the overall need for allogeneic blood.\textsuperscript{15} Of 78 patients in the ANH group of this study, only 15 required the use of allogeneic blood, compared with 22 of 77 in the standard infusion group. The ANH group used 33 units of allogeneic blood versus 63 units in the standard, and had a 14% postoperative complication rate versus 30% in the standard group.

Practice guidelines of a task force on perioperative blood transfusions concur with the current medical literature supporting the use of ANH. The guideline developers agreed that ANH could be efficacious in decreasing a patient's risk for exposure to allogeneic blood, and that evidence was inconclusive as to whether it decreases the number of patients transfused.\textsuperscript{16}

The American Association of Blood Banks recommends that the inclusion criteria for ANH include patients undergoing surgery where greater than 1,000-mL blood loss is expected, preoperative hemoglobin concentration is adequate (>9 g/dL), and no ischemic heart disease or active bleeding due to coagulopathy are present.\textsuperscript{17,18} Our facility recommends the exclusion of patients who are septic, in respiratory or cardiac failure, or in hemorrhagic shock. Surgeries in which ANH should be considered include cardiac, and major orthopedic, neurosurgical, and urologic procedures.\textsuperscript{18,19}

Most blood banks have policies on ANH that practitioners can obtain and follow. Policies in our facility indicate that blood should be collected in Food and Drug Administration approved, single-draw CPDA-1 blood bags via a central venous or arterial access. The blood may be stored for up to 8 hours at room temperature.

The American Association of Blood Banks recommends using the following formula to determine the amount of blood to withdraw for reinfusion\textsuperscript{17} \( V = \frac{EBV \cdot (Hi - Hf)}{Hav} \), where \( V \) indicates volume of blood to be withdrawn; \( EBV \), estimated blood volume, typically 70 mL/kg multiplied by patient body weight (in kg); \( Hi \), initial hematocrit before the start of the procedure; \( Hf \), final desired hematocrit after hemodilution; and \( Hav \), average hematocrit during the hemodilution process.

**Conclusion**

Acute normovolemic hemodilution appeared to contribute to the positive outcome of the patient described in this case. The volume of blood reinfused at the end of the case theoretically increased his hemoglobin by 2 g/dL to 9.1 g/dL. In addition, the clotting factors returned to the patient probably helped maintain a dry surgical field at the end of surgery. Without ANH, the clinical course could have included anemia, hypovolemia, or fluid overload, thus exposing the patient to the additional risks of prolonged intubation, tissue hypoxia, infection, coagulopathy, and cardiac compromise.

The overall good health of our patient undoubtedly also contributed to the positive outcome. The use of ANH seemed an effective therapy to conserve hemoglobin and improve coagulation during this major surgery. As a therapeutic option for Jehovah's Witness patients, this blood conservation technique could be life-saving.

**REFERENCES**

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