

ADVANCES IN HEMATOLOGY

Current Developments in the Management of Hematologic Disorders

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Blood Component Support in Patients With Solid Tumors and Hematologic Malignancies: Lessons From the Treatment of Jehovah's Witnesses



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H&O When are blood products typically used in patients with solid tumors and hematologic malignancies?

KB We most commonly use blood products when therapy makes these patients anemic or thrombocytopenic, which can occur with bleeding from surgical procedures and as a result of chemotherapy or radiation therapy.

H&O Which blood products typically are used to treat these patients?

KB We usually use prestorage leukoreduced red blood cells to treat symptomatic anemia, and leukoreduced apheresis platelets or whole blood-derived platelets to treat thrombocytopenia. Plasma components are used less commonly, and their use generally is restricted to the treatment of bleeding associated with coagulation factor deficiencies—either isolated coagulation factors or multiple coagulation factors.

H&O How often do you see Jehovah's Witnesses as patients?

KB There are approximately 7.9 million Jehovah's Witnesses worldwide, but we do not see them very often at our hospital. We do make a point, of course, of recording religious identification if a patient wants to provide that information, and we specifically note when patients are Jehovah's Witnesses because they often will refuse whole blood and blood components. In addition, there are also

people who prefer to be treated without any blood administration for nonreligious reasons.

H&O Are all blood products banned for Jehovah's Witnesses?

KB Most Jehovah's Witnesses will refuse allogeneic whole blood, red blood cells, white blood cells, platelets, and plasma. They generally refuse preoperative autologous blood donation because this involves interruption of the blood's circulation. By contrast, they often accept intraoperative autologous transfusion—also known as blood salvage—which involves special instrumentation to maintain a continuous circuit of the patient's blood. They also generally allow for acute normovolemic hemodilution, in which tubing is used to maintain continuous direct contact between the patient and his or her blood. There will always be some individual variation when it comes to these rules; one chart review of 61 Jehovah's Witnesses who gave birth at Mount Sinai School of Medicine found that 10% were willing to receive whole blood and 39% were willing to accept some blood products.

H&O What is the religious rationale behind the rejection of blood?

KB My understanding is that the belief is based on several passages from Biblical scripture stating that people must not eat blood. For Jehovah's Witnesses, this has been interpreted as a prohibition of blood transfusion. The religion requires all Jehovah's Witnesses to refuse allogeneic blood,

and allows for individual decisions about plasma derivatives, such as albumin (including vaccines that might be suspended in albumin) and clotting factor concentrates.

H&O What are the challenges in treating patients with solid tumors or hematologic malignancies who are Jehovah's Witnesses, and how is their health care affected?

KB These patients are at increased risk for morbidity and mortality caused by severe anemia and thrombocytopenia. Years ago, our hospital did a retrospective study of the 58 Jehovah's Witness oncology patients we had seen at our hospital from October 1986 through February 1994. Of the 15 patients who had transfusion requirements, 9 refused blood. One older woman had a postoperative stroke and a young woman died, likely because of the combination of severe anemia and thrombocytopenia. Long-term prognosis also may have been affected. We did find that younger patients were more likely than older ones to accept transfusion, and parents were more likely to accept transfusion for their children than for themselves.

We found that 10 of the 58 patients we evaluated had their treatment limited because of their refusal of blood. For example, surgery was restricted or not performed, chemotherapy was withheld or the dose was lowered, or radiation therapy was withheld because the physician did not want to create a situation in which the patient would need a blood transfusion.

Other groups of researchers have looked at larger patient populations. One study, which was reported in 2002 in *Transfusion*, looked at more than 2000 surgical patients with postoperative hemoglobin levels of 8 g/dL or lower who had declined red blood cell transfusions for religious reasons. This study found that as the hemoglobin level fell to 7 g/dL or lower, the adjusted risk increased 2.5-fold for every 1 g/dL decrease. When the hemoglobin level fell to 3 g/dL or lower, the in-hospital mortality at 1 month was 64%. This study did not find any immediate adverse effects as long as the patients' hemoglobin level was greater than 7 g/dL.

H&O What steps can be taken to minimize the need for blood products in these patients?

KB We want to optimize patient blood stores prior to any treatment, which begins by minimizing the number of preoperative blood draws and the amount of blood sampled. For example, we certainly should not perform a type and screen or type and crossmatch if there is no possibility of a transfusion. We also need to evaluate the patient for correctable forms of anemia and address these prior to surgery, chemotherapy, or radiation therapy

Table. Blood Components, Blood Derivatives, and Procedures Commonly Accepted and Refused by Jehovah's Witness Patients

Usually Refused
Whole blood
Red blood cells
Platelets
Plasma
Cryoprecipitated antihemophilic factor
Granulocytes
Fibrin glue/sealant
Predeposited autologous blood/components
Usually Accepted
Acute normovolemic hemodilution ^a
Intraoperative cell salvage ^a
Erythropoiesis-stimulating agents ^b
Hemodialysis ^c
Cardiopulmonary bypass ^c
^a Usually accepted if patient remains continuously in contact with blood.
^b Synthetic hormone can be suspended with or without albumin.
^c Provided that a non-blood prime is used.
Individual Decision
Albumin
Immune globulins
Factor concentrates
Organ and tissue transplants
Therapeutic apheresis

through the use of iron, vitamin B₁₂, or folate supplementation, as appropriate. The use of erythropoiesis-stimulating agents and/or conjugated estrogens should be considered, although these require advance planning in order to benefit the patient.

When surgery is needed, steps that help minimize the need for blood transfusion include maintaining the patient's temperature, maintaining blood volume, and reducing the risk of major blood loss by breaking down a complex procedure such as a bilateral mastectomy into stages. As I mentioned earlier, acute normovolemic hemodilution and intraoperative blood salvage also may help, provided that there is a closed circuit. Postoperatively, it may be helpful to consider oxygen supplementation. In addition, every effort should be made to identify and treat infection immediately.

For both surgical and nonsurgical patients with bleeding, hemostatic agents—such as aprotinin, desmopressin acetate (DDAVP), the synthetic antifibrinolytic agents aminocaproic acid and tranexamic acid, and recombinant activated factor VII—should be considered.

H&O Are these steps that should carry over to the care of patients who are not Jehovah's Witnesses?

KB Absolutely; with the exception of acute normovolemic hemodilution, which generally has fallen out of favor, any of these techniques have the potential to benefit patients without blood product limitations.

H&O What lessons have we learned from the care of patients who are Jehovah's Witnesses?

KB One lesson we have learned is that we often can allow patients' hemoglobin thresholds to drop to levels lower than what we once considered safe—it appears that a threshold of 7 g/dL is safe for almost all patients, and many patients have minimal adverse events provided that the threshold is at least 5 g/dL.

H&O Are there products that can be used in place of autologous blood for transfusion?

KB We can maintain blood volume using colloids such as hydroxyethyl starch or crystalloid solutions such as normal saline or lactated Ringer's solution, but these products work only transiently and will not benefit patients who need red blood cells or platelets. If the patient needs red blood cells, the only option we have right now is allogeneic red blood cells. That is why acute normovolemic hemodilution and intraoperative blood salvage are such important techniques during surgical procedures.

Intraoperative blood salvage has been somewhat controversial in oncology patients because there is concern that any malignant cells collected could be reinfused and cause metastasis. One way to mitigate this risk might be to restrict salvage of the patient's red blood cells to the periods before the tumor site has been reached and after the tumor has been removed.

A study of intraoperative blood salvage in radical prostatectomy that was published in *Transfusion* in 2012 found that long-term survival appears to be unaffected. This study included 42 patients who underwent radical prostatectomy for prostate cancer. There was no increased risk of biochemical failure, disease dissemination, or mortality at 5 years after surgery as a result of intraoperative blood salvage use.

H&O What other concerns are there when caring for patients who are Jehovah's Witnesses?

KB We have to pay special attention to the issue of informed consent. Many hospitals require documented informed consent for blood transfusion. In consideration of the Jehovah's Witness population, it is very important to document informed refusal of blood transfusion and to clearly specify whether the patient will accept certain blood components or plasma derivatives and what they are.

There are additional legal considerations when the patient is a minor or a pregnant woman. The courts have decided that in general, a woman has the right to make decisions for herself and for the fetus. When the woman is at risk for dying and the fetus might survive, however, a consideration is whether the father of the child or another family member would be supporting the newborn, or if the woman's death would cause any minor children to become wards of the state. In some of these situations, we may want to have legal counsel.

H&O Is it psychologically difficult for health care providers to care for patients who refuse certain medical treatments?

KB That is something that I know personally can be difficult to watch. We certainly need to respect the patient's wishes, however. As long as the patients are making an informed decision about refusing one type of medical care, we have to respect that decision.

Suggested Readings

- Benson K. Management of the Jehovah's Witness oncology patient: perspective of the transfusion service. *Cancer Control*. 1995;2(6):552-556.
- Bodnaruk ZM, Wong CJ, Thomas MJ. Meeting the clinical challenge of care for Jehovah's Witnesses. *Transfus Med Rev*. 2004;18(2):105-116.
- Carson JL, Noveck H, Berlin JA, Gould SA. Mortality and morbidity in patients with very low postoperative Hb levels who decline blood transfusion. *Transfusion*. 2002;42(7):812-818.
- Gyamfi C, Berkowitz RL. Responses by pregnant Jehovah's Witnesses on health care proxies. *Obstet Gynecol*. 2004;104(3):541-544.
- Gyamfi C, Gyamfi MM, Berkowitz RL. Ethical and medicolegal considerations in the obstetric care of a Jehovah's Witness. *Obstet Gynecol*. 2003;102(1):173-180.
- Nash MJ, Cohen H. Management of Jehovah's Witness patients with haematological problems. *Blood Rev*. 2004;18(3):211-217.
- Raval JS, Nelson JB, Woldemichael E, Triulzi DJ. Intraoperative cell salvage in radical prostatectomy does not appear to increase long-term biochemical recurrence, metastases, or mortality. *Transfusion*. 2012;52(12):2590-2593.