

Jehovah's Witness Patients

Interventions for successful stem cell transplantation without blood product transfusions for hematologic malignancies

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BACKGROUND: Jehovah's Witnesses are members of a religion that prohibits them from accepting blood product transfusions. This refusal makes them a particularly compelling population in the context of hematologic malignancies and stem cell transplantation, because blood product transfusions are a mainstay of supportive treatment.

OBJECTIVES: This article presents preventive and supportive measures allowing Jehovah's Witness patients the opportunity to receive a stem cell transplantation without blood product transfusions.

METHODS: A literature review was done that included evidence focusing on optimizing hematopoiesis, blood loss prevention, alterations in chemotherapy regimens, and implications for nursing practice.

FINDINGS: With proper preventive and supportive care measures, Jehovah's Witness patients can receive stem cell transplantations for hematologic malignancies without blood product transfusions.

KEYWORDS

Jehovah's Witness; hematologic malignancies; stem cell transplantation

JEHOVAH'S WITNESSES ARE A FUNDAMENTALIST CHRISTIAN RELIGIOUS GROUP that was founded in Pittsburgh, Pennsylvania, in 1872. Among the many tenets of the religion, followers are prohibited from accepting blood transfusions, based on their literal interpretation of the bible. According to Genesis 9:4 (King James Version), "only flesh with its soul—its blood—you must not eat." Jehovah's Witnesses interpret this to mean that they cannot accept transfusions of whole blood or its primary components (red and white blood cells, plasma, and platelets). The decision about whether to accept minor blood components, such as albumin, clotting factors, cryoprecipitate, and stem cells, is left up to the individual as a matter of conscience (Lin, Kaye, & Baluch, 2012). Many Jehovah's Witness patients are willing to accept the infusion of stem cells because they are perceived to come from the marrow rather than being considered a blood product. Blood product refusal was not always the religion's mandate; the Governing Body of Jehovah's Witnesses officially banned blood product transfusions in 1945 (Wright, 2016).

This blood product refusal can lead to ethical and moral distress when the healthcare team treats these patients, because denying a life-saving transfusion can be perceived as irrational. However, general agreement exists among ethicists that the wishes of competent, well-informed adult patients to decline blood products should be respected because of the preeminence of patient autonomy in medical decision making (Sagy, Jotkowitz, & Barski, 2016). There have been favorable outcomes for Jehovah's Witness patients in complex bloodless surgeries, including cardiac and vascular surgeries and solid organ transplantations (Brunetta et al., 2015; Madueño, Tomás, & Velázquez, 2013; Spasovski, Stankov, & Masin-Spasovska, 2014; Tanaka et al., 2015). The common thread among all these bloodless procedures is the ultimate goal of minimizing blood loss and optimizing hematopoiesis to attain the best possible outcomes for these patients while forgoing transfusions.

Although Jehovah's Witnesses constitute just 0.8% of the population in the United States (Pew Research Center, 2015), their refusal of blood product transfusions makes them a particularly compelling community in the context of stem cell transplantation (SCT). Blood and platelet transfusions are mainstays

of supportive therapy in hematopoietic SCT (HSCT), because high doses of chemotherapy required to minimize any residual hematologic cancer also wipes out the patient's bone marrow. After the patient receives conditioning chemotherapy, blood and platelet transfusions along with other therapies, such as antibiotics, bridge the gap until the transplanted stem cells start producing adequate numbers of red blood cells (RBCs), white blood cells, and platelets. This dependence on blood product transfusions is a complicating factor for Jehovah's Witness patients diagnosed with a hematologic malignancy because their religious beliefs conflict with the traditional standard of care for patients receiving an SCT.

The Transplantation Process

Indications for autologous or allogeneic transplantation vary by disease and are determined by various factors, such as cytogenetic abnormalities, response to previous therapy, disease status and prognostic factors, patient age and performance status, and availability of a suitable graft source (Perumbeti & Sacher, 2018). Prior to receiving a transplantation, patients receive conditioning chemotherapy to prepare their marrow to accept the stem cells. Conditioning chemotherapy for SCT can be classified into myeloablative, nonmyeloablative, and reduced-intensity regimens. Myeloablative regimens cause irreversible cytopenia and require a stem cell transfusion for the patient's bone marrow to recover (Atilla, Atilla, & Demirer, 2017). Nonmyeloablative regimens cause minimal cytopenia and do not require stem cell support (Atilla et al., 2017). Reduced-intensity regimens do not fit the criteria of either myeloablative or nonmyeloablative regimens; the cytopenia is reversible, but stem cell transfusion is still required for the patient's marrow to recover (Atilla et al., 2017). After conditioning chemotherapy, patients either receive an autologous transplantation with their own previously harvested stem cells or an allogeneic transplantation with stem cells from another donor. Neither option requires special handling specifically for Jehovah's Witness patients. The decision about whether to perform an autologous or allogeneic transplantation without the support of blood products largely rests on the risks associated with prolonged pancytopenia and the resultant danger of death from anemia and bleeding. Because of the variation within the Jehovah's Witness community regarding which blood components they will or will not accept, it is crucial that the treatment team has a comprehensive discussion with the patient prior to the transplantation process about the patient's preferences. In addition, precautions can be taken for Jehovah's Witness patients that allow specialized programs to offer these patients the option to receive SCT without transfusions (see Figure 1).

Preventive and Supportive Measures

Optimizing Hematopoiesis

Anemia is a significant cause of death for patients who decline blood product transfusions. In a study by Carson, Noveck, Berlin,

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and Gould (2002) of postoperative Jehovah's Witness patients who abstained from transfusions, mortality increased 2.5 times for every 1 g/dl of hemoglobin below 8 g/dl. Fortunately, with erythropoiesis-stimulating agents, it is possible to boost RBC production prior to chemotherapy and during recovery from transplantation. Erythropoietin (EPO) is a mainstay of bloodless SCT and is used to elevate patients' hemoglobin to give them the best possible chance at survival without RBC transfusion (Al-Nawakil et al., 2013; Ford, Grant, Mick, & Keck, 2015; Garelius, Grund, & Stockelberg, 2015; Jillella et al., 2017; Mazza, Palazzo, Minoia, Amurri, & Pisapia, 2016). Elemery et al. (2017) established a specific trigger point to use erythropoiesis-stimulating agents during transplantation when the hemoglobin of Jehovah's Witness patients dropped below 11 g/dl. However, there are limitations to the efficacy of EPO because it takes two to six weeks of use to raise the patient's hemoglobin levels and the medication carries a black-box warning for increased risk of mortality or tumor progression in patients with cancer (Amgen, 2012). Therefore, providers may order EPO based on a careful analysis of risks and benefits of EPO administration.

Folate, vitamin B₁₂, and iron can play a crucial role in erythropoiesis (Koury & Ponka, 2004). During transplantation, these supplemental vitamins and minerals, along with EPO, can optimize hematopoiesis. IV iron is a pillar of SCT in Jehovah's Witness patients and is used in conjunction with EPO to boost hemoglobin production (Elemery et al., 2017; Ford et al., 2015; Garelius et al., 2015; Jillella et al., 2017). Folic acid also is used as an aid in RBC production (Elemery et al., 2017; Jillella et al., 2017). Elemery et al. (2017) used vitamin B₁₂ to prevent megaloblastic anemia in Jehovah's Witness patients receiving SCT.

Thrombopoiesis is also possible but not routine. In one small study (Al-Nawakil et al., 2013), Jehovah's Witness patients who underwent SCT were given romiplostim, a thrombopoietin receptor agonist, to help boost their platelet count. Ten of

13 patients received the medication before transplantation, and 4 of 13 received romiplostim after transplantation. None of the 13 patients experienced hemorrhagic complications, and their period of severe thrombocytopenia was shorter and less profound than thrombocytopenia reported in previous studies (Al-Nawakil et al., 2013).

Minimizing Blood Loss

Jehovah's Witness patients undergoing SCT are at high risk for complications secondary to bleeding because they decline platelet transfusions to help stem bleeding and RBC transfusions to replenish lost blood. Not only is blood loss due to high-volume hemorrhage a risk, but low-volume persistent blood loss also must be prevented. Precautionary measures can be taken to help lower the risk of bleeding. These measures include the use of antifibrinolytics, vitamin K supplements, and cryoprecipitate (if the patient agrees), and minimization of phlebotomy, gastrointestinal bleed, and epistaxis prophylaxis.

Because Jehovah's Witness patients do not accept platelet transfusions, other interventions are necessary to aid in blood clotting to prevent hemorrhage. Antifibrinolytics, such as aminocaproic acid (Amicar®), slow hemorrhaging when blood clots break down. Amicar is frequently prescribed for Jehovah's Witness patients after SCT when their platelets drop below $10 \times 10^9/L$ or with clinical evidence of bleeding (Elemery et al., 2017; Ford et al., 2015; Jillella et al., 2017). Vitamin K plays an important role in the formation of proteins that promote blood clotting, so it can be included in the treatment protocol for Jehovah's Witness patients receiving SCT to prevent bleeding (Elemery et al., 2017; Ford et al., 2015). Some Jehovah's Witness patients may choose to accept cryoprecipitate even though it is prepared from frozen plasma because it is not one of the expressly forbidden blood products and is left up to individual conscience. Cryoprecipitate has been used prophylactically to prevent bleeding when patients' platelets drop below $10 \times 10^9/L$ (Elemery et al., 2017) and as a treatment option for refractory bleeding in the setting of platelet transfusion refusal (Ford et al., 2015). Desmopressin (DDAVP®) can be used in the presence of active bleeding to attempt to reduce blood loss (Elemery et al., 2017). DDAVP improves hemostasis by stimulating release of clotting factor VIII, tissue plasminogen activator, and von Willebrand factor (Lawson & Ralph, 2015).

Prevention of iatrogenic blood loss reduces the degree of anemia when Jehovah's Witness patients receive SCT. Phlebotomy has been associated with changes in hemoglobin and hematocrit for hospitalized patients and can contribute to anemia (Thavendiranathan, Bagai, Ebidia, Detsky, & Choudhry, 2005). Limiting phlebotomy and using pediatric tubes for laboratory draws can further reduce anemia (Ford et al., 2015; Jillella et al., 2017; Mazza et al., 2016). Elemery et al. (2017) specified that drawing baseline blood work before SCT, then limiting

peripherally drawn blood draws to twice a week, prevents blood wasting from central line blood draws. To help reduce iatrogenic blood loss from frequent phlebotomy, the interprofessional team can collaborate and coordinate, eliminating unnecessary tests.

For Jehovah's Witness patients receiving SCT, the treatment plan includes preventing blood loss from epistaxis, gastrointestinal bleed, and menstruation. Epistaxis prevention using saline nasal sprays and xylometazoline nasal spray is common if a patient experiences active bleeding because it causes local vasoconstriction (Elemery et al., 2017). Gastrointestinal bleeds can be prevented when providers prescribe proton pump inhibitors and stool softeners (Elemery et al., 2017; Ford et al., 2015). Progesterone is given to premenopausal women to prevent any blood loss from menstruation, however minimal (Ford et al., 2015).

Altering Chemotherapy Regimens

Some studies made alterations to the intensity and length of chemotherapy regimens for Jehovah's Witness patients because they are unable to receive blood products and, therefore, are thought to be unlikely to survive more prolonged

FIGURE 1. PREVENTIVE AND SUPPORTIVE MEASURES FOR TREATING JEHOVAH'S WITNESS PATIENTS RECEIVING STEM CELL TRANSPLANTATION WITHOUT BLOOD PRODUCT TRANSFUSIONS

OPTIMIZING HEMATOPOIESIS

- Erythropoietin
- IV iron
- Folic acid
- Vitamin B₁₂

MINIMIZING BLOOD LOSS

- Antifibrinolytics, such as aminocaproic acid (Amicar®)
- Vitamin K
- Cryoprecipitate prophylactically or in the setting of bleeding
- Desmopressin (DDAVP®) in the setting of active bleeding
- Reduced laboratory draws
- Epistaxis prevention with saline nasal spray and xylometazoline nasal spray
- Gastrointestinal bleed prevention with proton pump inhibitors and stool softeners
- Progesterone for premenopausal women to prevent menstrual blood loss

ALTERING CHEMOTHERAPY REGIMENS

- Shortened length of conditioning chemotherapy, not intensity
- Reduced-intensity conditioning

Note. Based on information from Al-Nawakil et al., 2013; Elemery et al., 2017; Ford et al., 2015; Garelius et al., 2015; Jillella et al., 2017; Mazza et al., 2016.

and profound cytopenia. One case study (Garelius et al., 2015) presented a 28-year-old Jehovah's Witness patient with acute monocytic anemia who underwent an allogeneic SCT with reduced-intensity azacytidine conditioning. The patient survived transplantation without transfusion and went into remission but relapsed and died within eight months. The researchers concluded that a lower overall risk of severe cytopenia must be thoroughly weighed against the higher risk of relapse. Mazza et al. (2016) reported a different treatment plan. The plan shortened the length of the treatment without reducing the overall treatment intensity by overlapping chemotherapy drugs rather than administering them in sequence for patients with lymphoblastic lymphoma, acute lymphoblastic leukemia, and acute and chronic myeloid leukemias who were receiving allogeneic SCT. Study results did not report relapse rates of the patients who received the shortened myeloablative chemotherapy versus those who received reduced-intensity conditioning, but the results did conclude that treatment-related mortality was dependent on disease status, with the worst outcomes among those who had refractory disease.

Discussion

The number of Jehovah's Witness patients with a hematologic malignancy requiring SCT is exceptionally small. Hematologic malignancies are a minority among cancer diagnoses; leukemias, lymphomas, and myelomas total just 10% of new diagnoses every year (Siegel, Miller, & Jemal, 2018). Jehovah's Witnesses account for less than 1% of the total U.S. population (Pew Research Center, 2015). Therefore, the number of patients who are diagnosed with a hematologic malignancy who are also Jehovah's Witnesses is limited. A retrospective case-control study of risk-adjusted clinical outcomes for patients who declined blood product transfusions showed similar or better outcomes for those patients at equivalent or lower costs when appropriate blood conservation measures were used (Frank et al., 2014).

Limitations

The small number of Jehovah's Witness patients with a hematologic malignancy requiring SCT does set some limitations on study. Most studies involving these patients have small sample sizes or are limited case studies. Subsequently, drawing definitive conclusions from their results can be difficult. In a study by Ford et al. (2015) of 125 Jehovah's Witness patients with Hodgkin lymphoma, multiple myeloma, and amyloidosis who received an autologous SCT, the patients were found to have a higher treatment-related mortality rate (4.8%) than the national rate of 1%–3.5%. However, the authors concluded that this was likely acceptable because of the population's unique characteristics and treatment requirements. In an update of a 2003 study, Mazza et al. (2016) reported that their 100-day mortality rate for Jehovah's Witness patients with various cancer diagnoses undergoing SCT

IMPLICATIONS FOR PRACTICE

- Assess patients thoroughly for changes in mental status, including asking patients and family members about any changes in mentation that the patient may not notice.
- Administer antiemetics and antitussives as needed to prevent patients from coughing and retching, which can increase intracranial pressure.
- Prevent patient falls through the use of bed alarms and standby assistance for patients who are severely thrombocytopenic.

was 15% (2 of 13) for autologous SCT, 20% (1 of 5) for myeloablative allogeneic SCT, and 14% (1 of 7) for reduced-intensity conditioning. Although these two studies have larger sample sizes compared to other studies involving Jehovah's Witness patients undergoing SCT, the sample sizes are still small enough that wide variation exists in their results. Study of Jehovah's Witness patients receiving SCT would benefit from larger sample sizes to draw consistent conclusions; however, the exceptionally small available patient population is a significant limiting factor.

Implications for Nursing

Nurses play a vital role in the safe care of Jehovah's Witness patients undergoing SCT. Thorough and perceptive assessment is the cornerstone of nursing practice and is particularly critical with this patient population. Nurses caring for Jehovah's Witness patients receiving SCT should be vigilant for signs of bleeding or subtle changes in patient condition. Special attention should be paid to preventing patients from coughing, retching, straining, or bending over; all of these activities can increase intracranial pressure and put patients at higher risk for hemorrhage (Roytowski & Figaji, 2013). Appropriate administration of antiemetics and antitussives as needed and thorough patient education about activity limitations are crucial nursing interventions that can help prevent bleeding. Similarly, measures such as use of bed alarms and standby assistance for severely thrombocytopenic Jehovah's Witness patients can be effective tools to prevent patient falls with potential for subsequent injuries and potential blood loss.

The specialized and complex care needed for patients receiving SCT requires a comprehensive and detailed onboarding process for new staff, as well as continuing education. Clifford, Acheson, and Hall (2013) recommended a formalized orientation process that combines didactic content in a classroom format with clinical experience at the bedside for all nurses caring for patients undergoing SCT. Because Jehovah's Witness patients are an even more specialized community within the transplantation population, it is imperative that transplantation programs provide specialized education to nurses regarding religious beliefs, cultural sensitivity, and implications for nursing practice.

The extent to which nurses caring for this population experience moral distress, its impact, and strategies to address it is an interesting and largely unexplored avenue for further research. Jameton (1984) defined moral distress as the emotional state that arises when one knows the right thing to do but is constrained from doing it. A research gap exists regarding the moral distress

that nurses may experience when caring for adult Jehovah's Witness patients undergoing SCT who forgo blood product transfusions in potentially life-threatening situations, such as profound anemia or bleeding. However, a vast amount of research exists regarding moral distress in nursing as a whole, which may be beneficial to nurses caring for Jehovah's Witness patients undergoing SCT. The SUPPORT model addresses moral distress by acknowledging its existence, fostering a supportive culture of care, and developing nurses' resilience to challenging circumstances through education, support, and collaboration (Pavlish, Brown-Saltzman, So, & Wong, 2016).

Conclusion

Using various strategies to optimize hematopoiesis and minimize blood loss in conjunction with modified chemotherapy regimens, Jehovah's Witness patients can undergo SCT without blood product transfusions. Bedside nursing interventions play a crucial role in successful transplantation for these patients, both in patient education and prevention of falls and hemorrhage. The modalities that contribute to the success of bloodless SCTs for Jehovah's Witness patients, such as optimizing hematopoiesis and minimizing blood loss, could be broadly applied to patients who accept blood product transfusions and may offer improvements in care. Specialized nursing education provides a foundation for nurses to best care for Jehovah's Witness patients receiving SCT. That education also can address potential issues of nurses' moral distress as a result of patients forgoing blood product transfusions in life-threatening situations. Because studies about this population have small sample sizes, results of those studies are difficult to generalize. Therefore, nurses can lead and contribute to further research about this population.

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