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Utilizing Bloodless Medicine to Decrease Infection Rates in Hematopoietic Stem Cell Transplantation: A Literature Review

Samantha Saint Fort
University of Central Florida

UTILIZING BLOODLESS MEDICINE TO DECREASE INFECTION RATES IN HEMATOPOIETIC STEM CELL TRANSPLANTATION: A LITERATURE REVIEW

by

SAMANTHA SAINT FORT

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Thesis Chair: Heather Peralta, DHSc, MSN, RN

ABSTRACT

Aim: To determine if a significant relationship exists between bloodless medicine practices and decreased infection rates in oncology patients following hematopoietic stem cell transplantation by performing a literature review.

Background: It is not uncommon for healthcare professionals to encounter Jehovah's Witnesses (JW) seeking medical treatment in the acute care hospital setting and outpatient clinics alike. However, JW's pose a unique challenge to healthcare providers. Their refusal of blood transfusions makes them a population of interest within the medical community. The refusal of blood transfusions also poses a serious challenge to successful treatment in oncology JW patients, and many hospitals will refuse to perform a procedure as complex yet beneficial as a hematopoietic stem cell transplant in this population.

Methods: An extensive electronic literature search in the CINAHL Plus database was completed and included the keywords infection, blood transfusion, stem cell transplant, bloodless medicine, Jehovah's Witnesses, and transfusion reactions. The available literature was carefully examined for interventions performed and compared for ultimate results to be finalized as a written report.

Significance: The results of this research can not only optimize healthcare for the population of Jehovah's Witnesses, but also assist in reduced blood transfusions and improved cost management in all patients with a cancer diagnosis.

Conclusions: All studies concluded that autologous hematopoietic stem cell transplantation can be performed safely without the use of blood products. Their conclusion was based off of the data they collected following patients post-stem cell transplant. More research is needed to explore outcomes in this population as a result of blood transfusion refusal following stem cell transplantation in comparison with those who receive blood transfusion support.

Key words: Jehovah's Witnesses, Bloodless Medicine, Stem Cell Transplantation, Outcomes

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INTRODUCTION

There are presently 8,699,048 Jehovah's Witnesses (JWs) practicing in 239 lands around the globe (Jehovah's Witnesses [JW], n.d.). Therefore, it is not uncommon for healthcare professionals to encounter JWs seeking medical treatment in the acute care hospital setting and outpatient clinics alike. However, JWs pose a unique challenge to healthcare providers and their refusal of blood transfusions makes them a special population of interest within the medical community. The refusal of blood transfusions also poses a serious challenge to successful treatment in oncology JW patients, and many hospitals will refuse to perform a procedure as complex yet beneficial as a hematopoietic stem cell transplant in this population.

Hematopoietic stem cell transplantation is a rigorous and effective procedure used in treating hematological cancers such as leukemias, lymphomas, and multiple myeloma among other disorders. It involves the use of stem cells being infused into the body following high dose chemotherapy in order to replace dysfunctional cancerous cells. Stem cells are cells that have the ability to differentiate into a wide variety of specialized cells in the human body. Hematopoietic stem cells are found in the bone marrow and can develop into platelets, red blood cells, or white blood cells. Before a high dose of chemotherapy is given, stem cells are extracted directly from the bone marrow, from the blood stream, or even from umbilical cord blood (American Cancer Society, 2020). Hematopoietic stem cell transplants can be done autologous or allogenic. During an autologous transplant, stem cells are taken from the patient themselves prior to receiving high dose chemotherapy and reinfused after completion of high dose chemotherapy. Contrastingly, during an allogenic transplant, stem cells are removed from a matched donor and infused into the patient.

Stem cell transplants pose a serious risk to the recipient. The use of high dose chemotherapy beforehand ensures that any undetectable remaining cancerous cells following

previous treatment are eradicated, but it also kills healthy blood cells in the process. In the days following the procedure, patients become dangerously pancytopenic and it can take many weeks for the stem cells to begin differentiating and the blood counts to rise once again. Some patients succumb to fatal complications during the process including anemia, bleeding as a result of thrombocytopenia, and infection due to neutropenia. Still, “it is the best hope for a cure or a longer life” (National Library of Medicine [NLM], 2017) for many patients.

BACKGROUND & SIGNIFICANCE

There is much literature exploring the benefits of following bloodless medicine practices within different domains of medicine such as before, during, and after cardiac surgery. A study by Galas et al. (2013) sought to further examine the effect of blood transfusions on patients post cardiac surgery. Patient data was organized into three categories: the high transfusion group (received > 3 units of red blood cells), the low transfusion requirement group (received 1-3 units), and the non-transfusion group (received 0 units). They found that as the units of red blood cells transfused increased, the length of stay experienced an increase as well.

Additionally, clinical research has shown that immunomodulation and immunosuppression can possibly occur following blood transfusions leading to cancer recurrence and metastasis as well as a reduced ability to fight common infections. However, it is of note that the "exact mechanisms of transfusion immunomodulation are still unknown" (Refaai & Blumberg, 2013).

Research has also shown that blood transfusions are costly. A study by Jefferies et al. (2001) found that bone marrow transplants were attributed to the highest cost of blood transfusions with a median blood cost of $4444 and mean of $6183. They concluded that "considering those conditions with the highest cumulative transfusion costs (e.g., BMT, liver transplant, acute leukemia, and cardiothoracic procedures), changes in transfusion practices that affect these particular patient categories may have a significant impact on global blood transfusion costs" (para. 4). Another journal article highlighted that the frequent use of allogenic blood products "has been underestimated in cost and overestimated in effectiveness" (Hofmann et al., 2013). From testing donated blood to managing adverse transfusion reactions, it is evident that blood transfusions cost both the patient and the hospital a considerable sum. Therefore, its frequent overuse is not beneficial to either party.

Blood product alternatives are being implemented at bloodless medicine programs across the United States. While blood product alternatives have also been well researched, it is evident that more research is needed to explore outcomes in this population as a result of blood transfusion refusal specifically following stem cell transplantation in comparison with those who receive blood transfusion support. The result of this vital research can not only optimize healthcare for the JW population, but also assist in reduced blood transfusions, improved cost management, and better outcomes in all patients.

PURPOSE

The purpose of this literature review is to determine if a significant relationship exists between bloodless medicine practices and improved outcomes in adults hospitalized on oncology units. It is hypothesized that adults hospitalized for stem cell transplantation who receive blood transfusion support are more likely to exhibit symptoms of infection and an increased length of stay compared to adults who implement bloodless medicine practices.

METHODS

An extensive electronic literature search was conducted using the CINAHL Plus with Full Text database and the MEDLINE database. These databases were chosen based off of their focus on leading nursing and medical journal articles. The search included various combinations of the keyword's infection, blood transfusion, stem cell transplant, bloodless medicine, Jehovah's Witnesses, and transfusion reactions. Preference was given to peer-reviewed articles. Exclusion criteria included articles not published in an academic journal, articles not written in English, and articles published before 2000. Additionally, the following PICO question was used to guide the research process: In adults hospitalized on oncology units, how does the use of bloodless medicine compared to the transfusion of blood products decrease complication and infection rates after hematopoietic stem cell transplantation? The titles and abstracts of resulting articles were examined and screened for their relevancy to this PICO question. All articles were also screened for their relevance to hematological cancers over solid tumors. Ultimately, four articles were chosen through Medline and one article was chosen through CINAHL Plus with Full Text. The information obtained from these articles was collected into a literature analysis table that examined factors such as study design, demographics, interventions, strengths, and limitations. The data collected within this table was synthesized to finalize this literature review.

RESULTS

The literature shows increasing data on this important topic. Ford et al. (2015) conducted a case series study between May 1996 to March 2014. The sample size was N=125 with an age range of 21-71 years old. Fifty-seven participants were males (45.6%) and 68 were females (54.4%). Among the sample, n= 68 multiple myeloma patients, n = 19 Hodgkin's lymphoma patients, n= 36 Non-Hodgkin's lymphoma patients, n= 2 amyloidosis patients and there was no control group used.

This study measured bleeding complications using the WHO grading system, cardiac complications using the National Cancer Institute's toxicity grading system, and transplantation-related mortalities in JW patients post-Autologous Stem Cell Transplant. Interventions and changes were made in the treatment protocol when it was noticed that cardiac associated mortalities were occurring among participants. It was decided that following the retrieval of stem cells, patients would not undergo transplantation until hemoglobin levels were 11g/dL or higher and platelets were greater than or equal to 100,000 per microliter (Ford et al. 2015).

Ford et al. (2006) conducted a retrospective case-control chart review during an unspecified duration of time. The sample size was N=46 with an unspecified age range, gender, or race/ethnicity. Among the sample, n= 22 multiple myeloma patients, n = 22 lymphoma patients, and n= 2 breast cancer patients. Among the control group, there were 75 patients. Specifically, 30 had multiple myeloma, 30 had lymphoma, and 15 had breast cancer.

This study measured the number of patients with at least one reported infection in each group. Furthermore, the data was categorized into bacterial, viral, fungal, and unknown infections per person. It is unclear if an infection assessment tool was used or necessary to determine what constituted as an infection. Interventions were not applicable as a retrospective comparison was performed using medical records.

Joseph et al. (2019) conducted a retrospective case-control chart review during August 2006 to August 2016. The sample size within the case group was N=24 with an age range of 37-71 years old. Ten participants were males (42%) and 14 were females (58%). Fifteen participants were black (63%) and 9 were white (37%). Among the sample, n= 23 multiple myeloma patients and n= 1 amyloidosis patient. Among the control group, there were 71 patients with an age range of 27-68 years old. Twenty-nine participants were males (40%) and 42 were females (60%). Forty-four participants were black (63%) and 26 were white (37%). Specifically, 68 had multiple myeloma, and 2 had amyloidosis.

This study compared engraftment parameters, cardiovascular complications, and hematologic complications, among the case group and control group. No discernible measurement tool was used for cardiac complications. For hematologic complications, the *National Cancer Institute Common Terminology Criteria for Adverse Events* was utilized for classification. Interventions were not applicable as a retrospective comparison was performed using medical records.

DISCUSSION

The study performed by Ford et al. (2015) showed that autologous stem cell transplantation can be done safely without the use of blood products. Continuous cardiac monitoring and appropriate medications can effectively manage potential and active cardiac complications. Notably, Ford et al. found that JWs were hospitalized between 5-35 days whereas non-JWs ranged from 6-76 days. This data warrants further examination as non JWs could possibly face longer hospital stays compared with JWs undergoing the same procedure. The treatment plan used during this study was explained thoroughly allowing other medical professionals to apply this knowledge in their professional practice in the future. The results of this study showed that those within the JW population facing hematologic cancers can safely receive autologous stem cell transplantation (SCT) without blood transfusion support. This study did not measure infection rates in the population of interest outside of specific bleeding or cardiac associated complications.

Ford et al. (2006) showed a considerable decrease in infection rates among those who used bloodless medicine practices compared with those who received blood product supported SCT. To the knowledge of the researchers, no other studies have examined reduced infection rates in patients following a bloodless SCT compared with transfusion supported SCTs. A retrospective chart review allowed them to introduce preliminary evidence that could form the foundation of deeper research moving forward. This finding could have major implications for the general population and oncologic healthcare moving forward. This study is subject to all the disadvantages of retrospective studies. Selection bias of the control group cannot be excluded. Confounding variables could also skew results. The sample sizes were also smaller compared to the other studies. It was stated that the demographics were similar but specific data regarding participants was not supplied.

Joseph et al. (2019) demonstrated bloodless SCT is possible if specialized steps are followed to reduce blood loss, like the use of pediatric tubes and less blood draws. This study did not find any statistically significant differences between the population of interest and the control group, concluding that outcomes are similar with both treatment options. Patient demographics were provided in detail for each group in the study. The study design was also explicitly stated. Clinical lab values were included within the data for consideration both at the time of malignancy diagnosis and pre-ASCT. No transplant-related mortalities were reported in either group and long-term outcomes and overall survival were similar, showing that bloodless SCT is very possible. This study is subject to all the disadvantages of retrospective studies. Selection bias of the control group cannot be excluded. The sample sizes used for the control group vs the case group differ greatly. It may not be accurate to compare the data of each group and form conclusions. Chart review is not sufficient to answer this research question as records could be missing certain pieces of information and misclassification bias is likely. Blinding was not used. Few blood transfusions were performed in the control group, making this group similar to the case group of interest.

CONCLUSION

In summary, one study used a case series design while the others took a retrospective case-control chart review approach. The latter study method has inherent limitations that suggest further research using improved study designs are recommended. Multiple myeloma and lymphoma were the most common malignancies among participants. Females were slightly more prevalent than males. The studies that used a control group had much larger sample sizes in comparison with their respective case group. Race and ethnicity did not seem to be a significant or relevant demographic among researchers. While one study did not mention the age range, gender, or race/ethnicity in either of the groups under observation, it was stated that the "closest data set in terms of patient demographics" (Ford et al., 2006) was chose for comparison, suggesting adequate similarities between each group. Two of the studies reviewed focused on the most common complications post-SCT including cardiac and hematological complications as well as transplant related mortalities. Only one study focused on measuring the data regarding infections in patients post-SCT and resulting outcomes compared with a control group who received blood product support. All studies concluded that autologous hematopoietic stem cell transplantation can be performed safely without the use of blood products. Their conclusion was based off of the data they collected following patients post-SCT. Two studies were subject to the limitations of retrospective study designs. Many studies did not take into account infection rates among the bloodless SCT patients compared with a control group.

It is important that nursing considerations be taken into account when preparing to implement effective interventions within the immunocompromised oncologic patient population. Patient advocacy has long been considered a pillar of the nursing profession. It is described as "promoting patient safety and quality care" by "protecting patients, being patients' voice…[and] educating patients" (Nsiah et al., 2019). An article written by Sharon Vernon, a registered nurse

and director and coordinator of the Center for Bloodless Medicine and Surgery (CBMS) at Columbia St. Vincent Charity Hospital at the time, and Gail Pfeifer, also a registered nurse, demonstrated one way this can be done within a bloodless medical center setting. The admitting nurse placed a blue wrist band on the patient, a blue sticker on his chart, and a blue placard at the head of the bed all of which "identified him as a patient in the CBMS program" (Vernon & Pfeifer, 1997). This intervention ensured that the entire medical team was aware of the patient's wishes and could proceed with the appropriate treatment techniques thus protecting the patient and ensuring that his voice was heard. Nurses can also advocate for visitors and other staff members to consistently wear masks, wash their hands according to CDC standards, and disinfect reusable equipment like stethoscopes before entering the patients' room when caring for oncologic patients.

In conclusion, outcomes across the literature reviewed were similar showing that bloodless SCT can be performed safely and successfully if blood conservation techniques are followed. However, further research is needed to focus on infection rates and cost differences between those who pursue a bloodless stem cell transplant compared with those who receive blood product support. The result of this vital research can not only optimize healthcare for the JW population, but also assist in reduced blood transfusions and improved cost management in all patients. This research is critical towards providing equal, high quality healthcare to everyone regardless of personal beliefs.

APPENDIX A: LITERATURE ANALYSIS TABLE

Author(s), year	Ford et al., 2015	Ford et al., 2006	Joseph et al., 2019
Study Design	Case series	Retrospective chart review, cohort study	Retrospective case-control
Duration	May 1996- March 2014	N/A	August 2006 and August 2016
Sample Size	N= 125	N=46	N= 24
Demographics	21-71 years 57 males (45.6%) 68 females (54.4%) No stated ethnicity	None provided	37-71 years of age 10 males (42%) 14 females (58%) 15 black (63%) 9 white (37%)
Condition(s)	n= 68 multiple myeloma patients n = 19 Hodgkin n= 36 Non-hodgkin n= 2 Amyloidosis	n= 22 MM n= 22 lymphoma n= 2 breast cancer	n= 23 MM n= 1 amyloidosis
Controls	N/A	N= 75 patients myeloma (30), lymphoma (30) breast cancer (15)	TS-ASCT Age: 27-68 years old Gender: 29 males (40%) 42 females (60%) Race: 44 black (63%) 26 white (37%) Condition: 68 MM (97%) 2 amyloidosis (3%)
Outcome Measures	This study measured bleeding complications using the WHO grading system, cardiac complications using the National Cancer Institute's toxicity grading system, and transplantation-related mortalities in JW patients post-ASCT.	This study measured the number of patients with at least one reported infection in each group. Furthermore, the data was categorized into bacterial, viral, fungal, and unknown infections per person.	This study compared engraftment parameters, cardiovascular complications, and hematologic complications, among the case group and control group. Hematologic complications were measured using the National Cancer Institute Common Terminology Criteria for Adverse Events.
Intervention (if applicable)	Treatment plan-Interventions and changes were done in the treatment protocol when it was noticed that cardiac associated mortalities were occurring among participants.	N/A- a comparison was performed	N/A- a retrospective comparison was performed

Results	Autologous stem cell transplantation can be done safely without the use of blood products. Continuous cardiac monitoring and appropriate medications can effectively manage potential and active cardiac complications. Notably, Ford et al. found that JWs were hospitalized between 5-35 days whereas non-JWs ranged from 6-76 days. This data warrants further examination as non JWs could possibly face longer hospital stays compared with JWs undergoing the same procedure.	This study showed a considerable decrease in infection rates among those who used bloodless medicine practices compared with those who received blood product supported SCT.	This study showed that bloodless SCT is possible if specialized steps are followed to reduce blood loss, like the use of pediatric tubes and less blood draws. This study did not find any statistically significant differences between the population of interest and the control group, concluding that outcomes are similar with both treatment options.
Strengths	The treatment plan used during this study was explained thoroughly allowing other medical professionals to apply this knowledge in their professional practice in the future. The results of this study showed that the JW population facing hematologic cancers can safely receive autologous stem cell transplantation without blood transfusion support.	To the knowledge of the researchers, no other studies have examined reduced infection rates in patients following a bloodless SCT compared with transfusion supported SCTs. A retrospective chart review allowed them to introduce preliminary evidence that could form the foundation of deeper research moving forward. This finding could have major implications for the general population and oncologic healthcare moving forward.	Patient demographics were provided in detail for each group in the study. The study design was also explicitly stated. Clinical lab values were included within the data for consideration both at the time of malignancy diagnosis and pre-ASCT. No transplant-related mortalities were reported in either group and long-term outcomes and overall survival were similar, showing that bloodless SCT is very possible.

Limitations	This study did not measure infection rates in the population of interest outside of specific bleeding or cardiac associated complications.	This study is subject to all the disadvantages of retrospective studies. Selection bias of the control group cannot be excluded. Confounding variables could also skew results. The sample sizes were also smaller compared to the other studies. It was stated that the demographics were similar but specific data regarding participants was not supplied.	This study is subject to all the disadvantages of retrospective studies. Selection bias of the control group cannot be excluded. The sample sizes used for the control group vs the case group differ greatly. It may not be accurate to compare the data of each group and form conclusions. Chart review is not sufficient to answer this research question as records could be missing certain pieces of information and misclassification bias is likely. Blinding was not used. Few blood transfusions were performed in the control group, making this group similar to the case group of interest. No discernible measurement tool for cardiac complications

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