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Hemoglobin matters: Perioperative blood management for oncology patients

by Jennifer Stephens, Ruby Tano

ABSTRACT

As the number of cancer cases rise each year in Canada, so does the number of surgical oncology cases. Surgery presents a unique and heightened stressor for the body already experiencing volatility from factors such as disease and treatments. Perioperative red blood cell (RBC) transfusions are critical to stabilize hemoglobin levels and correct anemia, as well as provide a buffer against anticipated intraoperative blood loss. Thoroughly examining and anticipating risk factors related to the potential need for perioperative blood transfusions is necessary to improve outcomes. Research evidence in recent years related to perioperative blood management of oncology patients has specifically recommended active, coordinated programs to reduce the need and amount of blood transfusions administered pre-, intra-, and post-surgery. Coordination between surgical oncologists and a local or provincial patient blood management (PBM) program is an important strategy that allows patients at risk of perioperative complications to be identified and receive early interventions and ongoing observation.

Keywords: oncology, perioperative oncology, surgical oncology, blood management, blood transfusions, anemia, nursing, oncology nursing

INTRODUCTION

Despite amazing advancements in diagnostics and treatment, cancer has overtaken heart disease as the leading cause of death for adults in Canada (Canadian Cancer Society, 2020). More than 225,800 Canadians will be diagnosed with malignancies in 2020 and most of these will require some type of surgical intervention (Brenner et al., 2020; Prashad et al., 2019). Surgery is a major form of treatment for many solid tumour cancers. Major cancer types that feature surgery as a primary intervention include gynecologic cancers (uterine, ovarian, cervical, and vulvar), thoracic, breast, and gastrointestinal cancers (e.g., rectal, stomach, esophageal, oropharyngeal, and others).

Perioperative complications arising from comorbidities or pre-existing conditions can occur and include the potential need for blood product transfusions. Many oncology patients in Canada receive blood transfusions as part of their perioperative experience. This can be due to surgical complications, as well as to pre-existing anemia, which occurs in an estimated 30 to 90% of oncology patients (Knight et al., 2004). In some cases, it is possible to anticipate the need for blood products and intervene pre-operatively to decrease the need for transfusions. Some Canadian provinces, including Ontario, have established programs that provide patients with such preparation and education before they go to surgery. The purpose of this article is to explore the role of blood transfusion for oncology patients, and then to discuss the option of perioperative patient blood management (PBM) in specific relation to the oncology population.

BACKGROUND

Surgery is routinely performed as a major treatment strategy to remove malignant tumours (curative or primary surgery), for cancer staging and diagnosis, for debulking masses, and in palliative care to reduce suffering. In many cases, surgical interventions are combined with other treatment modalities including chemotherapy, radiation, targeted therapy, and hormone therapy to treat solid tumour cancers. Before taking a patient to surgery, the oncology team considers many factors including the quality of the tumour (type, size, location, grade, and stage), as well as the overall health of the patient, their age, level of physical fitness, and comorbidities.

Blood Transfusions in Surgical Oncology

According to the Transfusion Transmitted Injuries Surveillance System (TTISS), in 2015 there were 1,150,285 blood components transfused in Canada (Public Health Agency of Canada, 2019). According to the Canadian Blood Services Annual Report (2019), approximately 726,548 units were red blood cells (RBCs) and confirmed a growing need for donors who can continue to provide this supply. Therefore, the transfusion of red blood cells is an important aspect of modern medical care in Canada, one that can be successful for saving lives and improving patient comfort. A multicentre study in the United States estimated the cost of delivery of a unit of red blood cells to a patient ranges from $522–$1,183 depending on the clinical setting (Shander et al., 2010). Similar estimates of delivery cost for a unit of RBCs in Canada is around $500 CAD (Hall, 2008). Transfusions can be costly and are not without inherent dangers.

AUTHOR NOTE

Jennifer Stephens, MA, PhD, RN, OCN, Assistant Professor and BN Program Director, Faculty of Health Disciplines, Athabasca University, Athabasca, AB

Ruby Tano, MN, RN, Patient Blood Management Coordinator, Patient Blood Management Program, Sunnybrook Health Sciences Centre, Toronto, ON

Address for correspondence: Jennifer Stephens, Athabasca University, 1 University Drive, Athabasca, AB T9S 3A3

Email: **jstephens@athabascau.ca**

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An escalating use of surgery for oncology cases, combined with tremendous advancements in surgical technique and equipment, has resulted in an overall increase in the number of oncology surgeries. Surgery constitutes a stressful event for the body and amplifies the release of inflammatory mediators, catecholamines, and angiogenesis activators. These stress-chemicals compound a difficult period for the body, which is already undergoing some level of immunosuppression due to cancer treatments or the cancer process itself (Cata et al., 2019). The release of chemicals causing inflammation is particularly damaging to delicate tissue in the lungs, heart, and kidneys (Garraud et al., 2016). Shah and colleagues (2017) have explored how blood transfusion can significantly alter immune function causing both immunosuppression, as well as general immune dysregulation and overexpression.

Since the 1980s, the academic literature has blossomed with articles detailing risks associated with blood transfusions for surgical oncology patients (Wu & Little, 1988). Although blood transfusions can be lifesaving in many cases, research evidence indicates that potential complications and impacts to mortality and longevity arising from transfusions are becoming better understood. For example, allogeneic transfusion-related immunomodulation is considered a factor resulting in increased perioperative morbidity and poorer long-term outcomes for oncology patients (Ecker et al., 2016). Other complications include secondary infection, human errors, hemolytic transfusion reactions (HTR), transfusion-related acute lung injury (TRALI) and transfusion-related graft-versus-host disease (GVHD). In some cases, blood transfusions have been implicated in cancer recurrence (Weber et al., 2007; Wu et al., 2018). According to the literature, oncology patients who receive blood transfusion during surgery are more likely to develop complications including both venous and arterial thromboembolism (Barber & Clarke-Pearson, 2017; Cata & Gottumukkala, 2014; Khorana et al., 2008; Sheth et al., 2017).

The Role of Anemia

As stated previously, anemia refers to low hemoglobin levels. There are multiple types of anemia arising from both hypo-cellular disease (e.g., aplastic anemia or sickle cell anemia) and hypo-hemoglobular disease (e.g., thalassemia in which RBCs are destroyed by the spleen). Vitamin-deficient anemia occurs in persons who lack proper levels of folate, vitamin B-12, or vitamin C and results in a lack of RBC production. In cases where iron is not available for the bone marrow to construct hemoglobin, RBCs lack a proper oxygen carrying capacity. This iron-deficiency anemia occurs from blood loss such as might happen during a surgery, but it can also occur from inadequate dietary iron, poor gastrointestinal absorption of iron, inflammatory bowel disease, celiac sprue, or chronic blood loss such as through parasitic infection or micro-bleeding.

Most oncology patients suffer from some type of anemia, as part of their cancer illness trajectory, with researchers estimating between 30% to 90% of patients at risk (Knight et al., 2004). In many cases, anemia can be the result of myelosuppression from chemotherapy or radiotherapy or it can be a result of the cancer disease process (Rizzo et al., 2008; Weber et al., 2007). Disease or treatment-related nausea, vomiting, diarrhea, malnutrition, and excessive bleeding are also identified causes of anemia for oncology patients (Gilreath & Rodgers, 2020). Anemia can be a result of, or exacerbated, by surgery and can lead to a host of symptoms including fatigue, weakness, arrhythmias, dyspnea, headaches, and dizziness. In turn, these can impact quality of life and raise safety concerns. It has been shown that a direct relationship exists between hemoglobin levels and quality of life (Crawford et al., 2002).

Over the past decade, an increasing number of medical professionals have called for limits on the transfusion of erythrocytes during surgery (Carson et al., 2012; Napalitano et al., 2009). There are multiple reasons for this recommendation, but overall, the research literature supports the notion that RBC transfusion preoperatively is associated with increased morbidity and mortality. However, the descriptive factors for this association are complex. For example, O'Shea and colleagues (2018) revealed a positive connection between ovarian cancer patients receiving neoadjuvant chemotherapy and perioperative blood transfusions. The researchers suggested that anemia be corrected, and hemoglobin levels monitored before surgery to decrease the need for transfusion perioperatively. Similarly, Aquina and colleagues (2017) reported a similar statistic that causes alarm. These authors reviewed chart records of 24,230 patients who had colon resection surgery between 2004 and 2011 and concluded that perioperative blood transfusions were correlated with increased rates of postoperative sepsis and decreased survival. Recommendations from this study strongly suggested a purposeful reduction in perioperative blood transfusions for oncology patients through practice modifications. Several other studies over the past five years have also recommended increased perioperative blood management for oncology patients (Buchner et al., 2017; Elmi et al., 2016; Patel et al., 2017; Prescott et al., 2015; Prescott et al., 2019; Towe et al., 2018; Wallace et al., 2018).

PATIENT BLOOD MANAGEMENT

Patient blood management is a best practice approach to enhance and improve the care of patients at risk from transfusions (American Association of Blood Banks, 2020; Franchini et al., 2019). PBM practices include all features of clinical management and patient evaluation surrounding the decision-making process for transfusion. Increasingly, academic literature suggests that blood transfusions may be linked to increased patient morbidity, mortality, length of stay, costs, and blood shortages. Based on these issues, the core of PBM practice seeks to reduce the need for blood transfusions in three ways: by treating anemia in the preoperative phase, by minimizing blood loss during surgery, and through encouraging the appropriate use of blood in the postoperative period (Althoff et al., 2019; Freedman, 2016).

Preoperative anemia is being recognized as an associated risk factor for worse perioperative outcomes (Fowler et al., 2015; Musallam et al., 2011; Mueller et al., 2019; Njølstad et al., 2013) and is a major focus for patient blood management. Preoperative anemia, as defined by the World Health

Organization (WHO), is a hemoglobin less than 13g/dL for males and 12g/dL in females who are scheduled to undergo what is considered a high blood loss surgery (Butcher & Richards, 2017; International Society for Blood Transfusion, n.d.; WHO, 2011). Current PBM options of treatment of cancer anemia include iron replacement and erythropoietic stimulating agents (ESAs), like epoetin alfa (Eprex). Studies have suggested that the use of oral or intravenous iron therapy may play a role in the treatment of anemia (Muñoz et al., 2017). Prompt recognition and management of preoperative anemia has been associated with improved clinical outcomes (Busti et al., 2018).

A variety of surgical methods are available during an oncology surgery to reduce perioperative blood loss. These may include point-of-care testing to assess coagulation, topical hemostatic agents, hemostatic drugs, and perioperative blood salvage (Freedman, 2016). Anesthetic agents and techniques can also have an impact on perioperative blood loss. Literature suggests that anesthetic techniques including anesthetic types, types of ventilation, patient positioning, and avoiding hypothermia affect intraoperative blood loss (Shah et al., 2020).

In the postoperative period, oncology patients benefit from being involved in a PBM program in several ways. First, PBM guidelines and various pivotal clinical trials support a restrictive transfusion threshold/trigger with a hemoglobin concentration 7–8 g/dL for clinically stable adult patients (Goodnough et al., 2014; Mueller et al., 2019). The threshold serves as a guide in the context of the patient's clinical condition (Freedman, 2016). Over the years, several trials have shown that restrictive versus liberal RBC transfusions have at least equal patient outcomes, and restrictive RBC transfusion practices showed a decrease in mortality and morbidity rates in patients (Freedman, 2016). Secondly, risks associated with transfusions are dose dependent. Several recent studies suggest that each blood transfused unit is associated with an increased risk for adverse events (Aquina et al., 2017; Cata et al., 2016; Fernandez et al., 2018; Linder et al., 2013; Reeh et al., 2017). One landmark study, called the Transfusion Requirements After Cardiac Surgery (TRACS), consisted of a randomized control trial with two arms: one in which cardiac surgery patients were transfused liberally and another in which transfusions were sparing (Hajjar et al., 2010). The TRACS outcomes indicated a strong correlation between transfused units and mortality. Current PBM guidelines therefore support restrictive transfusion and single-unit transfusion approaches for clinically stable patients with clinical reassessment of patients before subsequent transfusions (Freedman, 2016; Zacharowski & Spahn, 2016).

PBM practices are continually evolving to improve patient outcomes. PBM practices support patients through the preoperative setting by managing anemia, utilizing surgical techniques to reduce blood loss, and employing the recommended use of transfusions in the postoperative period.

ONCOLOGY NURSING IMPLICATIONS AROUND PBM PROGRAMS IN CANADA

Adequate treatment strategies around perioperative blood management are important given the impact of quality of life, disease progression, and survival in cancer patients (Busti et al., 2018). A formal or informal PBM strategy for an oncology patient can provide added benefits to surgery, as a treatment or palliative strategy. Currently in Canada, many provinces have active PBM programs that routinely engage with oncology patients. These programs include specialty-trained nurses and physicians who collaborate and strategically coordinate strategies aimed at improving surgical outcomes. The implementation of PBM programs provides optimal care and support to patients and families anticipating transfusion in the perioperative setting. Engaging focused nursing coordinators dedicated to PBM's best practices adds value and benefit to the PBM process (Bielby & Moss, 2018; Freedman, 2016; Miller et al., 2015). Currently, PBM programs exist throughout the U.S., Canada, Europe, and Australia (Althoff et al., 2019).

Patient, family, and staff education around perioperative blood transfusion combined with increased surveillance of side effects and outcomes are essential aspects of core PBM practices. Specialized PBM nurse coordinators play a critical role in ensuring a PBM culture within healthcare organizations (Freedman, 2016). Within Canada, the PBM nurse coordinators work to ensure patients and families receive focused support and education both before and after their planned surgery. In this way, the nurse coordinator collaborates with the surgical team to identify when preoperative transfusion or iron supplementation will be beneficial to correct ongoing anemia concerns. The nurses may administer treatments such as intravenous iron transfusions or give prescribed injections of RBC boosters such as epoetin alfa (Eprex). The nurses may also teach patients or support members to administer these shots themselves according to a specific schedule in anticipation of a surgery date. For many patients enrolled in a perioperative transfusion program, the nurses will perform regular blood work (i.e., complete blood count with differential, or CBC with differential) to monitor RBC counts and hemoglobin levels, which allows for modifications in the pre-operative anemia treatment plan.

In addition to working directly with patients, the PBM nurse coordinators also educate other healthcare professionals about PBM strategies and work closely with referring physicians, pharmacists, nurses, and assessment clinics to meet the needs of preoperative patients. While PBM programs exist in some larger urban areas in Canada, in general, many oncology patients will not have access to a PBM-specific nurse coordinator or team. For this reason, there exists opportunity for oncology nurses to gain heightened awareness concerning blood transfusion practice and the impact that perioperative transfusion can potentially have on cancer patient complications and outcomes. By keeping core principles of PBM in mind during the preoperative phase, oncology nurses can assist in treating preoperative anemia, advocating for minimal blood loss during surgery, and for careful RBC transfusion postoperatively (Althoff et al., 2019; Freedman, 2016). For example, oncology nurses play a key role for ensuring appropriate lab work is completed in a timely manner throughout the perioperative period. This will include a CBC with differential, but also a group and screen (G&S), as well as a host of other potential indicators like serum iron, serum ferritin,

total iron-binding capacity (TIBC), or transferrin saturation. Additionally, C-reactive protein (CRP) and albumin should be examined throughout the operative journey as indicators of inflammatory response (Ferraris et al., 2013; McSorley et al., 2020). The oncology nurse is also critical in assessing for signs and symptoms of anemia such as low iron, low hemoglobin, or erythrocytopenia, as well as other potential complicating factors such as poor nutrition, coagulation disorders, neutropenia, and thrombocytopenia. As with the PBM nurse coordinator, the oncology nurse may act to provide preoperative support in the form of iron infusions, blood transfusions, or ESAs.

The role of the oncology nurse intraoperatively can be a support to the team for a wide variety of surgical procedures (Pirschel, 2018). Postoperatively, the oncology nurse is instrumental in monitoring patients for potential complications not only related to the surgery, but to RBC transfusions. In the immediate hours and days after surgery, patients may experience post-transfusion reactions related to secondary infections (with fevers, rashes, rigors, hypotension, dyspnea, and tachycardia) indicative of postoperative systemic inflammatory response syndrome (SIRS). Current rationale supports perioperative blood transfusion linked SIRS to as the most likely cause for increased morbidity and mortality (Ferraris, Ballert, & Mahan, 2013; McSorley et al., 2020). The oncology nurse further educates patients around post-operative activity and complications related to potentially new-onset anemia (from blood loss) or unintended diseases such as iron-overload (Crane & Selanders, 2017; Woei-A-Jin et al., 2020).

CONCLUSION

Cancer is the leading cause of death in Canada, and the number of surgical oncology cases continues to rise each year. Addressing the potential need for perioperative blood transfusions is critical to ensure patient safety and decrease potential for poor outcomes. Coordination between surgical oncologists and a local or provincial PBM programs allows patients at risk of perioperative complications to be identified and receive early interventions that can improve surgical outcomes and the overall patient care experience.

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