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Impact of a Conservative Red Blood Cell Transfusion Strategy in Children Undergoing Hematopoietic Stem Cell Transplantation

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A 2008 randomized trial of critically ill, but stable, children reported the safety of transfusing red blood cells at a hemoglobin threshold of 7 g/dL. In 2009, we adopted the same transfusion criteria in our hematopoietic stem cell transplantation patients. Regression modeling was used to compare data obtained during primary admission for hematopoietic stem cell transplantation in calendar years before and after our practice change. Sixty-six patients admitted in the preintervention year were compared with 75 postintervention. Pre- and postpatients were similar in diagnoses and type of transplantations. Postintervention, median hemoglobin pretransfusion significantly decreased from 8.8 g/dL to 6.8 g/dL ($P < .0001$). In addition, transfused red blood cell units received by patients dropped from 4 (interquartile range [IQR] 3, 8) to 3 (IQR, 2, 5), ($P = .002$), and number of transfusion days per patients decreased from 4 (IQR, 2,5) to 3 (IQR, 2, 5), ($P = .01$). There were no differences in length of stay, time to engraftment, or 100-day mortality. Median blood product charges per patient significantly decreased ($3,624 [IQR, $2,265, $6,040] to $2,185 [IQR, $1,812, $3,997], $P = .004$). Our initial experience suggests that implementation of a conservative transfusion strategy in otherwise stable children undergoing hematopoietic stem cell transplantation appears safe and lowers transfusion exposures.

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BACKGROUND

Red blood cell (RBC) transfusions are an essential and virtually universal component of supportive care for patients undergoing myeloablative hematopoetic stem cell transplantation (HSCT) [1]. Although such transfusions are generally well tolerated, there are associated short- and long-term risks. Acutely, patients are susceptible to volume overload and transfusion reactions including rare but serious complications such as anaphylaxis, viral transmission, and transfusion-related lung injury [2]; long-term sequelae include transfusion-associated immune compromise [3] and iron overload [4]. Blood products are also a limited and expensive healthcare resource. Because of the potential for harm and associated cost, transfusion exposures should be minimized. In recent years, conservative RBC transfusion strategies have been implemented in a variety of populations including pediatric intensive care unit patients, premature newborns, and infants undergoing reparative cardiac surgery [2,5-7]. Although patients undergoing HSCT represent one of the most heavily transfused groups in pediatrics, there have been no studies of the impact of using conservative thresholds for transfusions in these children.

Several well-controlled studies have shown that limiting blood transfusions in critically ill, but stable patient populations does not affect morbidity and

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mortality [2,5,8,9]. Most of these studies excluded critically ill and unstable patients who were bleeding, severely hypoxic, and/or in shock requiring vasopressors. A 1999 multicenter randomized controlled trial in critically ill adults found a restrictive strategy of maintaining hemoglobin (Hgb) concentrations between 7 and 9 g/dL resulted in a trend toward decreased mortality when compared with more liberal transfusion strategies designed to maintain a hemoglobin level >10 g/dL, excepting in patients with active coronary ischemic syndromes [9]. In 2007, a multicenter noninferiority randomized trial was conducted in children in the pediatric intensive care unit comparing outcomes using a conservative hemoglobin threshold of 7 g/dL with that of 9.5 g/dL. The results suggest that use of the lower hemoglobin threshold reduced tranfusions by 44% without affecting a number of clinical outcomes, including rates of organ failure, ventilator days, and mortality [5].

Before 2009, patients in our HSCT unit received routine RBC transfusions when hemoglobin levels were <9 g/dL. In February 2009, following a month-long review of the pediatric critical care literature and discussion among physician and nursing staff, we implemented a practice change to use a routine transfusion hemoglobin threshold of <7 g/dL in HSCT patients who were not clinically unstable. We subsequently performed the following pre/postanalysis to assess the impact of changing our transfusion strategy in children undergoing HSCT at our institution. We hypothesized that adopting a more conservative transfusion strategy in this patient population would lead to less use of blood products and decreased healthcare charges without negatively affecting patient outcomes.

METHODS

As part of a quality improvement initiative, we compared census and transfusion data for all patients admitted for HSCT to our unit during the calendar year before and for 1 year after a written change in transfusion protocol dated 2/10/2009. Before the practice change, our standard operating procedure stipulated that clinically stable patients undergoing transplantation should be transfused when hemoglobin levels were <9 g/dL. Subsequently, a revised standard operating procedure recommended limiting routine transfusions for hemoglobin levels <7 g/dL. We chose two 12-month study periods: 1/1/2008-12/31/2008 before the change, allowed a 2-month washout period, and compared 3/1/09-2/28/10 following practice change. Results of our analysis were extensively presented internally within our institution. We also discussed any human subjects review requirements with our hospital's institutional review board in preparation for dissemination of our findings externally. Per the policy at our institution, because this was implemented as a quality improvement initiative and not a research project, our institutional review board stated that it was exempt from and declined the opportunity for full review.

We included patients admitted to the HSCT unit at our hospital for a first transplantation during the study periods, excluding patients who had a second transplantation even if it was part of their original transplantation protocol and patients admitted for other indications such as suspected sepsis. We examined the entire length of stay for each patient according to HSCT database maintained for the purposes of FACT (Foundation for the Accreditation of Cellular Therapy; www.factwebsite.org) accreditation. Transplantation-related deaths, in particular, were reviewed to determine any possible relationship to transfusion practice.

All specific transfusion decisions for individual patients during both study periods were made at the discretion of physician attendings. Blood product orders were placed by either hematology-oncology fellows or by pediatric housestaff rotating through the unit. Transfusions in this pediatric population were generally ordered on a mL/kg basis, and there was no change in the practice of ordering transfusions during the study period.

Data from both periods were collected and analyzed using the methods established by the PRUDENT© (Patient Resource Use—Determination of Effective and Necessary Targets) project team at Children's Hospital Boston. Data abstracted from medical records included patient demographics, type of blood products transfused, the number and dates of transfusions, the temporal relationship between transfusions and mortality, and patient hemoglobin levels both before and after transfusion. Data obtained from our institution's blood bank registry included dates and numbers of units of blood products transfused. Additional data collected from our HSCT database included primary diagnosis, date of transplantation, type of transplantation (autologous versus sibling donor versus matched unrelated donor), time to engraftment, intensive care unit days, and 100-day mortality. We also collected data on patient healthcare charges at our institution from the Pediatric Health Information System, an administrative database affiliated with the Child Health Corporation of America (Shawnee Mission, KS), a business alliance of children's hospitals that contains inpatient, emergency department, ambulatory surgery, and observation data.

Statistical Analysis

Categoric patient characteristics and outcomes were reported as counts and percentages, and were compared by χ^2 or Fisher exact test between groups. Continuous and count data were summarized using median and interquartiles ranges (IQR), and were