



The Effect of Diagnostic Blood Loss on Anemia and Transfusion Among Postoperative Patients With Congenital Heart Disease in a Pediatric Intensive Care Unit



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ABSTRACT

Purpose: To evaluate whether diagnostic blood loss can lead to anemia and consequent blood transfusion among postoperative patients with congenital heart disease (CHD) in the pediatric intensive care unit (PICU).

Design and Methods: This prospective observational study was conducted in a university-affiliated tertiary hospital between January and August 2016. CHD patients aged < 12 years, undergoing cardiac surgery, with a PICU stay > 48 h were included ($n = 205$). Multivariate logistic regression analyses were used to determine the effect of diagnostic blood loss on anemia and transfusion.

Results: The mean daily phlebotomy volume was 5.40 ± 1.94 mL/d during the PICU stay (adjusted for body weight, 0.63 ± 0.36 mL/kg/d). Daily volume/kg was associated with cyanotic CHD, Pediatric Risk of Mortality III score, and Pediatric Logistic Organ Dysfunction (PELOD)-2 score. In total, 101 (49.3%) patients presented with new or more severe anemia after admission to PICU, which was not associated with phlebotomy volume. Forty-one (20.0%) children received one or more RBC transfusions during their PICU stay. Multivariate analysis indicated that PELOD-2 score > 5, new or more severe anemia, and daily volume/kg of phlebotomy > 0.63 mL/kg/d were significantly associated with transfusion after 48 h of admission to PICU.

Conclusions: Our findings indicate that diagnostic blood loss is not related to postoperative anemia in children with CHD; however, this factor does correlate with blood transfusion, since it somewhat reflects the severity of illness.

Practice Implications: Strategies should be applied to reduce diagnostic blood loss, as appropriate.

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Introduction

Anemia is defined as an abnormally low level of hemoglobin (Hb), which is at least two standard deviations (SD) less than the average level for an age group (Bateman et al., 2008), and is a very common comorbidity in intensive care units (ICU), presenting in 70%–98% of critically ill patients (Bateman et al., 2008; Corwin et al., 2004; Thomas, Jensen, Nahirniak, & Gibney, 2010). Reduction of oxygen carrying capacity because of anemia, can lead to compensatory increases in cardiac output, heart load, and consequent increased risk of cardiovascular disease (DeBellis, 2007; Kaiafa et al., 2015; McEvoy & Shander, 2013). Conversely, patients with cardiovascular disease are also unable to adequately tolerate anemia (Kaiafa et al., 2015). Recent evidence indicates that anemia increases the risk of death in patients with acute myocardial infarction (AMI) (Ducrocq et al., 2015; Mamas et al., 2016;

Uchida et al., 2015) or congenital heart disease (CHD) (Miyamoto, Inai, Takeuchi, Shinohara, & Nakanishi, 2015), and in those undergoing cardiac surgery (Karkouti, Wijeyesundera, Beattie, and Reducing Bleeding in Cardiac Surgery (RBC) Investigators, 2008; Miceli et al., 2014). Severe anemia commonly requires therapeutic red blood cell (RBC) transfusion. It is estimated that blood transfusion occurs in 20–62% of ICU patients (McEvoy & Shander, 2013). Although blood transfusion can save life, transfusion-related complications can also occur. A meta-analysis revealed that blood transfusion was related to inferior survival of patients with myocardial infarction (Chatterjee, Wetterslev, Sharma, Lichstein, & Mukherjee, 2013). Thus, strategies to reduce the development of anemia and unnecessary blood transfusion may improve the prognosis of heart disease.

Many factors can result in anemia in patients in ICU, including nutritional deficiencies, bone marrow suppression, destruction of RBCs, and blood loss (DeBellis, 2007; McEvoy & Shander, 2013), and diagnostic blood loss is recognized as an important cause of anemia in critically ill patients (Salisbury et al., 2011; Thavendiranathan, Bagai, Ebidia, Detsky, & Choudhry, 2005). Combined with multiple complications

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and rapid changes, patients in the ICU undergo frequent phlebotomy, which is humorously referred to as ‘ICU vampirism’ (Ranasinghe & Freeman, 2014). It is estimated that Hb concentrations reduce by approximately 7 g/L with every 100 mL of diagnostic blood loss (Thavendiranathan et al., 2005). A multicenter study of 17,676 patients revealed that blood drawn significantly raised the risk of moderate to severe hospital-acquired anemia during AMI, with an increase of approximately 18% for every 50 mL of phlebotomy (Salisbury et al., 2011). AMI is one of the most common heart diseases in adult ICU (Ding, Kader, Christiansen, & Berlowitz, 2015), whereas CHD is more frequent in pediatric ICU (PICU) (Axelrod et al., 2014). After adjustment for body weight, diagnostic blood loss from children is markedly more than that from adults. Hence, we hypothesized that critically ill children would be more vulnerable to phlebotomy-mediated anemia and consequent blood transfusion; however, the association between phlebotomy and hospital-acquired anemia in postoperative children with CHD is not well understood. Therefore, we carried out this study to determine the effect of diagnostic blood loss on anemia and transfusion in these patients.

Materials and Methods

Design

This was a prospective observational study to evaluate whether diagnostic blood loss could lead to anemia and consequently result in blood transfusion among postoperative children with CHD.

Setting

This study was conducted in a 26-bed PICU of a university-affiliated tertiary hospital, and was approved by the Ethics Committee of this hospital.

Sample

We enrolled children with CHD admitted to our PICU between January and August 2016. Patients were included if: (1) they received cardiac surgery, (2) the duration of their PICU stay was >48 h, and (3) they were younger than 12 years. Patients were excluded if: (1) they had chronic anemia before surgery, (2) they underwent a second operation after admission to ICU, and (3) they refused blood transfusions due to religious belief, or other reasons.

Data Collection

Clinical patient data were collected, including age, sex, weight, cyanotic category of CHD, Pediatric Risk of Mortality (PRISM) III score, Pediatric Logistic Organ Dysfunction (PELOD)-2 score, daily volume of phlebotomy, total volume of postoperative drainage, Hb levels, numbers and volume of RBC transfusions, length of PICU and hospital stays, and the presence or absence of nosocomial infections during ICU. Cyanotic CHD is defined as transposition of the great arteries, tetralogy of Fallot, univentricular heart, and truncus arteriosus/common arterial trunk (Madsen et al., 2016). The PRISM III score is a mortality risk model applied during the first 24 h after admission to PICU, which includes 17 physiologic variables corresponding to five features: cardiovascular/neurologic vital signs, acid-base/blood gas analyses, chemistry tests, hematology tests, and other factors (Pollack, Patel, & Ruttimann, 1996). The PELOD-2 score is assessed at eight time points during PICU stay, and consists of ten variables to evaluate the severity of neurologic, cardiovascular, renal, respiratory, and hematologic dysfunctions (Leteurtre et al., 2013). There are different criteria for anemia in CHD adults with or without cyanotic disease (Broberg et al., 2011; Miyamoto et al., 2015); however, there are no such separate criteria for children with cyanotic disease. Therefore, regardless of cyanotic

disease, a unified criteria for anemia was adopted as follows: 145 g/L for newborns, initially decreasing to 90 g/L at 2 months of age, subsequently increasing to 105 g/L at 6 months of age, and then 115 g/L at 2–12 years of age (Bateman et al., 2008). Patients were stratified into several groups according to the severity of anemia as follows: severe anemia (Hb < 70 g/L), moderate anemia (Hb, 70 to <100 g/L), and mild anemia (Hb, 100 g/L to the lower limit of the normal range) (Bateman et al., 2008).

Statistical Analysis

The Mann-Whitney *U* test was used to analyze continuous variables. Categorical variables are presented as frequency counts and percentages, and bivariate correlations were analyzed using the Chi-squared test. If appropriate, Fisher’s exact tests were performed. Multivariate analysis was performed by logistic regression, including only factors statistically significant at the 0.1 level ($P \leq 0.1$) in univariate analyses. For multivariate analysis, sample size should be approximately 10–20 times the number of predictive factors (age, sex, PRISM III score, PELOD-2 score, postoperative drainage volume, cyanotic category of CHD, and total volume, daily volume, and daily volume/kg of diagnostic blood loss); therefore, the estimated required sample size was 180. All statistical tests were performed using SPSS v17.0 (SPSS, Inc., Chicago, IL).

Results

Patient Characteristics

Between January and August 2016, 546 children with CHD were admitted to our PICU. In total, 210 patients met the inclusion criteria. Five patients who received second operation after admission to ICU were excluded. The median age of the remaining 205 eligible patients was 15 months (range, 0 to 138 months), 115 (56.1%) patients were male, and 66 (32.2%) cases had cyanotic CHD. On admission to PICU, the mean PRISM III score was 5.67 ± 4.40 (median, 5; range, 0–21), mean body weight was 10.69 ± 5.92 kg (median, 9.0 kg; range, 2.7–32.0 kg), and mean Hb concentration was 121.22 ± 17.09 g/L (median, 119 g/L; range, 80–183 g/L). Patient characteristics are listed in Table 1.

Diagnostic Blood Loss

Mean total volume of blood drawn was 33.05 ± 25.23 mL/patient during the PICU stay, with a mean daily volume of 5.40 ± 1.94 mL/d (adjusted for body weight, 0.63 ± 0.36 mL/kg/d). Daily volume/kg of diagnostic blood loss was significantly higher in patients with cyanotic disease, and those with higher PRISM III score on admission to PICU and PELOD-2 score during the PICU stay (Table 2).

Anemia and Transfusion

Among the 205 patients, 80 (39.0%) cases never became anemic, 24 (11.7%) were anemic on admission, but did not deteriorate during their PICU stay, and 101 (49.3%) developed new (69, 33.7%) or more severe (32, 15.6%) anemia after admission to PICU. Daily volume/kg of phlebotomy in patients with new or more severe anemia during the PICU stay was similar to that in the other patients (0.67 ± 0.37 mL/kg/d vs. 0.59 ± 0.35 mL/kg/d, $P = 0.058$). The results of univariate analyses for new or more severe anemia are listed in Table 3. Multivariate analysis indicated that PELOD-2 score >5 during the PICU stay [(odds ratio (OR) = 1.838, 95% confidence interval (CI) = 1.030–3.280, $P = 0.039$)] and postoperative drainage volume >258 mL (OR = 2.674, 95% CI = 1.424–5.023, $P = 0.002$) were independent risk factors for developing new or more severe anemia during the PICU stay.

In total, 41 (20.0%) children received one or more RBC transfusions during their PICU stay, and 23 (11.2%) patients received transfusions

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