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Storage duration of transfused red blood cells is not significantly associated with postoperative adverse events in pediatric cardiac surgery patients

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ABSTRACT

The aim of this study was to evaluate the association of storage duration of transfused red blood cells with the risk of postoperative serious adverse events in pediatric cardiac surgery patients. We studied 517 patients and found that 22 patients (4.3%) had at least one serious adverse event. The maximum and mean storage duration of transfused red blood cells did not differ significantly between patients with and without serious adverse events (maximum, $p = 0.89$; mean, $p = 0.81$). In our study of pediatric cardiac surgery patients, the storage duration of transfused red blood cells was not significantly associated with the risk of serious adverse events.

1. Introduction

Transfusion of red blood cells (RBCs) is a common clinical intervention. Transfusion can restore tissue oxygenation in some cohorts, especially when oxygen demand exceeds supply [1]. However, recent studies have raised concerns that morbidity and mortality may be higher in patients who receive blood transfusions [2,3].

It is standard practice in blood banks to use the oldest RBCs first. During storage, RBCs and their supernatant are altered biochemically and biomechanically, a development referred to as storage lesions [4,5]. The major characteristics of storage lesions include decreased levels of 2,3-diphosphoglycerate with impaired oxygen delivery, decreased intracellular adenosine triphosphate (ATP) levels, increased RBC rigidity, and release of proinflammatory cytokines into the supernatant. Thus, there are potential safety concerns when transfusing RBCs with longer storage durations to critically ill patients.

A number of studies have assessed the storage duration of transfused RBCs (tRBCs) and its association with clinical outcomes in adult cardiac surgery patients [6–8]. However, few studies have been performed to evaluate the association between storage duration of tRBCs and postoperative outcomes in pediatric patients who have undergone congenital cardiac surgery [9,10].

Accordingly, we conducted a retrospective observational study to evaluate the association between tRBC storage duration and the incidence of postoperative serious adverse events (SAEs). We hypothesized that longer tRBC storage duration would be associated with increased risk of SAEs in pediatric patients who had undergone congenital cardiac surgery.

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2. Methods

2.1. Study design

This study was a retrospective observational investigation to determine the association between tRBC storage duration with the incidence of postoperative SAEs. Our study has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. This study was approved by the Human Research Ethics Committee of Okayama University Hospital, which waived the need for informed consent.

2.2. Study population and data sources

This study was conducted in an 865-bed tertiary teaching hospital with 8 beds in the pediatric cardiac intensive care unit (ICU). We included pediatric patients admitted to the ICU after congenital cardiac surgery who received RBC transfusions intraoperatively or on the day of surgery, between January 1, 2009 and December 31, 2011. Exclusion criteria were 1) 18 years of age or older, 2) undergoing operations other than congenital cardiac surgery, or 3) no requirement for RBC transfusion during the operation or on the day of surgery.

Patient demographics, including age, sex, body weight, duration of cardiopulmonary bypass (CPB), and probability of death calculated by a revised version of the pediatric index of mortality (PIM2) [11] were retrieved from the database which had been collected by trained physicians. Surgery types were coded based on RACHS-1 (Risk Adjustment Classification for Congenital Heart Surgery-1) categories, which is coding [12]. RACHS-1 was based on the categorization of undergoing surgical procedures. It was scored from one to six (higher score means more complex operation with higher expected mortality).

2.3. Transfused red blood cells and its indices

In our hospital, for pediatric patients, tRBCs were used beginning with the chronologically oldest RBC pack which was selected by blood transfusion department. In Japan, the expiration date of RBCs was 3 weeks. Thus, the age of tRBCs in the current study was less than 3 weeks. Additionally, the donor of RBCs was not allowed to donate the blood for 4 weeks after prior donation.

Information on tRBCs was retrieved from an electronic blood product database. The maximum (RBC_{MAX}) and mean (RBC_{MEAN}) storage duration of tRBC were calculated, indicating the highest or arithmetic mean storage duration of all tRBCs used during the study period. We also calculated the total number of tRBC donors (N_{donor}).

2.4. Outcomes

We defined the primary outcome as the incidence of at least one of three postoperative SAEs: 1) death, 2) cardiac arrest, or 3) requirement for extracorporeal membrane oxygenation (ECMO). The information on the incidence of these SAEs was included in the database which we prospectively collected as part of an established quality assurance activity.

We defined the secondary outcome as the postoperative 28 day ICU free survival days. The decision for discharge from the ICU was made by attending physicians, when a patient's physiologic status had stabilized and the patient was free from 1) requirement of mechanical ventilation or risk of re-intubation, 2) hemodynamic instability and 3) requirement of renal replacement therapy.

2.5. Statistical analysis

We first separated patients into those with and those without SAEs. Categorical variables were summarized as proportions and compared between groups using chi-square tests; continuous variables were summarized as medians (interquartile ranges (IQR)) and compared between groups using Wilcoxon rank-sum tests as appropriate. As the relationship between tRBC indices and outcomes might not be linear, we separated patients into four subgroups according to tRBC index quartiles. We compared the incidence of SAEs and the postoperative 28 day ICU free survival days (the number of days alive and free from the need for intensive care from day of operation to day 28 after operation) among them using chi-square tests and Kruskal–Wallis test.

We performed multivariate logistic regression analysis, adjusting for the following covariates: age, emergency operation, requirement for mechanical ventilation prior to surgery, RACHS-1 category, CPB time, and tRBC index. The dependent variable was the incidence of SAEs. The results of the multivariate models were reported as odds ratios (OR) with 95% confidence intervals. $p < 0.05$ was considered statistically significant. All statistical analyses were performed using commercially available statistical software (IBM SPSS Statistics for Windows, version 19.0; IBM Corp., Armonk, NY). Data were reported in accordance with Strengthening the Reporting of Observational Studies in Epidemiology guidelines [13].

3. Results

3.1. Patients

During the study period, 747 patients underwent congenital cardiac surgery. Among them, 230 patients did not require RBC transfusion and were excluded from this study. We included a total of 517 patients who received RBC transfusions intraoperatively or in the ICU on the day of surgery. The median age of the patients was 6 months, with a median RACHS-1 category of 3. There were no patients with missing values.

There were 22 patients (4.3%) with at least one SAE: 9 patients died in the ICU, 9 patients experienced cardiac arrests, and 10 patients required postoperative ECMO. There were 6 patients with two or three SAEs, rest of 16 were with one SAE. All these SAEs occurred after first transfusion of RBCs.

3.2. Patient demographics and potential confounders

Table 1 shows the demographics of patients with and without SAEs. Patients with SAE were significantly younger,

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