Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Association for Academic Surgery

A high ratio of plasma: RBC improves survival in massively transfused injured children

Megan E. Cunningham, MD,[a] *Eric H. Rosenfeld, MD,*[a] *Huirong Zhu, PhD,*[a] *Bindi J. Naik-Mathuria, MD,*[a] *Robert T. Russell, MD, MPH,*[b] *and Adam M. Vogel, MD*[a,*]

[a] *Department of Pediatric Surgery, Texas Children's Hospital, Houston, Texas*
[b] *Department of Pediatric Surgery, Children's of Alabama, Birmingham, Alabama*

ARTICLE INFO

Article history:
Received 1 March 2018
Received in revised form
2 July 2018
Accepted 1 August 2018
Available online xxx

Keywords:
Massive transfusion
Blood product ratio
Trauma
Pediatric
Hemorrhage
Damage control resuscitation

ABSTRACT

Background: Massive transfusion protocols with balanced blood product ratios have been associated with improved outcomes in adult trauma. The impact on pediatric trauma is unclear.
Material and methods: A retrospective review of the Pediatric Trauma Quality Improvement Program data set was performed using data from January 2015 to December 2016. Trauma patient's ≤ 18 y of age, who received red blood cells (RBCs) and were massively transfused were included. Children with burns, dead on arrival, and nonsurvivable injuries were excluded. Outcome data and mortality were assessed based on low (<1:2), medium (≥1:2, <1:1), and high (≥1:1) plasma and platelet to RBC ratios.
Results: There were 465 children included in the study (median age, 8 [2-16] y; median injury severity score, 34 [29-34]; mortality rate, 38%). Those transfused a medium plasma:RBC ratio received the greatest blood product volume in 24 h (90 [56-164] mL/kg; $P < 0.01$). Those in the low plasma:RBC group underwent fewer hemorrhage control procedures [56 (34%); $P < 0.01$], but ratio was not significant when controlling for age and other variables. Survival was improved for those who received a high plasma:RBC ratio ($P = 0.02$). Platelet transfusions were skewed toward lower ratios (95%) with no difference in clinical outcomes between the groups.
Conclusions: A high ratio of plasma:RBC may result in decreased mortality in severely injured children receiving a massive transfusion. Prospective, multicenter studies are needed to determine optimal resuscitation strategies for these critically ill children.

Introduction

Although the overall number of childhood deaths related to trauma is declining, it remains the leading cause of mortality among children. The top mechanisms of traumatic injury include motor vehicle collision, suicide, and homicide.[1-3] Over the last 3 decades, research has been conducted to further reduce mortality in the acutely injured patient by initiating damage control resuscitation.[4,5] The principal of damage control resuscitation is to reduce the effects of hypothermia,

* *Corresponding author*. Department of Pediatric Surgery, Baylor College of Medicine, 6701 Fannin Street #1210, Houston, TX 77030. Tel.: +1 832 822 3135; fax: +1 832 825 3141.
E-mail address: amvogel@texaschildrens.org (A.M. Vogel).
0022-4804/$ – see front matter
https://doi.org/10.1016/j.jss.2018.08.007

acidosis, and coagulopathy, known as the "lethal triad of death."[5] Exsanguination, a major contributor to the lethal triad, has been shown to result in mortality 3 to 6 h from hospital admission.[6-9] To combat death related to exsanguination, massive transfusion protocols (MTPs) have been set into place. These proactive standardized protocols have been well described in the adult literature[10-12] but are still in the early stages when it comes to studies and implementation in the pediatric populace.[13-18]

The ratio of blood products given during massive transfusion plays a key role in MTP design. Recent adult studies have shown an increase in early survival,[7] earlier hemostasis, and decreased death from exsanguination[8] when either a high or balanced (1:1:1) ratio of plasma:platelet: red blood cell (RBC) is administered. Similar studies involving pediatric trauma patients have not demonstrated such results. Most have shown no significant difference in mortality[16,19] with one study showing a trend toward increased mortality for those who received a high plasma:RBC ratio.[20] In 2014, a multicenter survey was performed to assess pediatric MTP policy. Of those institutions, only 78% and 54% used high (≥1:2) plasma:RBC and platelet:RBC ratios, respectively.[17] With such variations in protocol and paucity of literature involving child trauma patients, further investigation into the role of blood product transfusion ratios is warranted.

The goal of this study is to compare the characteristics and clinical outcomes, including mortality, of pediatric trauma patients who have received varying ratios of plasma:RBC and platelet:RBC. The hypothesis is that children who receive at least 1:1 replacement of either plasma or platelets experience a decrease in mortality and need for surgical hemorrhage control procedure.

Methods

Study sample

A retrospective review was performed using the American College of Surgeons Pediatric Trauma Quality Improvement Program (ACS TQIP-P) data bank.[21] The Baylor College of Medicine Institutional Review Board granted a study review exemption, as no patient identifiers were present in the data bank. Data from January 2015 to December 2016 were analyzed. Those included in the analysis were pediatric trauma patients ≤18 y, who received RBC within 24 h of admission and were also massively transfused according to the definition 40 mL/kg total blood product received within 24 h of admission.[22] The patient age range was chosen according to the ages available in the TQIP-P data set (0-18 y) and the age ranges used in previous studies.[19,23] Patients excluded had no signs of life on arrival, presented with burn as their primary diagnosis, or had an abbreviated injury scale (AIS) score of 6 (unsurvivable injury) in any body region and subsequently died. To prevent bias from human error in judgment, those with an AIS of 6 that survived were included, as they did not reach the true definition of an unsurvivable injury. Also of note, there were no patients with burn diagnosis once those not transfused RBC were excluded. The TQIP-P data bank does not allow input of patients with ≥20% body surface area burns.

Variables and data management

Data related to demographics, injury, vitals, and outcomes were collected for analysis. Significant demographics included age, gender, and weight. Injury severity score (ISS) (a derivative of the three highest AIS scores), Glasgow coma score (GCS), and mechanisms of injury were all used to describe injury at time of arrival. The pediatric age-adjust shock index[24,25] was included with standard vital data. Patient outcomes included ventilator, intensive care unit (ICU), and hospital-free days, in-hospital complication rates (acute kidney injury, acute respiratory distress syndrome, severe sepsis, infection, deep venous thrombosis/pulmonary embolism), hemorrhage control procedure rates, and mortality rates.

Blood products were recorded in either milliliter (mL) or units (U). Those in mL were converted to U using a given conversion factor according to the patient's institution. If no conversion factor was given or if the conversion factor was <10 while in units, the median of the known factors was assigned as follows: 300 mL/U RBC, 250 mL/U plasma, 200 mL/U platelets, and 50 mL/U cryoprecipitate. Those who had one blood product recorded as mL and another as U were excluded ($n = 10$) to prevent inaccurate proportions. Plasma:RBC and platelet:RBC ratios were calculated using blood volume at 4 and 24 h from admission. Patients were classified into one of three groups for both plasma and platelets; low (<1:2), medium (≥1:2 to <1:1), and high (≥1:1). Plasma and platelet ratios were independently evaluated according to the three cohort ratios to reflect the methodology of the PROMMTT trial and other pediatric studies looking at blood product ratio during massive transfusion.[7,19]

Missing data points were imputed using certain assumptions. If blood volume was blank for a given product, it was assumed none was given, and volume was placed as zero. If the patient's weight was blank, it was replaced with the CDC's 50th percentile weight for age and gender.[26] Angiography embolization was included with hemorrhage control surgeries to encompass hemorrhage control procedures. ICU, ventilator, and hospital-free days were calculated by subtracting actual days from 28 until a value of 0, with mortalities also assigned the value of 0. Vitals were adjusted for age and analyzed as bivariate data points being either normal or abnormal for age.[27]

Statistical analysis

Descriptive statistics were used to evaluate the study population. Categorical variables were analyzed using Chi-square and Fisher's exact test and are reported as, number (percentage). Continuous variables were analyzed using Kruskal–Wallis test and are reported as, median [interquartile range]. When comparing the three ratios (low, medium, and high), z-test and pairwise comparison were used. Kaplan–Meier curves were created to look at survival and were analyzed using log rank test. After controlling for factors clinically and by univariate analysis with $P < 0.1$ being significant, logistic regression was performed to determine independent predictors of mortality and hemorrhage control procedure. Adjusted odds ratio (AOR) and 95% confidence interval (CI) were calculated. A P value of <0.05 was considered significant for all data. Statistical analysis was performed