World J Surg (2008) 32:2185–2189
DOI 10.1007/s00268-008-9655-0

World Journal of Surgery

ORIGINAL SCIENTIFIC REPORTS

Outcome Analysis of Blood Product Transfusion in Trauma Patients: A Prospective, Risk-Adjusted Study

Grant V. Bochicchio · Lena Napolitano · Manjari Joshi · Kelly Bochicchio · Walter Meyer · Thomas M. Scalea

Published online: 24 June 2008

Abstract

Background Studies have confirmed adverse outcome associated with transfusion of packed red blood cells (PRBCs) in trauma; however, little data are available regarding other blood product transfusion, such as fresh frozen plasma (FFP) and platelets. The objective of this study was to examine risk-adjusted outcome in trauma with stratification by blood product type.

Methods Prospective data were collected daily for 1,172 consecutive trauma patients admitted to the intensive care unit (ICU) during a 2-year period, including transfusion rates of blood products (PRBCs, FFP, platelets). Outcome assessment included infection rate, ventilator days (Vdays), ICU and hospital length of stay (LOS), and mortality.

Results Blood products were transfused in 786 (67%) patients. The study cohort had a mean age of 43 ± 21 years and Injury Severity Score (ISS) of 24 ± 13. Although the majority of patients were men, women were more likely to be transfused ($p < 0.001$). Mean transfusion rates of PRBCs (5.5 ± 9.6 U), FFP (5.4 ± 11.4), and platelets (3.7 ± 11.1) were high. Univariate analysis identified that blood product transfusion (any type) was associated with a significantly greater infection rate (34% vs. 9.4%; $p < 0.001$), hospital LOS (18.6 vs. 9 days; $p < 0.001$), ICU LOS (13.7 vs. 7.4 days; $p < 0.001$), Vdays (12.9 vs. 6.3 days; $p < 0.001$), and mortality (19% vs. 8.3%; $p < 0.001$). Multivariate analysis (risk-adjusted for severity of injury by ISS, age, sex, and race, and stratified by blood product type) confirmed that risk of infection increased by 5%, and hospital LOS, ICU LOS, and Vdays increased by 0.64, 0.42, and 0.47 days, respectively, for every unit of PRBCs given. Risk of death increased by 3.5% for every unit of FFP transfused.

Conclusion There is a dose-dependent correlation between blood product transfusion and adverse outcome (increased mortality and infection) in trauma patients.

Presented, in part, at the meeting of the American Association for the Surgery of Trauma, Minneapolis, Minnesota, Sept 12–15, 2003.

G. V. Bochicchio (✉) · L. Napolitano · T. M. Scalea
R. Adams Cowley Shock Trauma Center Programs in Trauma, 22 South Greene Street, Baltimore, MD 21201, USA
e-mail: gbochicchio@umm.edu

M. Joshi · K. Bochicchio
R. Adams Cowley Shock Trauma Center Programs in Infectious Disease, Baltimore, MD, USA

W. Meyer
Department of Epidemiology, University of Maryland School of Medicine, Baltimore, MD, USA

Introduction

Blood transfusion is a major component in the treatment of acute traumatic hemorrhagic shock. Early use of blood transfusion in resuscitation protocols for acute trauma is advocated in the Advanced Trauma Life Support guidelines of the American College of Surgeons [1]. However, recent literature has documented severe immunologic responses to blood transfusion with resultant adverse outcomes [2, 3]. Transfusion of blood products, including shed blood, also has been found to be associated with deleterious effects on the immune system [4–8]. At the cellular level, immune cell proliferation is altered with significant effects on T-cell–related immunity and cytokine immunomodulation. Recently, inflammatory cytokine release has been shown to be amplified with the transfusion of old stored blood [9].

In trauma patients, blood transfusion has been confirmed as an independent risk factor for death, perioperative

infection, postinjury multiple organ failure, systemic inflammatory response syndrome, and admission to the intensive care unit (ICU) [10–15]. The association of blood transfusion with immunosuppression, hyperinflammation, and adverse outcome has led some to advocate caution for the liberal use of blood transfusion in injured patients [16].

The majority of research in the trauma population related to the transfusion of blood products has focused on the transfusion of packed red blood cells (PRBCs). To our knowledge, no previous studies have evaluated the impact of concurrent transfusion of specific individual blood component therapy (PRBCs, fresh frozen plasma (FFP), platelets) on trauma outcome. Thus, the goal of this study was to examine risk-adjusted outcome in trauma with stratification of transfusions by blood product type.

Materials and methods

Prospective (independent of trauma-registry) data were collected daily by a single individual on 1,172 consecutive trauma patients admitted >48 hours to the ICU at the R. Adams Cowley Shock Trauma Center during a 2-year period (2002–2004). Patients were stratified by age, sex, race, Glasgow Coma Score (GCS) score, and Injury Severity Score (ISS). The transfusion of individual blood product types (PRBCs in units, FFP in units, and platelets in equivalent units) were calculated daily. Transfusion of blood products was determined by the trauma or ICU team based on clinical grounds. No formal transfusion protocol for blood products was used. In addition, no specific protocol to transfuse leukocyte-reduced or plasma-reduced products was used. Admission base deficit, serum lactate, and shock index (HR/SBP) were collected as measures of shock severity.

Outcome was assessed by infection rate, ventilator days, ICU and hospital length of stay (LOS), and mortality. CDC definitions for infection were used to diagnose infection. Categorical variables were compared by using Pearson's χ^2 and contingency table analysis. Multiple logistic regression analyses were used for binary outcomes, using the covariates age, sex, race, and ISS as adjusters. The blood product variables (measured in number of units transfused) were entered into the regression equation so that the variance in outcome explained by these variables would be partialled out of the final model, thus allowing interpretation of the blood product of interest to be made independent of the effects of the other blood products. Continuous variables were compared by using Student's t test (to compare differences between transfused and nontransfused patients) and multiple linear regression analysis, using the same covariates as adjusters (Stata, Release 6.0, Stata Corp., College Station, TX).

Results

Demographics and blood product transfusion

The study cohort consisted of 873 men (74%) and 299 women (26%). The mean age of the study cohort was 43 ± 21 years with a mean Injury Severity Score (ISS) of 24 ± 13 (Table 1). Blunt trauma accounted for the majority of the injuries ($n = 914$, 78%). Blood products were transfused in 786 (67%) of the 1,172 patients with majority (88%) occurring during the first 48 hours of admission. Although the majority of the patients were men, women were more likely to be transfused ($p < 0.001$; Table 1).

Most patients ($n = 480$, 61%) received combination transfusion therapy, with more than one blood product type transfused. Transfusion of PRBCs only ($n = 246$), FFP only ($n = 56$), or platelets only ($n = 4$) was less common. The mean number of units transfused by product type was as follows: PRBCs = 5.5 ± 9.6 U, FFP = 5.4 ± 11.4 U, and platelets = 3.7 ± 11.1 equivalent units (Table 2).

Factors associated with blood product use

Trauma patients who received blood product transfusion had significantly higher mean ISS ($p < 0.001$, Table 1), lower admission hematocrit, lower admission platelet count, higher admission INR, increased lactate, increased shock index, and lower RTS and admission GCS (Table 3). Logistic regression analysis (adjusted for age, ISS, GCS,

Table 1 Admission characteristics and blood product transfusion

	Total ($n = 1,172$)	Blood product transfusion ($n = 786$)	No blood product transfusion ($n = 386$)	p value
Age (year)	43 ± 21	43 ± 21	42 ± 20	NS
Male	873	562 (64%)	311 (36%)	
Female	299	224 (75%)	75 (25%)	<0.001 vs. male
Injury Severity Score	24 ± 13	27 ± 13	19 ± 11	<0.001
Admission Glasgow Coma Score	12 ± 5	11 ± 5	12.5 ± 4	NS

NS, not significant

Table 2 Blood component utilization in trauma ($n = 786$ patients)

Blood product type	Units transfused	Patients transfused
Transfusion combination	NA	480 (61.1)
PRBCs only	5.5 ± 9.6 U	246 (31.3)
FFP only	5.4 ± 11.4 U	56 (7.1)
Platelets only	3.7 ± 11.1 equivalent U	4 (0.5)

PRBCs, packed red blood cells; FFP, fresh frozen plasma
Data are mean ± SD or number (%)

and all other variables present in the model) confirmed age, ISS, shock index, lactate, hematocrit, INR, and platelet count as independent predictors of blood product transfusion (Table 4).

Blood product use and outcome

Transfused patients had a significantly greater infection rate, hospital and ICU length of stay, ventilator days, and hospital mortality (Table 5). The most common type of infection was respiratory, followed by genitourinary, blood, intra-abdominal, and skin/wound (Fig. 1). When analyzed by multivariate logistic regression analysis, risk of infection and mortality increased significantly for every unit of PRBCs or FFP transfused (Table 6). Transfusion of PRBCs and FFP were associated with increased hospital and ICU length of stay. In contrast, transfusion of platelets did not adversely impact mortality and infection risk, after controlling for the transfusion of PRBCs and FFP in addition to age, GCS, and ISS.

Discussion

The impact of PRBC transfusion on outcome in the critically ill and injured patients has undergone intense investigation recently, but many of these studies are limited by retrospective data collection efforts and lack of evaluation of transfusion of other blood product types. To our knowledge, the current prospective study represents the first evaluation of the impact of blood product type (PRBCs, FFP, platelets) on outcome in the critically injured patient. This prospective study adds to the literature that transfusion of PRBCs and/or FFP are both associated with increased risk for mortality and infection, after controlling for numerous variables that affect trauma outcome. The authors realize the limitations of ISS as the principal injury severity scale; however, this score was used because it remains the standard in the majority of trauma studies.

PRBC transfusion has been confirmed an independent risk factor for death, perioperative infection, systemic inflammatory response syndrome, postinjury multiple organ failure, and admission to the ICU [10–14]. Blood transfusion within 24 hours of trauma admission ($n = 9{,}539$) was confirmed as a significant independent predictor of

Table 4 Risk factors for blood product transfusion in trauma patients

Variable	OR	95% CI	p value
Age (year)	1.03	(1.01–1.06)	<0.001
ISS	1.2	(1.02–1.31)	<0.001
Shock index	2.6	(1.98–2.83)	<0.001
Admission lactate	1.7	(1.57–1.87)	<0.001
Admission Hct	5.6	(4.5–5.88)	<0.001
Admission INR	4.8	(4.3–5.2)	<0.001
Admission platelet Count	4.1	(3.8–4.4)	<0.001

Multiple logistic regression analysis. Odds ratios were adjusted for all other variables present in the model

Table 5 Outcome analysis stratified by blood product transfusion versus no transfusion

	Blood product transfusion ($n = 786$)	No blood product transfusion ($n = 386$)	p value
Infection	230 (34%)	46 (9.4%)	<0.001
Ventilator days	12.9 ± 12	6.3 ± 6	<0.001
Hospital days	18.6 ± 14	9 ± 7	<0.001
ICU days	13.7 ± 11	7 ± 5	<0.001
ICU admission	724 (74%)	249 (26%)	<0.001
Hospital mortality	147 (21.4%)	32 (6.5%)	<0.001

Table 3 Admission variables stratified by blood product transfusion vs. no blood product transfusion (χ^2 analysis)

Variable	Blood product transfusion ($n = 786$)	No blood product transfusion ($n = 386$)	p value
Admission Hematocrit (%)	29 ± 8	37 ± 7	<0.001
Admission INR	1.8 ± 1	1.1 ± 0.09	<0.001
Admission Platelet Count	80 k ± 38 K/μl	148 k ± 77 K/μl	<0.001
Admission Serum Lactate	6.1 ± 4 mmol/l	3.2 ± 2 mmol/l	<0.001
Shock Index	0.9 ± 0.5	0.6 ± 0.3	<0.001
RTS	6.6 ± 1.5	7.2 ± 1.1	<0.001
GCS (admission)	11 ± 4.7	12.5 ± 4	<0.001

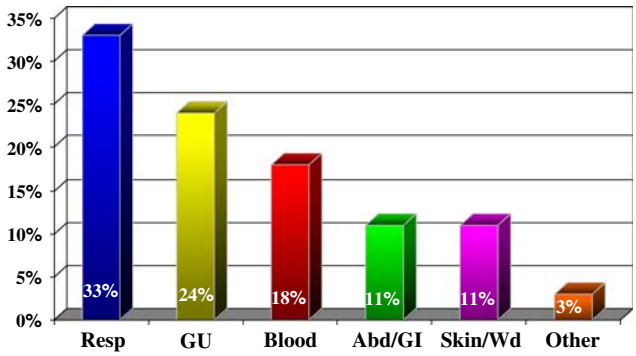

Fig. 1 Incidence of infection in transfused patients stratified by site ($n = 230$)

mortality, ICU admission, and ICU length of stay after stratification for ISS, GCS, and age by logistic regression analysis [15]. An additional study using a larger cohort ($n = 15{,}534$) and stratification for other variables that affect trauma outcome, including sex, race, and admission shock variables (admission base deficit, serum lactate, and shock index [HR/SBP]) also confirmed that blood transfusion was an independent predictor of mortality, ICU admission, ICU LOS, and hospital LOS in trauma [16].

Similarly, blood transfusion has been identified a strong independent predictor of mortality and hospital length of stay in patients with blunt liver and spleen injuries after controlling for indices of shock and injury severity [17]. Transfusion-associated mortality risk was highest in the subset of patients managed nonoperatively, and these authors recommended prospective examination of transfusion practices in treatment algorithms of solid organ injury.

Recently, Hill and colleagues performed a meta-analysis of 20 peer-reviewed articles published from 1986 to 2000 in which criteria for inclusion was defined as a control group (nontransfused) compared with a treated (transfused) group (total, $n = 13{,}152$) [18]. The effect of blood transfusion in trauma patients compared with other surgical patients was examined in a separate meta-analysis. The common odds ratio for all articles evaluating the incidence of postoperative bacterial infection was 3.45 with 17 of 20 studies demonstrating statistical significance. The common odds ratio for the subgroup of trauma patients was 5.26 with all studies showing a value of $p < 0.05$ (0.005 to 0.0001), confirming that allogenic blood transfusion was found to be a greater risk factor for the development of postoperative bacterial infection in the trauma patient compared with the elective surgical patient.

These data confirm that blood transfusion is associated with significant risk for increased mortality and infection after trauma, and this current study confirms these findings as well. These data suggest that we institute all efforts to reduce blood transfusion in trauma patients. Because blood transfusion is the only current therapy available for the treatment of hemorrhagic shock, other than crystalloid resuscitation, our efforts should focus on limitation of blood transfusion for the treatment of anemia in hemodynamically stable critically ill trauma patients.

A recent post-hoc cohort analysis of the trauma patient population from the prospective multicenter, randomized, controlled trial, Transfusion Requirements in Critical Care Trial (TRICC), was reported [19]. This study compared the use of restrictive and liberal transfusion strategies in resuscitated critically ill trauma patients with anemia. Critically ill trauma patients with a hemoglobin concentration <9 g/dl within 72 hours of admission to the ICU were randomized to a restrictive (hemoglobin concentration, 7 g/dl) or liberal (hemoglobin concentration, 10 g/dl) red blood cell transfusion strategy. The mean units of PRBCs transfused per patient (2.3 ± 4.4 vs. 5.4 ± 4.3; $p < 0.0001$) were significantly lower in the restrictive group than in the liberal group. The 30-day all-cause mortality rates in the restrictive group were 10% compared with 9% in the liberal group ($p = 0.81$). These data confirm that a restrictive red blood cell transfusion strategy seems to be safe for critically ill multiple-trauma patients. A randomized, controlled trial would provide the appropriate level of evidence with regard to the daily use of blood in this population of patients.

Similarly, a prospective multicenter observational study in 3,534 patients from 146 western European ICUs confirmed the common occurrence of anemia and the large use of blood transfusions in critically ill patients [20]. Additionally, this epidemiologic study provided evidence of an association between blood transfusions and increased mortality by using

Table 6 Risk of infection, hospital and ICU LOS, and mortality stratified by blood product type (adjusted for age, ISS, and admission GCS)

	PRBCs OR (CI)	FFP OR (CI)	Platelets OR (CI)
Infection	2.8 (1.96–3.94)*	1.02 (1.01–1.04)*	0.94 (0.96–1)
Hospital LOS	8.1 (6.6–9.03)*	1.3 (1.3–1.41)*	−0.15 (−0.023 to 0.07)*
ICU LOS	5.6 (4.2–7.06)*	1.25 (1.2–1.31)*	−0.08 (−0.14 to 0.01)*
Mortality	1.05 (1.03–1.07)*	1.03 (1.02–1.05)*	1.03 (1.02–1.04)

* $p < 0.001$

LOS, length of stay; ICU, intensive care unit; PRBCs, packed red blood cells; FFP, fresh frozen plasma; OR, odds ratio; CI, confidence interval

a matched cohort propensity analysis, with 28-day mortality rate 22.7% among patients with blood transfusions and 17.1% among those without ($p = 0.02$), with confirmation by the Kaplan-Meier log-rank test.

A prospective, multicenter, observational, cohort study (CRIT trial) performed in the United States also confirmed that the number of PRBC transfusions a patient received was independently associated with increased mortality and longer ICU and hospital LOS [21].

A post-hoc cohort analysis of all trauma patients enrolled in the U.S. CRIT trial confirmed that 55.4% of all trauma patients were transfused with a mean of 5.8 ± 5.5 units during the ICU stay [22]. Compared with the full study population, patients in the trauma subset were more likely to be transfused and received an average of 1 additional unit of blood. This current prospective study documents similar findings regarding PRBC utilization in trauma, but with a much wider range (5.5 ± 9.6 units PRBCs). Importantly, this prospective study also provides additional data regarding the utilization of other blood products (FFP, platelets) in trauma and its impact on outcome.

Conclusion

There is a dose dependent correlation between blood product transfusion (PRBCs, FFP) and adverse outcome (mortality, infection) in critically ill trauma patients after appropriate stratification for all other variables that affect trauma outcome. All efforts to reduce blood transfusion in critically ill trauma patients should be implemented.

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