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Examining 1:1 vs. 4:1 Packed Red Blood Cell to Fresh Frozen Plasma Ratio Transfusion During Pediatric Burn Excision

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Blood transfusions following major burn injury are common due to operative losses, blood sampling, and burn physiology. While massive transfusion improves outcomes in adult trauma patients, literature examining its effect in critically ill children is limited. The study purpose was to prospectively compare outcomes of major pediatric burns receiving a 1:1 vs. 4:1 packed red blood cell to fresh frozen plasma transfusion strategy during massive burn excision. Children with >20% total body surface area burns were randomized to a 1:1 or 4:1 packed red blood cell/fresh frozen plasma transfusion ratio during burn excision. Parameters examined include patient demographics, burn size, pediatric risk of mortality (PRISM) scores, pediatric logistic organ dysfunction scores, laboratory values, total blood products transfused, and the presence of blood stream infections or pneumonia. A total of 68 children who met inclusion criteria were randomized into two groups ($n = 34$). Mean age, PRISM scores, estimated blood loss (600 ml (400–1175 ml) vs. 600 ml (300–1150 ml), $P = 0.68$), ventilator days (5 vs. 9, $P = 0.47$), and length of stay (57 vs. 60 days, $P = 0.24$) had no difference. No differences in frequency of blood stream infection (20 vs. 18, $P = 0.46$) or pneumonia events (68 vs. 116, $P = 0.08$) were noted. On multivariate analysis, only total body surface area burn size, inhalation injury, and PRISM scores ($P < 0.05$) were significantly associated with infections.

INTRODUCTION

Massive blood loss plays a significant role in the development of the lethal triad consisting of hypothermia, acidosis, and coagulopathy. Homeostatic changes have subsequently been described in the trauma literature that further compound this triad by initiation of endothelial injury, factor consumption, and fibrinolysis.[1] The acute traumatic coagulopathy that follows can increase transfusion requirements, organ dysfunction, and injury severity scores.[2–4] Treatment strategies to manage the hemorrhagic shock that follows acute traumatic coagulopathy have employed the utilization of transfusion policies that favors the administration of fresh frozen plasma (FFP) with packed red blood cells (PRBCs) in a 1:1 ratio.[5–9] The aggressive replacement of blood component factors in a ratio that most resembles whole blood components is theorized to improve coagulation profiles, control hemorrhage, and improve survival.[10] Restrictive transfusion policies can be benefit massively burned patients. A recent comparison of restrictive to liberal transfusion strategies in massively burn injured patients showed no differences in blood stream infections, organ dysfunction, or mortality.[11,12]

The use of aggressive equal ratio blood product replacement strategies has been adopted in the operative setting to improve hemorrhage control in high blood loss procedures. This practice may in turn decrease the number of blood products transfused and improve acidosis.[13] Furthermore, blood transfusions are generally associated with immunosuppression and increased blood stream infections. The use of fewer blood products may result in a decrease in associated infectious complications.[14]

The impact of these transfusion policies in burn injured patients has had limited study. Restrictive transfusion strategies in adult burn injured patients may have benefit in reducing ventilator days, ICU days, and blood utilization.[11] Prospective, randomized trials examining these transfusion strategies in the pediatric population, however, remain limited. Following resuscitation, these patients experience burn excision and grafting with an associated hemorrhage that results in the loss of 2% blood volume per percent total body surface area (TBSA) burn excised from their body or 5% blood volume per percent excised from their head.[15] As a result, acute burn injury in the pediatric population offers a unique setting to analyze the impact of massive transfusion policies in the nontraumatic setting.

The practice of early massive excision involving burn sizes >20% TBSA is considered to be the standard of care.[16] Hence,

burn excision is a known massive transfusion situation, and blood loss could be ameliorated by using a 1:1 transfusion strategy. The reduction in blood products may result in a decrease in deleterious effects such as infectious complications. Our goal is to understand the impact of an aggressive blood product transfusion policy during massive intraoperative blood loss on outcome measures such as blood utilization, organ function, and infectious complications.

METHODS

This is a randomized, prospective study comparing patient outcomes following a 1:1 or 4:1 PRBC to FFP transfusion strategy and represents a planned safety interim analysis extended from our previous publication.[17] Following institutional review board approval, this trial was conducted at an American Burn Association verified pediatric burn center.

Subject Selection

Patients were examined and scrutinized for trial eligibility following presentation to our pediatric burn center. Patients ≤ 18 years of age, who sustained an acute burn injury totaling 20% TBSA or larger, and presented within 72 hours of injury were approached for consent. Patients were excluded if they were older than 18 years of age, unable or unwilling to receive blood products, on hemodialysis, were pregnant, had a previous or ongoing hematologic disease, were brain dead, had a closed head injury with a calculated Glasgow coma scale score < 9, or were deemed nonsurvivable by the managing attending burn surgeon. Within 72 hours of admission, informed consent was obtained by research personnel before any surgical intervention was performed. If a child was older than 8 years of age and able to communicate, consent was obtained from them. Following consent, the patient was assigned either to a 1:1 or a 4:1 PRBC/ FFP transfusion group and followed prospectively for outcomes.

Admission and Ongoing Data Collection

Parameters obtained following enrollment included demographic information such as age, sex, TBSA burn size, the presence of inhalation injury, admission weight, and past medical history. The pediatric risk of mortality (PRISM) score was used to determine disease severity at admission and the pediatric logistic organ dysfunction (PELOD) score was measured daily following admission to assess organ dysfunction.[18,19] The admission weight was used as the basis for calculation of all blood and transfusion volumes. The presence of infection utilizing definitions established by the ABA burn consensus conference was recorded daily.[13] When multiple values in a 24-hour period were present, the highest level of dysfunction was recorded for study purposes. Clinical and laboratory parameters were recorded daily. Additional parameters monitored included fluid balance, mechanical ventilation usage, dialysis, any procedures performed, and additional blood product transfusions such as platelets and cryoprecipitate.

Resuscitation and Surgical Procedures

All patients enrolled in the study underwent resuscitation per institution protocol. Resuscitation fluids were initiated for patients who presented within 24 hours of injury based on a calculation incorporating the Parkland formula with evaporative losses incurred while admitted. This was then titrated down to a calculated maintenance fluid rate based on urine output. Nasoduodenal feeding tubes were placed and enteral nutrition began within 4 hours of admission. Excision and grafting of full thickness burns were performed at the discretion of the managing attending burn surgeon within 3 days of admission. All identifiable third-degree burns were excised at the initial operation if possible. Excised burns were then grafted with autograft, xenograft, allograft, or a dermal matrix substitute as deemed appropriate.

Multiple strategies to mitigate blood loss during burn excision were employed. These include the use of subcutaneous epinephrine solution injection and tumescence, utilization of epinephrine solution soaked gauze, topical fibrin sprays, topical hemostatic dressings, compressive elastic bandages, tourniquets, extremity elevation, and judicious use of monopolar electrocautery following excision. A combination or all of these hemostatic strategies were employed on a case-by-case basis at the discretion of the operating burn surgeon. Intraoperative hemostatic techniques did not differ between groups. Subsequent procedures may have included further excision of burns following conversion of what was initially identified as more superficial burn wounds, amputations, or tracheostomies. Postoperative wound care consisted of dressing management for 5 to 7 days for close observation of healing wounds and to maximize skin graft maturation prior to any further excision and grafting. As such, any additional procedures necessary usually occurred ~1 week following the initial excision and grafting. This study was specifically confined to analysis following this initial tangential excision and grafting procedure and did not follow any re-excisions, graftings, or other procedures thereafter.

The perioperative period was defined as the start of the initial excision of the burn wound completed within 3 days of admission and up to 12 hours after the patient left the operating room. Perioperative parameters recorded included what procedure was performed, estimated blood loss, and the amount of PRBC and FFP that was transfused into a patient during the course of their procedure and the 12 hours that followed. Additional products, such as platelets or cryoprecipitate, were noted if given during the course of a procedure as well. A calculated estimated blood loss was also determined based on formulae developed by Gross to provide a more reliable comparison of blood loss.[20] Operative reports were scrutinized for percent TBSA or square area of burn excised. Unfortunately, the initial burn excision was not always done by the same burn surgeon and there was variability in reporting style. As such, the percent TBSA or square area of burn excised could not be reliably recorded. Since the height, weight, and body surface area of each patient were known, as well as the percent of full thickness of injury, an estimation of square area of full thickness excised was calculated for study comparison purposes.

Adherence to the transfusion protocol was conducted with the assistance of a research nurse in coordination with the attending anesthesiologist during the course of the procedure and perioperative period after. Both during and following the procedure, clinical laboratory values were obtained that included a complete blood count (CBC), arterial blood

gas, prothrombin time (PT), partial thromboplastin time (PTT), international normalized ratio (INR), fibrinogen, antithrombin III, and protein C. Following the procedure, laboratory values were obtained at 1, 12, and 24 hours and 1 week postoperatively.

Transfusions occurred during the perioperative period, both over the course of a procedure where tangential excision and grafting were performed as well as within the immediate postoperative up to 12 hours after. The decision to transfuse was based on evaluation of the patient's vital signs, degree of blood loss, clinical laboratory values, and a discussion between the attending burn surgeon and anesthesiologist following guidelines previously described.[17] The trigger for transfusion during the course of a procedure included concerning laboratory values such as a hemoglobin value ≤7 g/dL, if it was felt that the patient was observed to be bleeding significantly during the course of the case, or if there was a concomitant contextual clinical physiologic insult such as tachycardia or hypotension. The trigger for postoperative transfusion followed a similar protocol encompassing concerning clinical laboratory values, physiologic derangements, or observed significant bleeding.

Transfusion Protocol

If a patient was assigned to the 1:1 PRBC/FFP transfusion group, they received 1 unit of FFP (200 ml) for every unit of PRBC (400 ml) transfused to maintain a 1:1 ratio. If a patient received <1 unit of PRBCs, an equivalent fraction of FFP was transfused. Patients in each transfusion group followed a pediatric weight-based protocol as previously described.[17] Platelets were only transfused if the platelet count was <50,000K/μl with major intraoperative bleeding or 20,000K/μl outside the operating room. Cryoprecipitate was transfused if the patient was bleeding and their fibrinogen level was <100 mg/dl. All transfusions were given individually at a time. If a transfusion was required after a procedure, product was delivered based on their randomization category. In the case of life-threatening bleeding, additional product was given at the discretion of the managing attending burn surgeon.

Outcome Measures

Outcome measures examined included the amount of PRBC and FFP transfused, whether transfusion ratios were maintained, the presence of any coagulopathy, hospital length of stay, organ dysfunction, pulmonary dysfunction as measured by days requiring mechanical ventilation, mortality, and any infectious episodes as manifested by the presence of a blood stream infection or pneumonia occurrence.

Statistics

Data analysis was conducted by utilizing the R statistical package (www.r-project.org). For parametric categorical data, comparisons of means were performed using a standard Student's *t*-test when comparing two groups. For nonparametric categorical data between groups, the Mann–Whitney *U*-test was employed. To assess the association between discrete categorical values, the chi-square test was used. The Shapiro–Wilk test of normality was used to assess data normality.

To compare continuous outcome variables with independent continuous and categorical predictor variables, multivariate linear regression analysis was performed. Outcome variables included the following: number of infections in total, number of blood stream infection occurrences, and number of pneumonia occurrences. Independent variables for these models included the following: transfusion group, total TBSA, presence of inhalation injury, age, PELOD score, and PRISM score. Multivariate logistic regression analysis was performed to determine the association between having an infection and the following independent variables: transfusion group, total TBSA burn size, presence of inhalation injury, age, PELOD score, and PRISM score. A linear regression analysis of clinical laboratory data was also performed comparing CBCs (white blood cell count, hemoglobin, hematocrit, and platelet count), INR, PT, PTT, fibrinogen, antithrombin III, and protein C. Independent variables were transfusion group, postoperative day, and the interaction between transfusion groups and postoperative day. Independent and significant input variables associated with outcome variables and the Akaike information criterion were used for final model determination in both multivariate linear and logistic regression analysis.

RESULTS

A total of 68 children who met inclusion criteria were enrolled into this study with 34 children randomized into either the 1:1 or 4:1 groups. The mean age of presentation was 7.4 ± 5.5 years in the 1:1 group vs. 8.2 ± 5.3 y in the 4:1 group. TBSA burn size was 39 ± 16% in the 1:1 group vs. 43 ± 24% in the 4:1 group. PRISM scores were 9.5 ± 6 in the 1:1 group vs. 11 ± 6 in the 4:1 group. The mean TBSA involvement of third-degree burns was 35 ± 16% in the 1:1 group vs. 36 ± 15% in the 4:1 group. No significant differences were identified in comparing age, TBSA burn size, PRISM score, and percent third-degree burns between groups by univariate analysis (Table 1). No deaths occurred in any patient during the course of the study.

Table 1. Patient demographics

	1:1 Group	4:1 group	*P*-value
N	34	34	
Age (y)	7.4 (5.5)	8.2 (5.3)	0.55
Total burn TBSA (%)	39 (16)	43 (24)	0.43
third degree (%)	36 (15)	37 (16)	0.77
Inhalation injury	1	3	0.61
Length of stay	57 (31)	60 (48)	0.24
Ventilator days (median)	5 (2–12.8)	9 (3–21)	0.47
Days to wound closure (median)	30 (16–40)	30 (7–48)	0.74
PELOD (median)	10 (1–12.5)	10 (1–12)	0.9
PRISM	9.5 (6)	11 (7)	0.26

Summary of patient demographics between patient groups. Significance was set at *P* < 0.05. Comparisons of means between two groups were performed using the Student's *t*-test. PELOD—pediatric logistic organ dysfunction score; PRISM—pediatric risk of mortality.

Inhalational injuries were identified in one child in the 1:1 group and three children in the 4:1 group. There were no significant differences noted in ventilatory days (5 days vs. 9 days, $P = 0.47$) between either group (Table 1). Preoperative measures of coagulation were obtained and compared to determine the presence of coagulopathy overall and whether there was any difference in coagulation profiles between transfusion groups. In comparing PT (11 ± 1.4 seconds vs. 12 ± 2.3 seconds , $P = 0.26$), PTT (41 ± 15 seconds vs. 45 ± 19 seconds , $P = 0.22$), INR (1.12 (1–1.2) vs. 1.13 (1–1.3), $P = 0.67$), platelet count (162 K/µL (124–213 K/µL) vs. 148 K/µL (114–225 K/µL), $P = 0.57$), fibrinogen level (422 mg/dL (505–1394 mg/dL) vs. 382 mg/dL (452–1929 mg/dL), $P = 0.41$), protein C level (57 ± 20 IU/dL vs. 51 ± 16 IU/dL), $P = 0.2$), or antithrombin III level (66 ± 26 IU/dL vs. 55 ± 22 IU/dL, $P = 0.22$), no abnormal coagulation profiles were identified in general or between groups prior to initial excision (Table 2).

In the operating room, both groups had similar estimated blood loss that did not differ significantly following the initial case (600 ml (400–1175 ml) vs. 600 cc (300–1150 ml), $P = 0.68$). The calculated blood loss similarly did not show any significant difference following the initial excision and grafting (805 ml (505–1394 ml) vs. 1136 ml (453 ml–1929 ml), $P = 0.47$). In determining estimated blood loss per square area excised, no differences were seen between observed estimated blood loss per square area (0.25 ± 0.16 ml/cm^2 vs. 0.2 ± 0.11 ml/cm^2, $P = 0.16$) or calculated blood loss per square area (0.32 ± 0.21 ml/cm^2 vs. 0.32 ± 0.2 ml/cm^2), $P = 0.98$). Both groups were able to generally maintain consistent transfusion ratios both in the operating room (1 vs. 2.8 units, $P = 0.002$) and in total afterwards (1.4 vs. 4.25 units, $P = 0.001$). There was also no significant difference in the median number of transfusions during the course of an operation (2 vs. 2 units, $P = 0.58$, Table 2).

Comparison of collated CBCs in total revealed no significant differences among white blood cell count (13 ± 3K/µl vs. 13.6 ± 5K/µl, $P = 0.75$), hemoglobin (9 ± 0.7 g/dl vs. 9.2 ± 2.3 g/dl, $P = 0.6$), hematocrit (26 ± 2% vs. 26 ± 2%, $P = 0.44$), and platelet count (415 ± 106K/µl vs. 409 ± 101K/µl,

$P = 0.77$). Measures of coagulation, PT (11.4 ± 1.4 seconds vs. 11.9 ± 2 seconds , $P = 0.2$) and PTT (33 ± 6 seconds vs. 34 ± 5 seconds , $P = 0.75$) were similarly nonsignificant. Further examination of coagulation measures such as fibrinogen (423 ± 89 mg/dl vs. 396 ± 61 mg/dl, $P = 0.159$), protein C (73 ± 19 IU/dl vs. 73 ± 16 IU/dl, $P = 0.9$), and antithrombin III (79 ± 12 IU/dl vs. 77 ± 11 IU/dl, $P = 0.5$) levels also did not show any significant difference (Table 3).

Clinical laboratory parameters were then stratified by their individual time points and a linear regression was performed comparing clinical laboratory data obtained at postoperative days 0, 1, and 7 between transfusion groups. In this analysis, there was significantly higher concentrations of antithrombin III (12.8 ± 5 IU/dl, $P = 0.02$) in the 4:1 transfusion group at day 7 compared with other time points and significantly lower PTT (9 ± 6 seconds , $P = 0.02$) values again in the 4:1 transfusion group at day 7 compared with other time points. No other significant differences were noted between transfusion groups when comparing clinical laboratory values by different time points.

An equal number of infections were identified in both populations (24 patients each). Broken down into infection type, no differences were noted in blood stream infection occurrences (20 vs. 18, $P = 0.46$) between either group. A higher number of pneumonia occurrences were identified in the 4:1 group (68 vs. 116), but this was not significant ($P = 0.08$; Table 4).

Linear multivariate regression analysis revealed a significant association between the number of infections and total TBSA burn size ($P = 0.000000007$) and PRISM score ($P = 0.007$). Additionally, there was a significant association between the number of blood stream infections and total TBSA burn size ($P = 0.0064$). There was also a significant association between the number of pneumonia occurrences and total TBSA burn size ($P = 0.02$), inhalation injury ($P = 0.02$), and PRISM score ($P = 0.02$). Logistic multivariate regression analysis was performed to look at the association of these variables with the risk of developing an infection. TBSA burn size was the only independent variable identified that was associated with an increased risk of infection (OR 1.17, $P = 0.005$). There

Table 2. Transfusion and perioperative characteristics

	1:1 Group	4:1 group	*P*-value
PRBC/FFP ratio (total transfused, median)	1.4 (1–1.8)	4.25 (1.2–6)	0.001
PRBC/FFP r(OR transfused, median)	1 (1–2)	2.8 (0.4–3.9)	0.002
Estimated OR blood loss (median, ml)	600 (400–1175)	600 (300–1150)	0.68
Calculated OR blood loss (median, ml)	805 (505–1394)	1136 (453–1929)	0.47
Preoperative PT (s)	11 ± 1.4	12 ± 2.3	0.26
Preoperative PTT (s)	41 ± 15	45 ± 19	0.22
Preoperative INR	1.12 (1–1.2)	1.13 (1–1.3)	0.67
Preoperative platelet count (K/µL)	162 (124–213)	148 (114–225)	0.57
Preoperative fibrinogen (mg/dL)	422 (505–1394)	382 (452–1929)	0.41
Preoperative protein C (IU/dL)	57 ± 20	51 ± 16	0.2
Preoperative antithrombin III (IU/dL)	66 ± 26	55 ± 22	0.22
Estimated EBL per cm^2 excised (ml/cm^2)	0.25 ± 0.16	0.2 ± 0.11	0.16
Calculated EBL per cm^2 excised (ml/cm^2)	0.32 ± 0.21	0.32 ± 0.2	0.98

Summary of transfusion characteristics between patient groups. Significance was set at $P < 0.05$. PRBC—packed red blood cell; FFP—fresh frozen plasma; PT—prothrombin time; PTT—partial thromboplastin time.

Table 3. Clinical laboratory data

	1:1 Group	4:1 group	*P*-value
WBC (K/µL)	13 (3)	13.6 (5)	0.75
Hemoglobin (g/dL)	9 (0.7)	9.2 (2.3)	0.6
Hematocrit (%)	26 (2)	26 (2)	0.44
Platelet (K/µL)	415 (106)	409 (101)	0.77
PT (s)	11.4 (1.4)	11.9 (2)	0.2
PTT (s)	33 (6)	34 (5)	0.75
Fibrinogen (mg/dL)	423 (89)	396 (61)	0.159
Protein C (IU/dL)	73 (19)	73 (16)	0.9
Antithrombin III (IU/dL)	79 (12)	77 (11)	0.5

Summary of clinical laboratory data compared between patient groups. Significance was set at P < 0.05. WBC—white blood cell count; PT—prothrombin time; PTT—partial thromboplastin time.

Table 4. Infectious presence and characteristics

	1:1 Group	4:1 group	*P*-value
Number of patients with an infection	24	24	
Number of infections (median)	2 (0–3)	1.5 (0–4)	0.75
Number of infections (total)	67	83	
No. of blood stream infections (median)	0 (0–1)	0 (0–0)	0.46
No. of blood stream infections (total)	20	18	
No. of pneumonia (median)	0 (0–2)	1 (0–5)	0.08
No. of pneumonia (total)	68	116	

Summary of the presence of infection and infectious type between patient groups. Significance was set at *P* < 0.05.

was no difference in any factor based on transfusion ratio. Multivariate analyses are summarized in Tables 5–8.

DISCUSSION

Pediatric patients with large burns require extensive burn excision and grafting. These procedures are by nature high blood loss procedures that place them at risk for the lethal triad of coagulopathy and harbor higher transfusion requirements. Here, we have examined the use of 1:1 vs. 4:1 transfusion strategies both during and after major burn excision. We have confirmed in our previous report of massive hemorrhage accompanying burn excision and skin grafting that children in the 1:1 group received more units of FFP and fewer units of PRBC than children in the 4:1 group.[17]

Direct comparisons of burn size, injury severity scores, and general demographic data did not show any significant differences between transfusion groups. In addition, laboratory coagulation parameters did not exhibit any major difference between PT, PTT, fibrinogen, antithrombin III, and protein C levels between the 1:1 and 4:1 groups. When

Table 5. Linear multivariate regression (dependent variable: number of infections)

	B (slope)	*P*-value
Transfusion ratio	0.18	0.675
Total TBSA	0.075	0.000000007
Inhalation injury	0.71	0.448
Age	−0.062	0.15
PELOD	−0.04	0.23
PRISM	0.18	0.007

Linear multivariate regression comparing outcomes while controlling for number of infections. Significance was set at *P* < 0.05.

Table 6. Linear multivariate regression (dependent variable: number of blood stream infections)

	B (slope)	*P*-value
Transfusion ratio	−0.16	0.5
Total TBSA	0.02	0.0064
Inhalation injury	−0.19	0.75
Age	−0.066	0.006
PELOD	0.03	0.04
PRISM	0.02	0.65

Linear multivariate regression comparing outcomes while controlling for number of blood stream infections. Significance was set at *P* < 0.05.

Table 7. Linear multivariate regression (dependent variable: number of pneumonia events)

	B (slope)	*P*-value
Transfusion ratio	0.25	0.79
Total TBSA	0.07	0.02
Inhalation injury	5.8	0.02
Age	0.1	0.26
PELOD	−0.09	0.19
PRISM	0.27	0.02

Linear multivariate regression comparing outcomes while controlling for the presence of pneumonia. Significance was set at *P* < 0.05.

Table 8. Logistic multivariate regression (dependent variable: risk of developing a blood stream infection or pneumonia)

	OR	CI	*P*-value
Transfusion ratio	0.9	0.22–3.64	0.88
Total TBSA	1.17	1.05–1.3	0.005
Inhalation injury	0.25	0.003–22	0.54
Age	1.08	093–1.23	0.3
PELOD	1.08	0.95–1.22	0.26
PRISM	0.98	0.79–1.2	0.82

Logistic multivariate regression comparing outcomes while controlling for the presence of infection. Significance was set at *P* < 0.05. PELOD—pediatric logistic organ dysfunction score; PRISM—pediatric risk of mortality.

stratified by time points, clinical laboratory parameters similarly did not show any differences between time points days 0, 1, and 7 except in antithrombin III and PTT at day 7. It

is likely that FFP transiently facilitates coagulation during the course of the procedure and shortly thereafter that may not necessarily be identified by clinical laboratory measures alone. This is similar to previous reports from massive transfusion in trauma where coagulopathy was more rapidly corrected by aggressive product transfusion.[8]

The impact of the increased use of FFP on other outcome parameters is not clear. On ventilator days, organ failure, hospital length of stay, and wound healing, trends are not sufficient to state that there were any significant effects present. Overall organ dysfunction, as measured by PELOD, similarly held no significant difference between groups. The findings of this study, however, demonstrate that increased use of FFP in children in a 1:1 ratio is safe, contrary to previous studies in the pediatric intensive care unit and our own retrospective burn transfusion studies.[21,22]

This study differed from the studies of massive transfusion in trauma in that we did not use a 1:1:1 ratio (PRBC:FFP:platelets) due to previous reports of increased mortality in children transfused with these products.[21–23] As such, this study does not examine the additional impact of platelets on coagulation during massive blood loss. Given the higher complication rate and antibody development associated with platelet transfusion in children, evaluation of this parameter will require separate study prior to adoption. Similarly, whole blood transfusion has been reported to be safe in burned children and could offer a different avenue for further investigation.[16]

Multivariate analysis suggests that increased TBSA burn size and PRISM scores may play a role in infection risk. Analysis demonstrates no statistical significance between infection rates between transfusion groups at this juncture. This study illustrates that CDC criteria for infection incidence calculation should not be used to compare treatment modalities for an individual patient, but that CDC calculations may, however, point to hospital-based differences. Evaluation of care processes between hospitals may then lead to trials that can identify optimal treatment paradigms for the individual.

There are a few things to note in examining patients in the pediatric burn population. Given that pediatric patients are smaller in size than adults, they will require a smaller number of transfusions for their smaller blood volumes. This in turn will result in less transfusion complications like transfusion-related lung injury that may occur in patients with greater transfusion needs. Additionally, the setting of this study is in the operative and perioperative setting, which allows rapid and immediate transfusion of patients when necessary compared to trauma patients who risk prolonged presentation of injury and hemorrhage prior to admission, thus prolonging the duration of any coagulopathy risk.[24] Hemodilution is another factor to consider in patients undergoing major excision. While early resuscitation can be a contributing factor to abnormal coagulation profiles, we compared collected clinical laboratory markers of coagulation prior to excision and showed no abnormal coagulation profiles in general and between groups prior to excision.

There are several limitations of this study. Though this remains an ongoing study examining the use of aggressive transfusion strategies in the pediatric burn population, the power of the study remains relatively low. Additionally, the study remains in place at a single institution. As such, data presented may not be as readily generalizable to other populations. Comparisons between groups generally compared aggregated laboratory values. The granularity of the study could increase with time-based comparisons relative to operative interventions, but the clinical utility of transient abnormal labs over brief time periods remain unclear. Review of operative notes also unfortunately revealed that percent TBSA burn excised as well percentage of grafting performed for each graft type was not reliably documented and therefore unable to undergo analysis. Given that we are unable to compare the similarity of these points between groups, this also represents a limitation of this study. We should additionally note that many patients presented as international transfers to our center. While patients were transferred as quickly as possible, we were unable to accurately assess what actual initial resuscitation volumes were started or how much fluid they received prior to arrival, making any hemodilution analysis from this perspective difficult. Finally, clinical laboratory analysis relies on static measures that require some time for laboratory results to appear. Dynamic analysis of clotting behavior by methods such as thromboelastography or thromboelastometry may provide more rapid and frequent analysis of coagulation behavior following operative intervention and transfusion. Further evaluation and patient enrollment will continue to further define trends and observations in this study.

In this study, we sought to address the impact of a restrictive transfusion strategy in a pediatric burn population. Our interim analysis has shown that a 1:1 PRBC/FFP transfusion strategy did not yield any significant differences in untoward outcomes when compared with a 4:1 transfusion strategy. The study itself, however, remains too underpowered to definitively establish noninferiority with a restrictive transfusion strategy and our hope is to complete the study to better answer this question. As such, this trial is set to continue, as it has not reached its endpoint for either safety or efficacy. More broadly, it is becoming apparent that coagulopathy in acutely burn injured patients is a nuanced topic. Coagulation and hemostasis in this patient population may be further modulated at the platelet, factor, or plasma level and itself may behave differently compared with what is known in trauma patients undergoing hemorrhage management. Given this, we are hoping to use this study as a foundation to ask more questions and further study the behavior of coagulopathy in this population through factor specific assays and thromboelastography.

CONCLUSION

In conclusion, a 1:1 PRBC/FFP transfusion strategy when compared with a 4:1 strategy is safe in children and did not yield any significant differences in outcomes. A 1:1 transfusion strategy may be associated with a decrease in overall blood product use and could not be linked to any untoward outcomes. Additional studies on the effects of different transfusion ratios will be necessary to further elucidate this information.

REFERENCES

1. Tejiram S, Brummel-Ziedins KE, Orfeo T, et al. In-depth analysis of clotting dynamics in burn patients. J Surg Res. 2016;202(2):341–351.
2. Brohi K, Cohen MJ, Ganter MT, et al. Acute coagulopathy of trauma: hypoperfusion induces systemic anticoagulation and hyperfibrinolysis. J Trauma. 2008;64(5):1211–7; discussion 1217.
3. MacLeod JB, Lynn M, McKenney MG, Cohn SM, Murtha M. Early coagulopathy predicts mortality in trauma. J Trauma. 2003;55(1):39–44.
4. Frith D, Brohi K. The acute coagulopathy of trauma shock: clinical relevance. Surgeon. 2010;8(3):159–163.
5. Holcomb JB, Tilley BC, Baraniuk S, et al.; PROPPR Study Group. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. JAMA. 2015;313(5):471–482.
6. Baraniuk S, Tilley BC, del Junco DJ, et al.; PROPPR Study Group. Pragmatic randomized optimal platelet and plasma ratios (PROPPR) trial: design, rationale and implementation. Injury. 2014;45(9):1287–1295.
7. Sperry JL, Ochoa JB, Gunn SR, et al.; Inflammation the Host Response to Injury Investigators. An FFP:PRBC transfusion ratio >/=1:1.5 is associated with a lower risk of mortality after massive transfusion. J Trauma. 2008;65(5):986–993.
8. Kutcher ME, Kornblith LZ, Vilardi RF, Redick BJ, Nelson MF, Cohen MJ. The natural history and effect of resuscitation ratio on coagulation after trauma: a prospective cohort study. Ann Surg. 2014;260(6):1103–1111.
9. Valparaiso AP, Vicente DA, Bograd BA, Elster EA, Davis TA. Modeling acute traumatic injury. J Surg Res. 2015;194(1):220–232.
10. Cap A, Hunt B. Acute traumatic coagulopathy. Curr Opin Crit Care. 2014;20(6):638–645.
11. Palmieri TL, Holmes JH, Arnoldo B, et al. Restrictive transfusion strategy is more effective in massive burns: results of the TRIBE multicenter prospective randomized trial. Mil Med. 2019;184(Suppl 1):11–15.
12. Palmieri TL, Holmes JH 4th, Arnoldo B, et al. Transfusion requirement in burn care evaluation (TRIBE): a multicenter randomized prospective trial of blood transfusion in major burn injury. Ann Surg. 2017;266(4):595–602.
13. Greenhalgh DG, Saffle JR, Holmes JH 4th, et al.; American Burn Association Consensus Conference on Burn Sepsis and Infection Group. American Burn Association consensus conference to define sepsis and infection in burns. J Burn Care Res. 2007;28(6):776–790.
14. Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. Crit Care Med. 2008;36(9):2667–2674.
15. Housinger TA, Lang D, Warden GD. A prospective study of blood loss with excisional therapy in pediatric burn patients. J Trauma. 1993;34(2):262–263.
16. Barret JP, Desai MH, Herndon DN. Massive transfusion of reconstituted whole blood is well tolerated in pediatric burn surgery. J Trauma. 1999;47(3):526–528.
17. Palmieri TL, Greenhalgh DG, Sen S. Prospective comparison of packed red blood cell-to-fresh frozen plasma transfusion ratio of 4: 1 versus 1: 1 during acute massive burn excision. J Trauma Acute Care Surg. 2013;74(1):76–83.
18. Pollack MM, Holubkov R, Funai T, et al.; Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network. The pediatric risk of mortality score: update 2015. Pediatr Crit Care Med. 2016;17(1):2–9.
19. Leteurtre S, Martinot A, Duhamel A, et al. Validation of the paediatric logistic organ dysfunction (PELOD) score: prospective, observational, multicentre study. Lancet. 2003;362(9379):192–197.
20. Gross JB. Estimating allowable blood loss: corrected for dilution. Anesthesiology. 1983;58(3):277–280.
21. Church GD, Matthay MA, Liu K, Milet M, Flori HR. Blood product transfusions and clinical outcomes in pediatric patients with acute lung injury. Pediatr Crit Care Med. 2009;10(3):297–302.
22. Palmieri TL, Lee T, O'Mara MS, Greenhalgh DG. Effects of a restrictive blood transfusion policy on outcomes in children with burn injury. J Burn Care Res. 2007;28(1):65–70.
23. Palmieri TL, Sen S, Falwell K, Greenhalgh DG. Blood product transfusion: does location make a difference? J Burn Care Res. 2011;32(1):61–65.
24. Galganski LA, Greenhalgh DG, Sen S, Palmieri TL. Randomized comparison of packed red blood cell-to-fresh frozen plasma transfusion ratio of 4: 1 vs 1: 1 during acute massive burn excision. J Burn Care Res. 2017;38(3):194–201.

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