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MULTICENTER COMPARISON OF EMERGENCY RELEASE GROUP A VERSUS AB PLASMA IN BLUNT INJURED TRAUMA PATIENTS

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Abstract

INTRODUCTION—Group AB plasma, the traditional universal donor plasma product, is a limited resource. We compared outcomes of Group A plasma transfusion in comparison to AB.

METHODS—Analysis of blunt-injured patients who received emergency release plasma from was performed. Multivariable logistic regression was utilized to identify associations with morbidity and mortality.

RESULTS—There were 191 patients; 115 Group A and 76 Group AB. No differences were seen in age, sex, plasma transfusions, uncrossmatched red blood cells (RBCs), and Glasgow Coma Scale (GCS). Patients who received Group A plasma had significantly lower Injury Severity Score, chest Abbreviated Injury Scale, and scene transfer rate but not head AIS, or abdomen AIS. In addition, significant differences were noted in terms of blood products transfused within 24 hours in those receiving Group A over AB. Development of acute respiratory distress syndrome (ARDS), but not mortality, was higher within the AB cohort. No hemolytic or transfusion associated-ARDS reactions were noted in either group. ARDS; RBC transfusion volumes and head AIS were independently associated with mortality.

CONCLUSION—Utilization of Group A plasma for emergency blood resuscitation is a safe option which may alleviate potential shortages of AB plasma.

INTRODUCTION

Balancing the supply and demand of plasma resources is critical to the successful management of any blood bank. With unpredictable massive transfusion (MTx) events (≥ 10 units of red blood cells [RBCs] transfused within 24 hours), transfusion of male group AB

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plasma, the most widely accepted universal plasma product, can overwhelm the blood bank system leading to severe shortages. [1] Regionally, the scarcity of AB units may persist for days given that replenishment is directly related to the incidence of Group AB in the population.[2] As a result, regional solutions have been developed in order to reduce chronic shortages in Group AB plasma availability. Solutions include the use of viable alternatives to plasma, improving the speed of blood typing to ensure rapid use of matched products, and minimization of unnecessary plasma transfusions. Additionally, utilization of alternatives to plasma, including prothrombin complex concentrates (PCC) and lyophilized plasma, as well as the expansion of the universal plasma product to include male Group A plasma, have been proposed.[3,4,5]

The transfusion of male Group A plasma for emergency purposes is becoming more popular, particularly in rural environments where MTx events are less predictable.[6,7] The transfusion of potentially incompatible Group O apheresis platelets and its corresponding incompatible plasma containing anti-A and anti-B antibodies has become routine. The risk of this potentially incompatible transfusion, however, carries at least an equivalent, and likely greater, risk when compared to potentially incompatible Group A plasma and its corresponding anti-B (but not anti-A) antibodies. With this realization, several trauma centers have adopted Group A plasma as the universal plasma product in order to ensure adequate supply of Group AB plasma when indicated.[8,9] Nevertheless, to date, the clinical experience in the use of Group A plasma is limited to small cohorts in retrospective, single center reviews. [3, 4,10] To discriminate outcomes between practices using either the traditional universal plasma product (i.e. Group AB) and an alternative universal plasma product (i.e. Group A) in bluntly injured trauma patients, we performed a multi-institutional retrospective review. Both institutions are certified as Level I Trauma Centers by the American College of Surgeons but utilize either Group A or Group AB preferentially as their emergency release plasma products. We hypothesized that there would be equipoise in morbidity and mortality between bluntly injured patients regardless of the type of emergency release plasma transfused.

METHODS

Institutional Review Board permission was obtained from both institutions to review the medical records of bluntly injured trauma patients, age 18 or older, who received at least one emergency release plasma unit (i.e. unknown blood type at the time of transfusion) between January and September of 2012. Data was obtained from the respective, prospectively collected trauma databases at each institution as well as through medical record review. The trauma databases at both institutions employ full time chart abstractors, as mandated by the American College of Surgeons, and are used for institutional standardization as part of the National Trauma Databank (NTDB) and the Trauma Quality Improvement Project (TQIP).[11] The Mayo Clinic transfuses male donor-only Group A plasma exclusively to patients with unknown blood type while the University of Cincinnati transfuses gender nonspecific-donor Group AB plasma. Clinical parameters including age, sex, blood type, emergency department Glasgow Coma Scale (GCS), Injury Severity Score (ISS), blood product transfusion volumes, time in the trauma bay, time at referring hospital (if applicable), intensive care unit (ICU) length of stay (LOS), hospital LOS, as well as the

outcomes of complications and mortality rates, were compared based on type of plasma transfused. The Berlin Classification was utilized to define the acute respiratory distress syndrome (ARDS).[12,13] Positive end-expiratory pressure (PEEP) and PaO_2/FiO_2 (P/F) ratios were defined as the highest and lowest values, respectively, within 7 days of injury. Both institutions utilize similar plasma storage techniques. Fresh frozen plasma is thawed and stored nearby the trauma bay for immediate transfusion to patients meeting indications for plasma transfusions using massive transfusion and Coumadin reversal protocols. Thawed plasma is transferred to another area of the hospital by day 4 to ensure utilization and reduce waste. Univariate analysis was performed using Pearson's Chi-square test or Fisher's exact test for categorical variables and Student's t test or Wilcoxon rank-sum test for continuous variables. Variables were reported as rates or means with standard deviations (SD) where appropriate. Statistical significance was defined as $p \leq 0.05$. Statistically and clinically significant features were identified and used to perform a multivariable nominal logistic regression analysis to identify risk factors associated with mortality, the primary outcome.

RESULTS

In total, 191 patients were identified at both institutions including 115 who received Group A (60%) and 76 who received Group AB (40%) plasma. No differences were noted in age, sex, GCS, or probability of survival based on Trauma Score Injury Severity Score (TRISS) methodology between patients who received Group A versus Group AB emergency release plasma (Table 1). There were, however, significant differences in chest injury severity (Abbreviated Injury Scale [AIS)]) and there was an overall greater Injury Severity Score (ISS) in those who received Group AB plasma.

The distribution of patient blood types at both institutions were similar except for the greater incidence of Type AB at the University of Cincinnati (Table 2). The number of units of emergency release plasma transfused in the 24 hour period following injury was similar between cohorts; however, more plasma was transfused to Group AB plasma patients (Table 3). As expected, the utilization of compatible, non-identical plasma was greater in the emergency release AB plasma patients. In regards to RBC and apheresis platelet transfusions, the number of units of emergency release RBCs and platelets were similar but there was greater utilization of RBCs and platelets in the 24 hours following injury in the patients exposed to Group AB emergency release plasma. Emergency release Group A plasma patients received more crystalloid; tranexamic acid utilization was similar.

There were significant differences in outcomes between emergency release plasma blood groups. While mortality was equivalent (17% vs. 26%, p=0.15), there was a greater rate of sepsis, acute renal failure, deep venous thrombosis and pulmonary embolus in the patients who received Group AB emergency release plasma (Table 4). There was a non-statistically significant greater rate of ARDS in emergency release Group AB plasma groups (2% vs. 8%, $p = 0.06$). The P/F ratios were similar between groups but there was a greater highest PEEP within 7 days of injury in the Group A plasma group. Additionally, the ICU LOS was greater in the AB group. There was no evidence of transfusion associated ARDS nor hemolytic reactions in either group.

Multivariable analysis demonstrated several independent clinical features associated with mortality including ARDS, RBC transfusion volumes and head AIS (Table 5). The emergency release plasma group used for resuscitation (A vs. AB) did not contribute to mortality.

DISCUSSION

Over the last several years, there has been a substantial increase in the use of Group AB plasma. Despite the overall decline in the use of plasma, utilization of Group AB plasma increased 27% between 2006 and 2011 and now represents up to 25% of the overall plasma supply even though only 3–4% of the donor population nationwide is blood type AB.1,[2,14] While signs exist of this trend slowing, if the pace continues at this rate, demand will outstrip supply.

The cause of this marked increase in Group AB plasma use is likely related to the advent of MTx protocols which rely heavily on the traditional universal plasma donor, Group AB.[15] This blood product lacks anti-A and anti-B antibodies which potentially could cause minor ABO incompatibility; as a result, hemolytic reactions can be avoided. The trend for increased transfusion of Group AB plasma was noted after release of Holcomb et al's work describing improved survival in patients receiving plasma to RBC ratios approximating whole blood as part of MTx practices.[16] Less recognized from the authors' collective wartime experience, however, is the use of both Group AB and A plasma to correct the early coagulopathy of trauma.[17]

Though the transfusion of incompatible plasma in apheresis platelet units when type specific platelets are unavailable is acceptable, and ABO compatibility between donor and recipient platelets is considered of "minor importance" in adults, this practice has been slow to permeate plasma transfusions.[18] The reasons for this reluctance are likely related to the differences in storage requirements of platelets and plasma. While evidence exists that the current platelet storage guidelines may be unnecessarily strict, the current standard for apheresis platelets storage is at room temperature on an agitator for up to 5 days; after which, the platelets are considered expired and must be discarded.[19] Conversely, plasma may be frozen for prolonged durations. When needed type-specific plasma can be thawed and transfused. As MTx protocols have evolved, however, this time lag was deemed inefficient and contributory towards failure to control traumatic coagulopathy. Instead, pre-thawed plasma has been widely adopted at high use centers to facilitate immediate transfusion.

The combination of increased need and diminished storage ability of traditional thawed universal plasma donor creates a need for an adjunct plasma product. While PCCs and lyophilized plasma may be viable options, the current standard of care relies on the use of plasma for the reversal of traumatic coagulopathy.[4, 5] Given these factors, an expanded universal donor product is required. We believe that Group A plasma provides all of the benefits of Group AB plasma without the anticipated drawbacks from major and minor isoagglutinin (i.e. anti-B) mediated ABO incompatibility.

The current study demonstrates safety and outcome equivalence at two institutions that have different protocols for emergency release plasma in bluntly injured patients. As hypothesized for both trauma centers during the period studied, mortality was similar between both practices and there were no hemolytic reactions. Despite this equivalence, there were significant differences between the two plasma cohorts. As demonstrated, there were significantly greater rates of complications such as DVT, PE, ARF and sepsis in the AB plasma group, likely a result of their more severe injuries, particularly chest, as based on the ISS. In order to attempt to control for confounding variables, we performed a multivariable analysis. The RBC volume transfused in 24 hours, ARDS development, and greater head AIS, but not the type of universal plasma donor units utilized, were independently associated with mortality.

The uncommon occurrence of blood type AB in the population potentially carries an advantage. While this rarity makes Group AB plasma scarce, it also contributes to a situation in which the vast majority of injured patients with an unknown blood type will lack the B antigen. Within the current study, there was a 4% incidence of blood type AB and 7% incidence of B. Therefore, there was an 11% chance that a patient carried the B antigen. In other words, the probability of a patient having a compatible plasma transfusion with a Group A donor was 0.89. Given the plasma practice differences between institutions, there were only 11 patients who received an incompatible plasma transfusion. Again, none of these 11 had a hemolytic reaction. In fact, the chances for a hemolytic reaction are so infrequent that, during the Vietnam War, there were only 38 hemolytic reactions (responsible for less than 2 deaths) out of 364,000 Group O whole blood transfusions which confer a much higher risk given the incidence of the A antigen and the greater pathogenicity of anti-A antibodies.[20,21]

The results of this study should be interpreted in the context of its limitations. Despite performing a multivariable analysis of mortality, there likely were factors we were unable to adequately control for which introduced potential bias. Given the differences in environment between the two trauma centers (i.e. rural versus urban), we did not include penetrating trauma in this study. In addition, despite the rarity, there was a significantly greater proportion of patients with AB blood type at the University of Cincinnati. This is likely a result of differences in racial demographics between institutions.[22] For instance, African-Americans can have up to a three times greater proportion of Group AB than Caucasians.[23] As a result, more patients at the University of Cincinnati received the appropriately identical plasma transfusion. Despite the similar mortality outcome, there were significantly greater rates of complications associated with Group AB plasma utilization. This can be explained not only by the greater ISS and chest AIS, but also institutional practice variations. The University of Cincinnati routinely screens for DVT with Doppler ultrasound (US) which increases the identification of DVTs. Similarly, we suspect that, in patients with known DVT based on the US results, there was a greater likelihood to undergo computed tomography to diagnose PE. It should be noted that both institutions have similar protocols for DVT chemoprophylaxis. Additionally, the University of Cincinnati does not have a step-down unit from the ICU which artificially increased their ICU LOS. Lastly, and most significantly, this study had insufficient power to detect a difference in rates of hemolysis. With only 38 reactions in the entirety of Vietnam War, over 9,500 patients would be

required at each institution even if we assumed a similar rate of hemolysis for the transfusion of Group O plasma rather than Group A. Similarly, to detect a difference in death resulting from hemolysis, well over 100,000 patients would be required.[20] The actual number of patients to show a difference, however, is likely substantially greater given the higher risk of hemolysis when transfusing Group O platelets or whole blood (with their corresponding anti-A and anti-B antibodies) to patients with A and/or B antigens on their red blood cells when compared to Group A plasma (and its anti-B antibody) to patients with B antigens on their red blood cells.

The consequences of the increasing use and decreased supply of Group AB plasma have led to the circumstance where an alternative universal plasma donor product must be identified.[3, 8, 9] Group A plasma can be substituted for the traditional donor given this and other study's data demonstrating the safety and appropriateness for the active reversal of coagulopathy in patients with unknown blood types. While further prospective studies are warranted as trauma centers develop their own Group A universal donor programs, this approach can reverse the trend of increased Group AB plasma utilization and therefore avoid unnecessary shortages.

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Table 1

Univariable analysis of features among Group A and Group AB emergency release plasma. Continuous variables are presented as means (standard deviation).

ARDS = Acute Respiratory Distress Syndrome; pRBC = packed Red Blood Cell; ISS = Injury Severity Score; AIS = Abbreviated Injury Severity Scale; TRISS = Trauma Score Injury Severity Score; PEEP = Positive End Expiratory Pressure; ICU = Intensive Care Unit; LOS = Duration of Stay; P/F = PaO_2/FiO_2;

Variable	Group A (n=115)	Group AB (n=76)	P value
Age	57.6 (25.5)	51.9 (20.0)	.102
Male sex	65%	67%	.876
ISS	20.3 (14.5)	26.8 (16.6)	.007
Head AIS (per unit)	2.0 (1.9)	1.8 (2.1)	.660
Abdomen AIS (per unit)	1.1 (1.6)	1.1 (1.6)	.962
Chest AIS (unit)	1.3 (1.6)	2.1 (1.6)	<.001
TRISS	0.80 (0.29)	0.75 (0.32)	.330
Glasgow Coma Scale	11.3 (5.3)	10.6 (5.2)	.371
Direct from scene	55%	71%	.032

Table 2

Patient blood types per institution. UC = University of Cincinnati.

Blood types	Total (n=191)	Mayo (n=115)	UC (n=76)	P-value
A	86 (45%)	55 (48%)	31 (41%)	.301
AB	8 (4%)	1 (1%)	7 (9%)	.007
B	14 (7%)	10 (9%)	4 (5%)	.414
O	81 (42%)	47 (41%)	34 (45%)	.882
Unknown	2 (1%)	2 (1%)	0 (0%)	.518

Table 3

Blood Product and Fluid Utilization. All volumes are given in units or milliliters (mL) given in the 24 hour period after injury. Continuous variables are presented as means (standard deviation). pRBC = packed red blood cell; mL = milliliter.

Fluid Type	Group A (n=115)	Group AB (n=76)	p-value
Plasma units			
Emergency release plasma	2.7 (2.5)	2.5 (1.9)	.485
Total compatible plasma	4.3 (5.7)	5.6 (6.9)	.173
Compatible non-identical plasma	0.17 (0.67)	1.5 (4.2)	.009
Total plasma	4.5 (5.7)	7.0 (9.0)	.031
pRBC			
Emergency release pRBC	2.3 (3.4)	2.3 (3.1)	.909
Total pRBC	4.0 (7.5)	6.6 (9.7)	.051
Platelets			
Total incompatible platelets	0.19 (0.75)	0.11 (0.42)	.316
Total compatible platelets	0.35 (0.82)	0.54 (0.88)	.133
Total platelets	0.52 (1.9)	1.05 (1.1)	.030
Total crystalloid (mL)	3845 (3163)	2501 (1569)	<0.001
Tranexamic acid	7%	8%	.833

Table 4

Outcomes. P/F ratio = PaO_2/FiO_2; ARDS = Acute Respiratory Distress Syndrome;

Feature	Group A (n=115)	Group AB (n=76)	p-value
Mortality	17%	26%	.150
Ventilator days	2.8 (7.0)	3.8 (6.0)	.310
ICU LOS	3.8 (7.7)	7.2 (8.8)	.007
Hospital days	8.2 (9.7)	9.5 (9.1)	.350
Highest PEEP	10 (4.6)	8 (3.1)	.002
Lowest P/F ratio	226 (145)	206 (97)	.326
ARDS	2%	8%	.060
Sepsis	0%	5%	.024
Pneumonia	7%	14%	.137
Acute Renal Failure	1%	11%	.003
Deep Venous Thrombosis	5%	16%	.021
Pulmonary Embolus	0%	5%	.013

Table 5

Multivariable analysis of variables associated with mortality.

Variable	OR	95% CI
Group A (vs AB plasma)	0.66	0.21–2.06
ARDS*	7.07	1.00–68.2
PRBC in 24° (per unit)*	1.25	1.04–1.52
Head AIS (per unit)*	1.46	1.13–1.91
Chest AIS (per unit)	1.30	0.94–1.84
Direct from scene	1.21	0.40–3.87
Age (per year)	1.01	0.99–1.04
Crystalloid in 24° (per L)	1.00	0.99–1.01
Plasma in 24° (per unit)	0.98	0.79–1.19
Abdomen AIS (per unit)	0.84	0.57–1.20
Platelets in 24° (per unit)	0.63	0.30–1.19

* $p < 0.05$