Impact of ABO-Identical vs ABO-Compatible Nonidentical Plasma Transfusion in Trauma Patients

Kenji Inaba, MD, FRCSC; Bernardino C. Branco, MD; Peter Rhee, MD; John B. Holcomb, MD; Lorne H. Blackbourne, MD; Ira Shulman, MD; Janice Nelson, MD; Demetrios Demetriades, MD, PhD

Hypothesis: Exposure to ABO-compatible nonidentical plasma will result in worse outcomes than transfusion with ABO-identical plasma only.

Design: Retrospective study.

Setting: Level I trauma center.

Patients: All patients requiring plasma (from 2000-2008) were identified. Propensity scores were used to match patients exposed to ABO-compatible plasma with those receiving exclusively ABO-identical plasma.

Main Outcome Measures: Mortality and complications (acute respiratory distress syndrome [ARDS]), sepsis, renal failure, and liver failure).

Results: A total of 284 patients who received ABO-compatible nonidentical plasma were matched 1:1 with patients who received ABO-identical plasma only (230 group O, 39 A, and 15 B). ABO-compatible plasma did not affect mortality (35.2% vs 33.5%, $P = .66$). However, the overall complication rate was significantly higher for patients receiving ABO-compatible plasma (53.5% vs 40.5%, $P = .002$). The ARDS and sepsis rates were also significantly increased (19.4% vs 9.2%, $P = .001$, and 38.0% vs 28.9%, $P = .02$, respectively). As the volume of ABO-compatible plasma infused increased, a stepwise increase in complications was seen, reaching 70.0% for patients receiving more than 6 U. Patients receiving more than 6 U also had a 4-fold increase in ARDS. All recipient blood groups had an increase in overall complications, ARDS, and sepsis with exposure. This was significant for group O recipients with a higher risk of overall complications and ARDS (50.9% vs 40.0%, $P = .03$, and 17.4% vs 7.8%, $P < .001$, respectively).

Conclusions: Exposure to ABO-compatible plasma results in an increase in overall complications, in particular ARDS and sepsis. There is a stepwise increase in the complication rate as exposure increases. Further prospective evaluation of the impact of limiting factor replacement to ABO-identical plasma only is warranted.

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Author Affiliations: Division of Trauma and Surgical Critical Care, University of Southern California, Los Angeles, California (Drs Inaba, Branco, and Demetriades); Division of Trauma, Critical Care and Emergency Surgery, University of Arizona, Tucson (Dr Rhee); Division of Acute Care Surgery, Center for Translational Injury Research, University of Texas Medical School at Houston (Dr Holcomb); US Army Institute of Surgical Research, Fort Sam Houston, San Antonio, Texas (Dr Blackbourne); and Department of Pathology, University of Southern California Medical Center, Los Angeles (Drs Shulman and Nelson).

AGGRESSIVE BLOOD COMPONENT therapy, centered around early plasma and red blood cell use, has become a mainstay in acute resuscitation of critically ill trauma patients who have sustained blood loss.[1-5] Aggressive plasma transfusion in particular, driven by an increasing evidence base derived both from military[6-8] and civilian[9-18] series, has become widely practiced. These studies demonstrate that, in patients who require a massive transfusion, plasma transfusion in ratios approaching 1:1 is associated with an improvement in survival.[6-18]

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As a direct consequence of this finding, plasma is being used earlier in the resuscitation sequence and in higher volumes. Ideally, plasma is dispensed as a group-specific product to be transfused along identical ABO lines. Thus, a patient with blood group A would receive A donor plasma, a group B patient would receive B donor plasma, group O patients would receive O plasma, and, although relatively rare, group AB patients would receive AB plasma. However, transfusion of plasma that is compatible but not ABO-identical is an approved practice. In compatible nonidentical plasma transfusion, group O patients could receive group A, B, or AB plasma. Group A and B patients in turn could receive AB donor plasma.

Few studies have examined the impact of compatible nonidentical plasma transfusion. In platelet transfusion,[19] the administration of compatible nonidentical platelets to patients undergoing coronary artery bypass grafting or valve replacement was associated with an increase in mortality and complications.[20] For

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plasma, the Scandinavian Donations and Transfusions database–derived retrospective cohort analysis[21] demonstrated that exposure to greater than 5 U of compatible nonidentical plasma in a mixed medical-surgical patient base resulted in a significant increase in mortality (relative risk, 1.15; 95% confidence interval, 1.02-1.95).

No data examining the impact of compatible nonidentical plasma transfusion in the injured patient population are available to date. With the aggressive replacement strategies being used for plasma in trauma resuscitation today, a clear understanding of the impact of plasma transfusion across nonidentical ABO lines is critical to optimizing transfusion safety. The purpose of this study, therefore, was to examine the extent of compatible nonidentical transfusion occurring in trauma patients and to assess the impact of this exposure on outcomes. Our hypothesis was that the transfusion of compatible nonidentical plasma would result in worse outcomes than the transfusion of exclusively ABO-identical plasma.

METHODS

STUDY DESIGN AND PATIENTS

After institutional review board approval, a review of the institutional trauma registry and Blood Bank Database at the Los Angeles County + University of Southern California Medical Center, a level I trauma center, was performed. All trauma patients who received plasma between January 1, 2000, and December 31, 2008, were identified. We excluded patients who (1) had blood group AB (because exposure to compatible nonidentical plasma is not possible) and (2) received ABO-incompatible plasma. Patient variables abstracted included age, sex, blood group, mechanism, admission vital signs, Glasgow Coma Scale score, Injury Severity Score, Abbreviated Injury Scale score, type and volumes of blood products, duration of intensive care unit stay, duration of hospital stay, complications (acute respiratory distress syndrome [ARDS], sepsis, acute renal failure, and liver failure), and mortality. Continuous variables were dichotomized by using clinically relevant cutoff points: age (≥55 vs <55 years), systolic blood pressure at admission (<90 vs ≥90 mm Hg), Glasgow Coma Scale score (≤8 vs >8), Injury Severity Score (≥25 vs <25), and Abbreviated Injury Scale score (≥3 vs <3).

DEFINITIONS

We defined *ARDS* as (1) ratio of arterial oxygen pressure to fraction of inspired oxygen of 200 or less, (2) chest radiograph demonstrating bilateral infiltrates, and (3) no evidence of cardiac failure on pulmonary artery catheterization (pulmonary artery occlusion pressure ≤18 mm Hg) or by echocardiography or clinical examination. *Sepsis* was defined as the presence of infection plus at least 2 of the following: (1) heart rate greater than 90/min, (2) respiratory rate greater than 20/min, (3) temperature less than 36°C or greater than 38°C, and (4) white blood cell count less than 4000/μL or greater than 12 000/μL (to convert to cells $\times 10^9$ per liter, multiply by 0.001), or more than 10% immature neutrophils (to convert to a proportion of 1, multiply by 0.01). *Acute renal failure* was defined as (1) serum creatinine level 3-fold higher than the normal limit, or (2) glomerular filtration rate decrease greater than 75%, or (3) serum creatinine level of 4 mg/dL or more (to convert to micromoles per liter, multiply by 88.4) with an acute increase greater than 0.5 mg/dL, or (4) urinary output less than 0.3 mL/kg/h for 24 hours, or anuria for 12 hours. *Liver failure* was defined as (1) total bilirubin level greater than 3 mg/dL (to convert to micromoles per liter, multiply by 17.1) or (2) aspartate aminotransferase or alanine aminotransferase level 2-fold higher than the normal limits. The term *overall complications* was defined as the presence of any of the 4 complications described in this paragraph.

STATISTICAL ANALYSIS

Patients were divided into 2 cohorts: those who received at least 1 U of ABO-compatible nonidentical plasma and those who received only ABO-identical plasma. These 2 cohorts were compared for differences in clinical characteristics and transfusion requirements by univariate analysis. Fisher exact tests or χ^2 tests were used to compare proportions, and unpaired *t* or Mann-Whitney tests were performed to compare means.

Because the number of confounders was large in comparison with the number of events, patients receiving ABO-compatible nonidentical plasma were matched in a 1:1 ratio by means of propensity scores to patients who received ABO-identical plasma.[22] Included in the propensity score model were all variables that differed significantly (at the $P<.05$ level) between the 2 cohorts (blood group, Injury Severity Score, chest and abdomen Abbreviated Injury Scale score, total volume of packed red blood cells, plasma, platelets, cryoprecipitate, and factor VIIa received at 6 and 12 hours and during the total hospital stay).

Propensity scores (predicting the probability of receiving ABO-compatible nonidentical plasma) were calculated by binary logistic regression. Each patient receiving ABO-compatible nonidentical plasma was matched to a patient who received ABO-identical plasma within a 0.03 caliper of propensity without replacement. The caliper was equal to one-quarter of a standard deviation of the logit of the propensity (caliper was $0.10/4 \approx 0.03$).[23] Patients who received ABO-compatible nonidentical plasma for whom no suitable match could be found were excluded.

The 2 groups were compared for differences in clinical characteristics and transfusion requirements. McNemar χ^2 test was used to compare proportions and paired *t* test to compare means.

Outcomes (mortality, length of stay, and complications) between matched cohorts were compared by McNemar χ^2 test for proportions and Wilcoxon test for matched sample for means. Data were analyzed by means of SPSS for Windows, version 12.0 (SPSS Inc, Chicago, Illinois).

RESULTS

During the 9-year study period, 6094 (14.3%) of the 42 684 trauma patients admitted to the Los Angeles County + University of Southern California Medical Center received a blood transfusion. Of these, 2788 (45.7%) received a plasma transfusion. After exclusion of 97 patients (3.5%) who had blood group AB and 1 patient (0.04%) who received ABO-incompatible plasma, data from 2690 patients were available for analysis. Of those, 338 (12.6%) received at least 1 U of ABO-compatible nonidentical plasma and 2352 (87.4%) received only ABO-identical plasma. After propensity score matching, 284 matched pairs were available for analysis.

From 2000 to 2008, while the total number of injured patients remained constant, the overall usage of

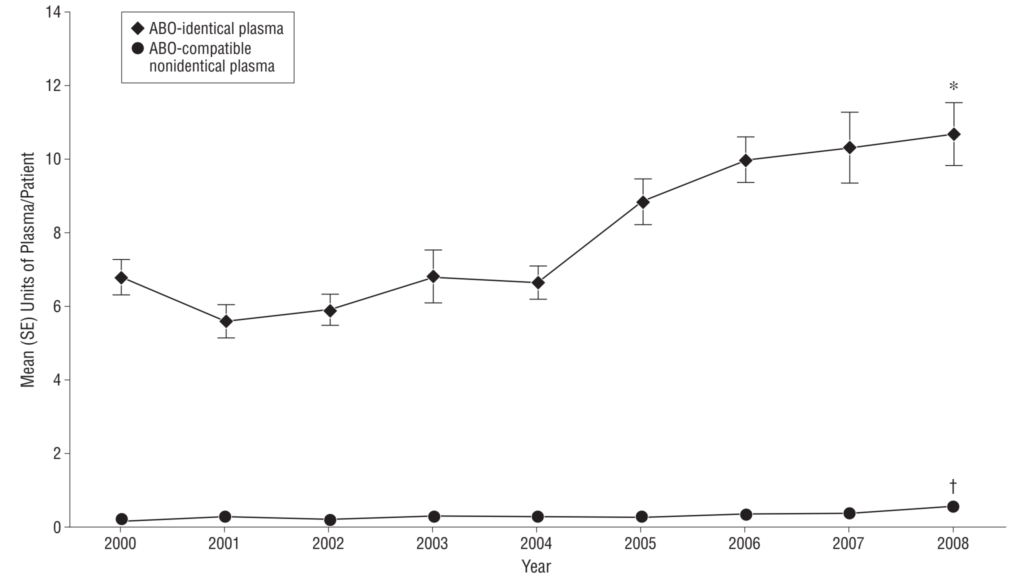

Figure 1. Increase in both ABO-identical and ABO-compatible nonidentical plasma utilization throughout the study period. *P* values were determined by post hoc analysis of variance. **P* < .001. †*P* = .001.

plasma increased. There was a 200% increase in use of ABO-compatible nonidentical plasma (mean [SE], from 0.2 [0.4] to 0.6 [0.8], *P* < .001) and a 57% increase in the use of ABO-identical plasma (from 6.8 [3.2] to 10.7 [5.9], *P* < .001) (**Figure 1**).

The average (SD) age of the matched patients receiving plasma was 34.0 (17.5) years, and 80.8% were male. Of the 284 matched pairs, 230 had blood group O, 39 blood group A, and 15 blood group B. At admission, 16.3% of the patients were hypotensive (systolic blood pressure <90 mm Hg), 36.2% had a Glasgow Coma Scale score of 8 or less, and 80.6% had an Injury Severity Score of 16 or more. The demographic and clinical characteristics before and after matching are summarized in **Table 1**.

Matched patients received a mean (SD) of 6.3 (8.7) U of packed red blood cells in the first 6 hours, 7.6 (9.7) U in the first 12 hours, and 14.8 (15.9) U during their total hospital stay. The mean number of units of apheresis platelets, cryoprecipitate, and factor VIIa transfused during their hospital stay was 1.2 (2.1), 4.1 (9.1), and 0.9 (3.1) U, respectively. Patients who received ABO-compatible nonidentical plasma had a mean of 2.8 (4.2) U of plasma transfused in the first 6 hours, 4.5 (5.2) U in the first 12 hours, and 13.5 (19.9) U during their total hospital stay. Patients who received ABO-identical plasma had a mean of 3.1 (4.1) U of plasma transfused in the first 6 hours, 4.7 (5.1) U in the first 12 hours, and 11.9 (12.8) U during their total hospital stay (**Table 2**).

When outcomes were compared between matched patients who received ABO-compatible nonidentical plasma and ABO-identical plasma, there was no difference with regard to mortality (35.2% for the ABO-compatible nonidentical group vs 33.5% for ABO-identical, *P* = .66). However, patients who received ABO-compatible nonidentical plasma had a significantly higher rate of overall complications than those who received ABO-identical plasma (53.5% vs 40.5%, *P* = .002). Patients who received ABO-compatible nonidentical plasma also had a significantly higher incidence of ARDS (19.4% vs 9.2%, *P* = .001) and sepsis (38.0% vs 28.9%, *P* = .02) (**Table 3**). There was a trend toward longer intensive care unit stay and hospital stay in patients who received ABO-compatible nonidentical plasma (15.6 [20.5] vs 12.7 [15.7] days, *P* = .07, and 24.2 [32.3] vs 20.0 [24.9] days, *P* = .09, respectively) (Table 3).

When the volume of ABO-compatible nonidentical plasma transfused was analyzed, there was a stepwise increase in complications with increasing transfusion, with a complication rate of 70.0% for patients receiving in excess of 6 U (**Figure 2**). Compared with patients who received only ABO-identical plasma, the risk of ARDS was 3-fold higher for patients receiving 4 to 6 U of ABO-compatible nonidentical plasma and 4-fold higher if patients received in excess of 6 U. The risk of sepsis also increased with increasing amounts of ABO-compatible nonidentical plasma, although statistical significance was not achieved. No dose-dependent difference in the complication rate was seen with ABO-identical plasma transfusion.

When analyzed by recipient blood group, there was an increase in the rates of overall complications (**Figure 3**), ARDS, and sepsis throughout all blood groups with the transfusion of ABO-compatible nonidentical plasma. This increase was significant for blood group O patients, who had a 2-fold higher risk of overall complications and a 3-fold higher risk of ARDS (50.9% vs 40.0%, *P* = .03, and 17.4% vs 7.8%, *P* < .001, respectively). When rates were compared between recipient blood groups, no significant differences were found for overall complications (61.5% for A vs 73.3% for B vs 50.9% for O, *P* value for trend = .11), ARDS (25.6% for A vs 33.3% for B vs 15.7% for O, *P* value for trend = .12), or sepsis (38.5% for A vs 66.7% for B vs 35.7% for O, *P* value for trend = .06).

Table 1. Demographic and Clinical Data of Patient Groups Receiving ABO-Compatible Nonidentical and ABO-Identical Plasma

	Unmatched			Matched[b]		
	ABO-C (n = 338)	ABO-I (n = 2352)	*P* Value[a]	ABO-C (n = 284)	ABO-I (n = 284)	*P* Value[a]
Age, y						
Mean (SD)	36.0 (18.3)	37.1 (18.6)	.34	33.9 (17.6)	34.2 (17.4)	.57
Median (range)	31 (1-91)	33 (1-98)		30 (1-91)	30 (1-92)	
≥55, No. (%)	56 (16.6)	400 (17.0)	.84	40 (14.1)	36 (12.7)	.71
Male sex, No. (%)	273 (80.8)	1934 (82.2)	.51	229 (80.6)	229 (80.6)	>.99
Blood group, No. (%)[c]						
A	39 (11.5)	813 (34.6)	**<.001**	39 (13.7)	39 (13.7)	>.99
B	15 (4.4)	323 (13.7)		15 (5.3)	15 (5.3)	
O	284 (84.0)	1216 (51.7)		230 (81.0)	230 (81.0)	
Blunt trauma, No. (%)	212 (62.7)	1505 (64.0)	.70	175 (61.6)	185 (65.1)	.38
Intubated on admission, No. (%)	69 (20.4)	430 (18.3)	.36	63 (22.2)	63 (22.2)	>.99
SBP on admission						
Mean (SD), mm Hg	120.6 (38.2)	121.2 (38.8)	.80	120.3 (39.3)	121.3 (39.7)	.77
Median (range), mm Hg	125 (0-280)	126 (0-284)		124 (0-280)	128 (0-211)	
<90 mm Hg, No. (%)	52 (15.4)	319 (13.6)	.23	42 (14.8)	48 (16.9)	.73
GCS score on admission ≤8, No. (%)	109 (32.2)	700 (29.8)	.31	102 (35.9)	102 (35.9)	.93
ISS						
Mean (SD)	26.0 (14.5)	22.8 (13.4)	**<.001**	26.1 (14.7)	27.3 (14.4)	.31
Median (range)	25 (1-75)	22 (1-75)		25 (1-75)	26 (1-75)	
≥16, No. (%)	267 (79.0)	1656 (70.4)	**<.001**	227 (79.9)	230 (81.0)	.75
AIS score ≥3, No. (%)						
Head	120 (35.5)	915 (38.9)	.27	112 (39.4)	125 (44.0)	.27
Chest	161 (47.6)	888 (37.8)	**<.001**	142 (50.0)	145 (51.1)	.80
Abdomen	149 (44.1)	813 (34.6)	**<.001**	116 (40.8)	119 (41.9)	.80
Extremity	104 (30.8)	663 (28.2)	.28	84 (29.6)	83 (29.2)	.95

Abbreviations: ABO-C, ABO-compatible; ABO-I, ABO-identical; AIS, Abbreviated Injury Scale; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; SBP, systolic blood pressure.

[a] *P* values that are significantly different ($P < .05$) are shown in boldface. For the unmatched cohorts, the *P* values for categorical variables were derived from χ^2 or Fisher exact tests; *P* values for continuous variables were derived from unpaired *t* or Mann-Whitney tests. For the matched cohorts, the *P* values for categorical variables were derived from the McNemar χ^2 test; *P* values for continuous variables were derived from the paired *t* test.

[b] Patients were matched for the variables that were significantly different (in boldface) and for the volume of packed red blood cells, plasma, platelets, cryoprecipitate, and factor VIIa transfused.

[c] Because of rounding, percentages may not total 100.

When group O recipients of ABO-compatible nonidentical plasma were analyzed according to the type of plasma received, there was no significant difference in overall complications (47.3% for A vs 57.6% for B vs 45.7% for AB, *P* value for trend=.34), ARDS (14.0% for A vs 19.7% for B vs 14.3% for AB, *P* value for trend=.38), or sepsis (33.3% for A vs 42.4% for B vs 31.4% for AB, *P* value for trend=.39).

COMMENT

Plasma transfusion has become an integral part of the early resuscitative strategy in critically injured patients. Although not universally accepted[24-26] and awaiting prospective validation, data from both the military[6-8] and civilian[9-18] settings, including a multicenter study published by Holcomb et al,[10] demonstrate that aggressive replacement of plasma in ratios approaching 1:1 is associated with an improvement in survival in patients requiring massive transfusions.

As a direct consequence of this aggressive resuscitation strategy, our time-dependent survey of plasma usage demonstrated an increase in the total volume of plasma being transfused despite the patient load receiving this plasma remaining constant during the study period. The increase was most marked between 2004 and 2005, around the time of publication of several reports outlining the importance of aggressive plasma transfusion. This increase was driven primarily by an increase in the transfusion of identical rather than compatible nonidentical plasma. However, although small relative to the volume of identical plasma transfused, there was a steadily increasing exposure of injured patients to compatible nonidentical plasma during the entire study period.

Patients who were exposed to compatible nonidentical plasma tended to be more severely injured, with a higher chest and abdominal Abbreviated Injury Scale score. As might be expected, these patients also required more blood products. To mitigate these differences, propensity scoring was used to allow a direct comparison between similar groups differing only in their exposure to compatible nonidentical plasma.

The exact mechanism responsible for the detrimental effect of compatible nonidentical plasma is not known. Plasma contains soluble blood group antigens and may contain residual fragments of red blood cell stroma.[27] Combined with antibodies in the recipient, circulating immune complexes result,[28] and these may in turn drive the negative immunomodulatory effects seen. In the study by Shanwell et al,[21] group O recipients who had a higher

Table 2. Transfusion Requirements of Patient Groups in Unmatched and Matched Populations

	Units Received					
	Unmatched			Matched		
	ABO-C (n = 338)	ABO-I (n = 2352)	*P* Value[a]	ABO-C (n = 284)	ABO-I (n = 284)	*P* Value[a]
Packed Red Blood Cells						
0-6 h						
Mean (SD)	6.7 (9.6)	4.6 (7.0)	**<.001**	5.9 (8.4)	6.7 (9.0)	.28
Median (range)	3 (0-71)	2 (0-82)		2 (0-45)	4 (0-45)	
0-12 h						
Mean (SD)	8.2 (10.9)	5.4 (7.7)	**<.001**	7.2 (9.3)	7.9 (10.0)	.39
Median (range)	4 (0-72)	3 (0-102)		4 (0-46)	4 (0-53)	
Total						
Mean (SD)	17.9 (20.1)	10.0 (10.3)	**<.001**	15.4 (18.0)	14.5 (14.5)	.53
Median (range)	12 (0-113)	7 (0-102)		10 (0-109)	10 (0-93)	
Plasma						
0-6 h						
Mean (SD)	3.4 (5.8)	2.0 (3.1)	**<.001**	2.8 (4.2)	3.1 (4.1)	.33
Median (range)	2 (0-46)	0 (0-34)		1 (0-26)	2 (0-30)	
0-12 h						
Mean (SD)	5.1 (7.0)	3.0 (3.9)	**<.001**	4.5 (5.2)	4.7 (5.1)	.50
Median (range)	3 (0-50)	2 (0-46)		2 (0-38)	4 (0-32)	
Total						
Mean (SD)	16.5 (22.1)	6.7 (7.6)	**<.001**	13.5 (19.9)	11.9 (12.8)	.25
Median (range)	10 (1-232)	4 (1-86)		8 (1-232)	7 (1-86)	
Platelets						
Mean (SD)	1.5 (2.6)	0.7 (1.2)	**<.001**	1.3 (2.5)	1.1 (1.6)	.36
Median (range)	0 (0-23)	0 (0-10)		0 (0-23)	0 (0-7)	
Cryoprecipitate						
Mean (SD)	5.3 (10.3)	2.0 (5.8)	**<.001**	4.6 (9.4)	3.9 (9.1)	.44
Median (range)	0 (0-80)	0 (0-60)		0 (0-50)	0 (0-60)	
Factor VIIa						
Mean (SD)	1.1 (3.6)	0.3 (1.9)	**<.001**	0.7 (3.0)	0.9 (3.0)	.56
Median (range)	0 (0-29)	0 (0-26)		0 (0-29)	0 (0-23)	

Abbreviations: ABO-C, ABO-compatible; ABO-I, ABO-identical.
[a] *P* values that are significantly different ($P < .05$) are shown in boldface. For the unmatched cohorts, the *P* values were derived from unpaired *t* or Mann-Whitney tests. For the matched cohorts, the *P* values were derived from the paired *t* test.

titer and avidity of anti-A and anti-B antibodies had an increased relative risk of dying if exposed to compatible nonidentical plasma when compared with other blood group recipients. In fact, when analyzed by recipient blood group, only the group O patients demonstrated a significant mortality difference. Likewise, in our subgroup analysis, although the A and B recipient groups were underpowered to demonstrate significance, when analyzed by recipient blood group, the increase in complications was significant only in group O recipients. Furthermore, when the Scandinavian group compared group O patients receiving AB donor plasma vs either A or B donor plasma with a smaller soluble antigen burden, they again found that the mortality impact resulted from AB donor plasma exposure only. This finding provides at least indirect evidence supporting the immune complex–mediated mechanism; however, no further mechanistic data are available at this time. In our analysis, no difference in the outcomes according to donor blood group could be detected.

Our study was designed to analyze the impact of compatible nonidentical plasma exposure in injured patients. Although no mortality effect could be extracted, exposure to compatible nonidentical plasma resulted in a significant dose-dependent increase in overall complications, in particular ARDS. The overall complication rate reached 70% in patients who received more than 6 U of compatible plasma, 3-fold greater than in those who did not; the ARDS rate was more than 4-fold higher than in those who did not. This rate difference was seen across all recipient blood groups but reached significance only in group O recipients.

This study was limited by its retrospective design. The complications used in our analysis were captured in real time by a team of experienced nurses. Despite this, there is the possibility that errors occurred in both the identification of complications and their entry into the database. It is expected, however, that this would have affected both groups equally. One of the primary complications under study was ARDS. Although standard diagnostic criteria for ARDS were used, transfusion-related acute lung injury can have a similar presentation. Because a definitive temporal relationship between blood product transfusion and the development of complications could not be made, the definitive diagnosis of transfusion-related acute lung injury was not possible.

Table 3. Outcomes Between Matched Populations[a]

	Total (N = 568)	ABO-C (n = 284)	ABO-I (n = 284)	OR (95% CI)	*P* Value[b]
Mortality, No. (%)	195 (34.3)	100 (35.2)	95 (33.5)	1.1 (0.8-1.7)	.66
Overall complications, No. (%)	267 (47.0)	152 (53.5)	115 (40.5)	1.7 (1.2-2.4)	**.002**
ARDS, No. (%)	81 (14.3)	55 (19.4)	26 (9.2)	2.4 (1.5-3.9)	**.001**
Sepsis, No. (%)	190 (33.5)	108 (38.0)	82 (28.9)	1.5 (1.1-2.2)	**.02**
ARF, No. (%)	59 (10.4)	31 (10.9)	28 (9.9)	1.1 (0.7-1.9)	.78
Liver failure, No. (%)	130 (22.9)	72 (25.4)	58 (20.4)	1.3 (0.9-2.0)	.19
				Mean Difference (95% CI)	
ICU days					
Mean (SD)	14.1 (18.3)	15.6 (20.5)	12.7 (15.7)	2.9 (0.3-6.2)	.07
Median (range)	7 (1-126)	8 (1-117)	7 (1-126)		
Hospital days					
Mean (SD)	22.1 (28.8)	24.2 (32.3)	20.0 (24.9)	4.2 (0.6-8.9)	.09
Median (range)	13 (1-216)	13 (1-216)	13 (1-180)		

Abbreviations: ABO-C, ABO-compatible; ABO-I, ABO-identical; ARDS, acute respiratory distress syndrome; ARF, acute renal failure; CI, confidence interval; ICU, intensive care unit; OR, odds ratio.

[a]The odds ratios, mean differences, and *P* values were obtained after matching for demographics, clinical variables, and blood transfusion requirements.

[b]*P* values that are significantly different ($P < .05$) are shown in boldface. The *P* values for categorical variables were derived from McNemar χ^2 test; *P* values for continuous variables were derived from Wilcoxon matched-pair test.

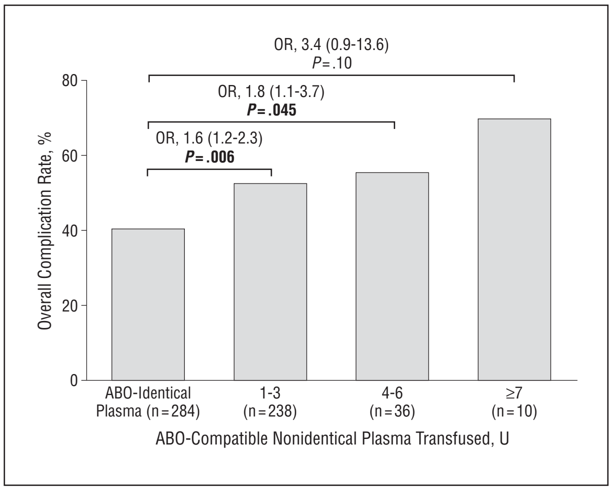

Figure 2. Overall complication rates stratified by number of units of ABO-compatible nonidentical plasma received. OR indicates odds ratio. The 95% confidence intervals are given in parentheses. *P* values that are significantly different ($P < .05$) are shown in boldface.

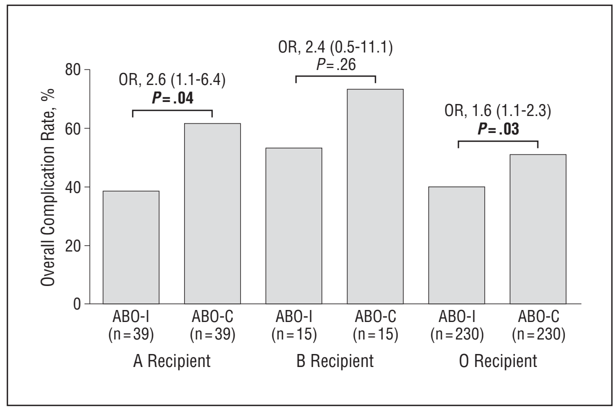

Figure 3. Overall complication rates between patients who received ABO-identical (ABO-I) and ABO-compatible nonidentical (ABO-C) plasma stratified by recipient blood group. OR indicates odds ratio. The 95% confidence intervals are given in parentheses. *P* values that are significantly different ($P < .05$) are shown in boldface.

As has been demonstrated in our previous analyses,[12,29] using the trauma registry for abstracting blood component transfusion data is highly inaccurate. In particular, concise volume determination is highly problematic. Consequently, to mitigate these errors, transfusion data were abstracted exclusively from the records maintained by the blood bank because dispensing and utilization data are regulated by the US Food and Drug Administration using tightly controlled criteria.

What was not available for analysis was the total crystalloid load received by the patients during their initial resuscitation. Crystalloids affect neutrophil activation, and,[30,31] although this was minimized in both the ABO-compatible and ABO-identical plasma groups, it is possible that a difference in the volume of crystalloids received by each group may have altered our results, especially the ARDS rates.

The exact reasons why patients received compatible nonidentical plasma could not be extracted from the data set, and as a direct consequence it is possible that a confounding factor was not corrected for in the analysis. Theoretically, patients bleeding faster may have required nonidentical plasma. At our facility, however, with the availability of prethawed plasma, this is less likely. Furthermore, within the limits of this study design, after propensity scoring and using blood product utilization as a surrogate marker for blood loss, the comparison groups were well matched for injury demographics as well as blood product transfusion.

This institution maintains an inventory of thawed plasma. Ten units of group O and 8 U of both A and B are kept thawed at all times. Although turnover is rapid and the functional differences between this thawed plasma and fresh frozen plasma are likely to be minor, during the study period a combination of thawed plasma and fresh frozen plasma was used. It is possible that differences in the relative amounts of each of these products could have affected the results. In addition, there may be a difference in male and female donor plasma and its effect on the recipient.[32,33] Donor sex was not available and could not be analyzed; however, most of our plasma inventory is obtained from male donors.

Finally, during the study period, apheresis platelets were used exclusively. Each apheresis unit contains a significant amount of plasma. Platelet transfusion across ABO lines may have occurred during the study period, diluting the magnitude of the effect seen.

The safety of our blood supply has undergone tremendous changes over time. Although major transfusion reactions are now relatively rare,[33,34] our understanding of the more subtle effects of transfusion on outcomes other than mortality is increasing. Clearly, for most patients receiving plasma, this product is lifesaving and has allowed for decreased allogeneic transfusion requirements. However, if outcomes can be improved by the transfusion of identical rather than compatible nonidentical plasma, technically this should drive a change in practice. Logistically, inventory management for fresh frozen plasma is relatively straightforward and the transfusion of identical plasma should in most cases be possible. Even for centers managing a liquid inventory of plasma, with the exception of massive transfusion cases, identical plasma transfusion is an achievable goal.

In summary, exposure to plasma that is compatible but nonidentical results in an increase in overall complications, in particular ARDS and sepsis. We found a stepwise increase in the complication rate as the extent of exposure increased, reaching 70% for patients who received in excess of 6 U. The mechanism behind this detrimental effect is unknown. Further prospective evaluation of the impact of limiting factor replacement to ABO-identical plasma is warranted.

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Correspondence: Kenji Inaba, MD, FRCSC, Division of Trauma and Surgical Critical Care, University of Southern California, 1200 N State St, Room CL5100, Los Angeles, CA 90033-4525 (kinaba@surgery.usc.edu).
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INVITED CRITIQUE

Is Transfusion of ABO-Compatible Nonidentical Plasma Truly Associated With an Increased Risk of Complications?

The transfusion of high ratios of plasma and platelets to packed red blood cells, known as hemostatic resuscitation, in patients requiring massive transfusion has become a standard of care in many trauma systems. This is a result of multiple retrospective analyses from both military and civilian databases that showed an association between high-ratio transfusion and improved survival. This very well-done study by Dr Inaba and his colleagues from the University of Southern California raises critical questions concerning the safety of hemostatic resuscitation.

The authors' data suggest that the practice of transfusing ABO-compatible nonidentical plasma results in an increased incidence of ARDS and sepsis compared with ABO-identical plasma and that the incidence of these complications increases as more nonidentical plasma is given. Although the authors' arguments are very persuasive, there are several factors that need to be considered before a change in practice is implemented.

Patients who received nonidentical plasma were more injured and received more blood products than patients who received identical plasma. It is likely that many of these patients were massively transfused. To correct for these fundamental differences between the populations, the authors performed propensity matching. This resulted in the exclusion of close to 90% of the patients who received identical plasma, introducing the potential for bias.

Also, this study was performed during the period from 2000 to 2008, during which transfusion practices changed significantly. For instance, blood banks are no longer transfusing plasma from women because of the risk of transfusion-related acute lung injury.[1] As the authors state, it is possible that many of the patients who were reported to have ARDS in this study actually had transfusion-related acute lung injury. This is supported by the fact that there was no difference in mortality, intensive care unit days, or hospital length of stay between the 2 groups. Also, this same group has reported a dramatic decrease in the incidence of ARDS at their institution during the same period. It would be interesting to evaluate whether the differences in complications reported persisted throughout the study period.

Another important consideration is the effect of time from thawing of plasma to transfusion. Most blood banks will store thawed plasma up to 5 days after thawing. It is possible that the increased complication rate seen in patients who received nonidentical plasma was a result of aged thawed plasma.

The group from the University of Southern California has truly remarkable resources in that they maintain approximately 26 U of thawed plasma that is almost equally distributed between types O, A, and B, allowing them to give type-specific plasma to most of their patients. Many trauma centers maintain 4 to 6 U of thawed AB plasma for use in patients who require massive transfusion, potentially placing them at increased risk for ARDS and sepsis. While some studies have shown an increased risk of ARDS and sepsis in patients who receive hemostatic resuscitation, one has to survive to manifest these complications. I look forward to a prospective randomized trial comparing ABO-compatible nonidentical and ABO-identical plasma in patients requiring massive transfusion.

Martin A. Schreiber, MD

Author Affiliation: Division of Trauma, Critical Care and Acute Care Surgery, Oregon Health & Science University, Portland.

Correspondence: Dr Schreiber, Division of Trauma, Critical Care and Acute Care Surgery, Oregon Health & Science University, 3181 SW Sam Jackson Rd, Mail Code L611, Portland, OR 97239 (schreibm@ohsu.edu).

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