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An association of ABO non-identical platelet and cryoprecipitate transfusions with altered red cell transfusion needs in surgical patients

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Abstract

Background—Transfusion of ABO non-identical plasma, platelets and cryoprecipitate is routine practice even though adverse effects can occur.

Methods and Materials—Our hospital changed transfusion practice in 2005 and adopted a policy of providing ABO identical blood components to all patients when feasible. We retrospectively compared the transfusion requirements, length of stay, and in-hospital mortality in relation to ABO blood group in surgical patients who received platelet transfusions before and after this change to determine if it resulted in any benefit.

Results—Prior to the change in practice both group B and AB patients received more ABO non-identical platelet transfusion ($p = 0.0004$), required significantly greater numbers of red cell transfusions ($p = 0.04$), and had 50% longer hospital stays ($p = 0.039$) than group O and A patients. Following the policy change, there was a trend for fewer red cell transfusions ($p = 0.17$) and length of stay in group B and AB patients than group O or A patients. Overall, the mortality rate per red cell transfusion decreased from 15.2 per 1000 to 11.0 per 1000 ($p = 0.013$).

Conclusions—These results, **in the context of previous findings**, suggest that providing ABO identical platelets and cryoprecipitate might be associated with reduction in transfusion requirements and improve outcomes **in surgical patients**.

Keywords

Transfusion; Transfusion reaction; Platelet transfusion; ABO-identical; Transfusion requirements; Blood products ratio

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INTRODUCTION

It is common practice to transfuse ABO non-identical platelets, fresh frozen plasma (FFP) and cryoprecipitate. The guiding principle has been to minimize the risk of hemolytic transfusion reactions by transfusing only ABO antigen compatible red blood cells, and less so, by transfusing only ABO antibody compatible plasma (e.g., **avoiding minor side incompatibility**). Whereas transfusion of group O FFP (about 250 ml in volume per donor unit) to non-O patients is strictly avoided, it is widely accepted practice to transfuse group O platelets to group A or B recipients for logistic reasons [1]. Infrequent reports of fatal [2] or near fatal [3] hemolysis due to ABO non-identical (**minor incompatible**) platelet transfusions continue to appear.

Several observations [4-8] led us to question whether infusion of ABO non-identical platelets and cryoprecipitate might actually impair, rather than improve hemostasis. First, exposure of platelets to immune complexes or platelet specific antibody can interfere with platelet function *in vitro* [4,5]. Second, in cardiac surgery patients receiving similar numbers of platelet transfusions, those receiving ABO non-identical platelets require 50% more red cell transfusions and have increased mortality [6]. Finally, patients with acute leukemia receiving prophylactic platelet transfusions largely without regard to ABO blood group have serious bleeding at a rate of 15-20% [7]. In contrast, the bleeding rate in patients receiving only ABO identical platelets is below 5% [8]. Recently, transfusion of group AB plasma to O patients has been associated with a significant 10% increase in mortality in a large national cohort study [9].

In April 2005, we implemented a policy of routinely transfusing, whenever feasible, only ABO identical transfusions to all patients. To determine if this practice change impacted outcomes, we compared red cell transfusion utilization by surgical patients receiving at least one platelet transfusion before and after its implementation.

METHODS

Because of reports of worse outcomes in patients receiving ABO mismatched platelets transfusions, we implemented a change in transfusion practice in April 2005. Prior to the change, a policy for transfusion of only ABO identical FFP was already in place, whereas afterward this policy expanded to include platelets and cryoprecipitate. To evaluate the effect of this change we compared transfusion needs and outcomes before and after implementation. We chose to closely evaluate surgical patients who needed at least one platelet transfusion during or after surgery. We retrospectively reviewed transfusion service and hospital demographic records of these patients and recorded platelet transfusion, red blood cell transfusion, length of stay, and mortality during the same hospital admission **prior to discharge**. The end point of this analysis was red blood cell utilization, discharge, and/or mortality.

We analyzed the data with trauma patients included or excluded, as these patients occasionally receive small numbers of ABO non-identical red cells in many instances, through use of “universal donor group O” units prior to the establishment of their ABO blood group. As the results did not differ we report the results on all patients, including those cared for by our trauma service. The current study was conducted as an element of transfusion service quality improvement activities and thus did not require institutional human subjects review.

Statistical analysis

The statistical significance between means among blood groups was determined by use of the 2-tailed Student *t* test. Deaths in hospital for each blood group were assessed using Chi Square analysis. Deaths per total red blood cell and per total blood components transfusions were analyzed by Fisher's Exact Test. A *P* value of less than 0.05 was considered statistically significant. No adjustment for multiple comparisons was performed.

RESULTS

2002-2003—No policy restricting transfusion of ABO non-identical platelets and cryoprecipitate to surgical patients

Patient Characteristics and Transfusions—Table 1 shows the demographics, transfusion, use, and outcomes of all 335 surgical patients who received at least one platelet transfusion during this period. All, but 2 patients, received red blood cell transfusion(s) as well. As expected, patients from groups B (*n* = 39) and AB (*n* = 15) were more likely to receive ABO non-identical transfusions (**mostly group O**). Blood group O and A patients required fewer red cells transfusions as compared with blood groups B and AB patients (*p* = 0.04). Total units of pooled platelets transfused during or after surgery in all groups were not significantly different (*p* = 0.802). However, O and A patients received fewer ABO non-identical platelets than B and AB patients (*p* = 0.0004). No significant differences were seen in ABO identical platelet transfusions between all groups (*p* = 0.527).

Red cell utilization by ABO blood group is shown in the left panel of figure 1. The majority of patients (176 of 335; 52.5%) received at least one ABO non-identical transfusion of cryoprecipitate or platelets. Of these 176, 135 received at least one ABO non-identical platelet transfusion and 88 received at least one non-identical cryoprecipitate transfusion. The proportion of patients receiving only ABO identical platelets and cryoprecipitate is shown by blood group in left panel of figure 2.

Length of Stay and In-Hospital Mortality—Group O/A patients had shorter lengths of stay as compared with B/AB patients (*p* = 0.039) (Table 2). In-hospital mortality did not differ between the two group (*p* = 0.40). Mortality per red cell transfused overall was 15.2 per 1,000, with significantly higher mortality among the O/A patients (*p* = 0.021). Mortality per total components transfused was 4.8 per 1,000 and was also higher in O/A patients (*p* = 0.05) (Table 2).

2005-2006—After institution of a policy to transfuse only ABO identical platelets and cryoprecipitate to surgical patients

Patient Characteristics and Transfusions—Table 3 shows the demographics, transfusion use, and outcomes of the 410 patients who required at least one platelet transfusion in the cohort receiving exclusively ABO identical blood components in so far as was logistically possible. Red cell utilization by ABO blood group is shown in the right panel of figure 1. The proportion of patients receiving only ABO identical blood platelets and cryoprecipitate is shown in right panel of figure 2. In contrast to the period when ABO non-identical platelets and cryoprecipitate were routinely transfused, blood groups O and A surgical patients now required more red cell transfusions than blood group B or AB patients (*p* = 0.051). The pattern of hemostatic component transfusion seen in the previous cohort receiving ABO non-identical platelets and cryoprecipitate routinely is the reverse of that seen in this cohort receiving primarily ABO identical platelets and cryoprecipitate. **Group O/A** patients in this later cohort received significantly more platelets, FFP and cryoprecipitate than did B/AB patients (Table 2). When calculations were made for each of

the four blood groups separately, the results for were largely identical to the grouped trends (Table 3).

All but 15 of 410 patients in this cohort received only ABO identical platelets and cryoprecipitate, and all patients received only ABO identical FFP (Figure 2).

Length of Stay and In-Hospital Mortality—Group O/A patients receiving ABO identical blood components had lengths of stay that were not significantly different from B/AB patients ($p = 0.81$) (Table 2). Also, in-hospital mortality did not differ between the two groups ($p = 0.33$). Mortality overall was 78 deaths per 7,089 red cells transfused (11.0 per 1,000), which is 28% lower than the cohort receiving many ABO non-identical **platelet and cryoprecipitate** transfusions prior to the change (15.2 per 1,000), ($p = 0.013$). Mortality per total components transfused yielded similar results (4.8 versus 3.6 per 1000, before and after the change, respectively, $p = 0.089$). In an exploratory subgroup analysis of massively transfused patients receiving 10-30 units of red cells (approximately 1-3 blood volumes), the mortality rates before and after the change were 25 of 137 (18.2%), compared with 18 of 161 (11.8%), ($p = 0.084$).

DISCUSSION

These results confirm previous observations **from multiple investigators** that exposure to ABO non-identical platelet or plasma transfusions is associated with increased red cell transfusion needs and morbidity in surgical patients [6][9,18-21]. When platelet and cryoprecipitate transfusions were given without regard to ABO blood group in the 2002-2003 cohort, group B/AB patients, who receive more non-identical transfusions, required significantly more red cell transfusions. This is despite the fact that group B/AB patients have markedly higher levels of von Willebrand factor, and are more likely to experience thrombosis in some treatment settings [11]. In contrast, group O/A patients required more red cell, platelet, FFP and cryoprecipitate transfusions than did group B/AB patients after the change in practice. This reversal of the pattern of red cell transfusion needs after implementation of a policy of ABO identical transfusions was striking and statistically significant. This observation benefits from the power of Mendelian randomization [12] as we examined red cell use, length of stay and mortality as a function of ABO blood group, not the non-random factor of whether ABO non-identical transfusions were given. ABO blood group itself is unrelated to transfusion needs in previous studies [13,14]. The finding that red cell utilization was strongly associated with ABO blood group, which itself determines the likelihood of ABO non-identical transfusions, is more robust because of the Mendelian randomization approach. A preliminary report from our center restricted to trauma patients from this study, containing more comprehensive clinical information, demonstrated increased multi-organ failure and red cell transfusion requirements in patients receiving ABO non-identical red cells and platelets [10].

Most importantly, after implementation of a rigorous ABO identical transfusion policy, the mortality rate per red cell or blood component transfused decreased by 28% and 25%, respectively, despite a greater acuity of illness (as measured by numbers of components transfused). Transfusion dose is a powerful predictor of clinical outcomes [15], as it is a surrogate measure of clinical acuity, and may have immunomodulatory/inflammatory/pro-thrombotic effects [16]. The finding of an unfavorable association of ABO non-identical transfusions with mortality is consonant with a recent large epidemiologic study demonstrating a 10% mortality increase when ABO non-identical plasma is transfused [9]. Virtually all studies demonstrated a dose response association between number of red cells or total blood components transfused and mortality in surgical patients [17]. Thus a 28% drop in mortality rate per red cell transfused is notable and unlikely to be explained by

confounding factors such as changes in case mix. Despite increased acuity of patient illness (as measured by blood transfusion needs), surgical mortality decreased by 2% overall, and 28% on a per transfusion basis in the cohort treated with ABO identical **platelet and cryoprecipitate** transfusions. Although the overall mortality results were not statistically significant, the per transfusion decrease in mortality rate approaches significance ($p = 0.084$), and this is consistent with previous reports of decreased morbidity, bleeding and mortality with use of ABO identical components [6,9,18-20].

One potential mechanism for increased red cell transfusion needs in patients receiving ABO non-identical platelets and cryoprecipitate is that platelet and/or endothelial dysfunction due to ABO antibody or immune complexes interferes with hemostasis. Similar findings regarding bleeding and red cell transfusion needs in patients receiving ABO non-identical platelet transfusions have been described in patients with acute leukemia [18] and during cardiac surgery [6]. ABO non-identical transfusions also have been associated with increases in mortality [19] and veno-occlusive disease [20] in stem cell transplantation, as well as in all patients in a national database [9]. In a recent report, *Inaba et al.*, showed significant increase in complications rate among trauma patients who received ABO-compatible nonidentical plasma ($n = 284$) versus patients who received ABO-identical plasma ($n = 230$), (53.5% vs 40.5%, $P = .002$, respectively). These complications tend to increase in patients receiving more than 6 units of ABO-compatible plasma. Higher incidences of acute respiratory distress syndrome (ARDS) and sepsis were also observed in ABO-compatible plasma recipient group (19.4% vs 9.2%, $P = .001$, and 38.0% vs 28.9%, $P = .02$, respectively). A four-fold increase in ARDS was seen in patients receiving more than 6 units of ABO-compatible plasma. No statistically significant effect on mortality was detected between the groups (35.2% vs 33.5%, $P = .66$). [21]

We speculate that transfusion of ABO non-identical platelets, FFP and/or cryoprecipitate may exacerbate bleeding, hemolysis (**minor side incompatible transfusions only**), and red cell transfusion needs, rather than correcting defects in hemostasis. Thus, a policy of transfusing only ABO identical blood components could reduce red cell transfusion needs and mortality in surgical patients. The use of ABO identical transfusions is primarily a logistical problem, but the cost and technical issues are comparatively minor. ABO non-identical **minor side incompatible** plasma, cryoprecipitate and platelet transfusions are well known to cause serious [3] or even fatal [2] hemolysis in rare instances. Developing procedures so that only ABO identical transfusions are administered, except in emergencies, has much to recommend it as a standard of practice, given findings previously reported by multiple groups, and these current data. We suggest that physicians carefully consider in each case the benefit to risk ratio of giving ABO non-identical transfusions versus withholding transfusion until ABO identical components are available.

The retrospective analysis of this data is one of the serious limitations in this study. The use of historical controls is another critical limitation. In addition, patients' clinical condition before surgery and the presence of other existing risk factors for bleeding and mortality were not evaluated. Nonetheless, the altered pattern of red cell utilization according to ABO blood group observed is an indication of a potentially causal association, taken in the context of previously published work by several groups. [6,9,18-21] A multi-center prospective randomized trial is needed to definitively evaluate these findings .

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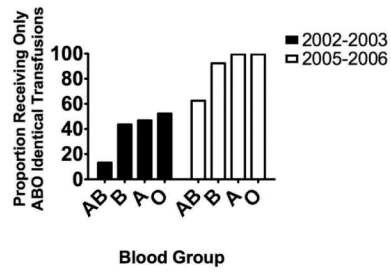


Figure 1.

The mean \pm SD number of red cell transfusions is shown by ABO blood group of the patient, grouped by the time period and ABO transfusion policy applicable to those patients. N = 15 (AB), 39 (B), 128 (A), 153 (O) for 2002-2003 and 24(AB), 52 (B), 158 (A), 175 (O) for 2005-2006. The overall ANOVA for the 2002-2003 data is significant ($p=0.040$). Employing Fisher's PLSD post-hoc test, the differences between blood groups A and B ($p=0.0047$) and O and B ($p=0.016$) are statistically significant. The overall ANOVA for the 2005-2006 data is not significant ($p=0.19$).

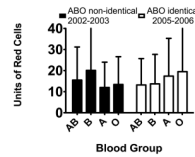


Figure 2.

The proportion of patients receiving only ABO identical transfusions is shown by blood group for the two time periods of the study (see Figure 1 for the N in each group, and here as well). For both periods, the proportion of patients in blood group AB who received only ABO identical components is statistically significantly smaller than for the other blood groups ($p = 0.034$ for 2002-2003; <0.0001 for 2005-2006 by Chi square). However the ratio of patients receiving only ABO identical transfusions in blood groups B, A and O to patients receiving only ABO identical transfusions in blood group AB is 3.3-4.0 fold in 2002-2003 as compared with 1.5 fold in 2005-2006.

Table 1

Characteristics of Surgical Patients by ABO Group from 2002 to 2003

Blood Group	O Mean± SD (n=153)	A Mean± SD (n=128)	B Mean± SD (n=39)	AB Mean± SD (n=15)	P value*
Age	59.2 ± 1.6	59.4 ± 1.7	53.8 ± 3.1	54.0 ± 5.0	0.318
Gender (M/F)	89 / 64	89 / 39	28 / 11	3 / 12	0.083
Red Cells Transfused (Units)	13.4 ± 1.2	12.0 ± 1.4	20.1 ± 2.5	15.5 ± 4.0	0.04
Total Platelets Transfused (Units)	13.8 ± 1.5	14.7 ± 1.6	17.1 ± 3.0	13.9 ± 4.8	0.802
ABO Non-identical Platelets Transfused (Units)	2.7 ± 0.6	4.0 ± 0.6	6.9 ± 1.2	9.2 ± 1.9	0.0004
ABO Identical Platelets Transfused (Units)	11.1 ± 1.3	10.6 ± 1.4	10.2 ± 2.5	4.7 ± 4.1	0.527
FFP Transfused (Units)	10.0 ± 1.3	6.9 ± 1.4	11.0 ± 2.6	5.1 ± 4.2	0.256
Total Cryoprecipitate Transfused (Units)	5.2 ± 0.7	4.4 ± 0.7	5.6 ± 1.3	3.9 ± 2.1	0.754
ABO Non-identical Cryo-precipitate Transfused (Units)	2.4 ± 0.4	2.2 ± 0.5	4.4 ± 0.9	3.6 ± 1.4	0.129
Post-Op Length of Stay (Days)	23.4 ± 3.0	20.3 ± 3.3	29.1 ± 6.0	45.1 ± 9.7	0.083
Deaths in Hospital	30 (20%)	31 (24%)	5 (13%)	4 (27%)	0.39
Death/1,000 Red Cell	15	20	6.4	17	0.07
Death/1,000 Components	4.5	6	2.3	5.7	0.089

*. Categorical data were compared by Chi square or Fisher's exact test as appropriate and continuous data by two-sided t tests.

Table 2
 Characteristics of Surgical Patients by O/A and B/AB groups for both periods (2002-2003 and 2005-2006)

	2002-2003 (n=335)			2005-2006 (n=410)		
	Blood Groups O and A	Blood Groups B and AB	P value*	Blood Groups O and A	Blood Groups B and AB	P value*
	Mean± SD (n=281)	Mean± SD (n=54)		Mean ± SD (n=334)	Mean± SD (n=76)	
Age	59.3 ± 19.0	53.9 ± 20.4	0.06	55.0 ± 20.5	56.4 ± 20.8	0.59
Gender (M/F)	178 / 103	40 / 14	0.13	211 / 122	44 / 32	0.79
Red Cells Transfused (Units)	12.8 ± 12.7	18.8 ± 25.1	0.0086	18.5 ± 20.9	13.6 ± 13.5	0.051
Total Platelets Transfused (Units)	14.2 ± 18.9	16.2 ± 16.1	0.47	15.6 ± 25.1	9.5 ± 7.7	0.036
ABO Non-identical Platelets Transfused (Units)	3.3 ± 6.2	7.5 ± 11	0.0001	0.0 ± 0.0	1.0 ± 2.8	0.0001
ABO Identical Platelets Transfused (Units)	11 ± 16	9 ± 12	0.35	15.6 ± 25.1	9.5 ± 7.7	0.036
FFP Transfused (Units)	8.6 ± 16.9	9.4 ± 13.5	0.75	13.3 ± 19.3	7.9 ± 9.5	0.017
Total Cryoprecipitate Transfused (Units)	6.0 ± 8.0	8.0 ± 9.2	0.79	7.3 ± 11.9	4.3 ± 7.7	0.04
ABO Non-identical Cryo-precipitate Transfused (Units)	2.3 ± 3.1	4.2 ± 5.1	0.02	0.06 ± 0.77	0.53 ± 3.6	0.03
Post-Op Length of Stay (Days)	22.0 ± 32.1	33.5 ± 57.8	0.039	22.8 ± 33.6	23.8 ± 33.8	0.81
Deaths in Hospital	61 (22%)	9 (17%)	0.40	66 (20%)	12 (16%)	0.33
Death/1,000 Red Cells	17	9	0.021	11	11.6	0.12
Death/1,000 Components	5.3	3.3	0.05	3.6	4.4	0.11

* Categorical data were compared by Chi square or Fisher's exact test as appropriate and continuous data by two-sided t tests.

Table 3

Characteristics of Surgical Patients by ABO Group from 2005 to 2006

Blood Group	O	A	B	AB	P value*
	Mean± SD (n=175)	Mean± SD (n=159)	Mean± SD (n=52)	Mean± SD (n=24)	
Age	53.5 ± 1.6	56.3 ± 1.6	58.0 ± 2.9	52.8 ± 4.2	0.414
Gender (M/F)	110 / 65	102 / 57	30 / 22	14 / 10	0.831
Red Cells Transfused (Units)	19.5 ± 1.5	16.8 ± 1.5	13.7 ± 2.7	13.2 ± 4.0	0.17
Total Platelets Transfused (Units)	17.4 ± 1.7	13.2 ± 1.8	9.2 ± 3.2	10.0 ± 4.7	0.068
ABO Non-identical Platelets Transfused (Units)	0.0 ± 0.1	0.0 ± 0.1	0.4 ± 0.2	2.5 ± 0.2	0.0001
ABO Identical Platelets Transfused (Units)	17.4 ± 1.7	13.2 ± 1.8	8.8 ± 3.2	7.5 ± 4.6	0.033
FFP Transfused (Units)	14.3 ± 1.4	12.2 ± 1.4	8.6 ± 2.5	6.4 ± 3.7	0.067
Total Cryoprecipitate Transfused (Units)	7.8 ± 0.9	6.7 ± 0.9	5.0 ± 1.6	2.9 ± 2.3	0.14
ABO Non-identical Cryo-precipitate Transfused (Units)	0.06 ± 0.1	0.1 ± 0.1	0.0 ± 0.2	1.7 ± 0.3	0.0001
Post-Op Length of Stay (Days)	21.8 ± 2.1	19.5 ± 2.2	23.9 ± 3.9	23.4 ± 5.7	0.736
Deaths in Hospital	40 (23%)	26 (16%)	9 (17%)	3 (13%)	0.36
Death/1,000 Red Cells	11.8	9.8	12.6	9.5	0.07
Death/1,000 Components	3.7	3	4.5	3.4	0.089

*. Categorical data were compared by Chi square or Fisher's exact test as appropriate and continuous data by two-sided t tests.