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Fresh frozen plasma (FFP) use during massive blood transfusion in trauma resuscitation

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ABSTRACT

Introduction: Recent retrospective studies have found high fresh frozen plasma (FFP) to packed red blood cell (PRBC) ratios during trauma resuscitation to be associated with improved mortality. Whilst this association may be related to a mortality bias present in these studies, there has been an overall tendency towards a 1:1 FFP:PRBC ratio in massive transfusion guidelines worldwide. The aim of this study was to retrospectively review the administration of FFP in patients undergoing massive transfusion during trauma resuscitation, to add to the evidence base for massive transfusion guidelines.
Materials and methods: Multi-trauma patients who were administered blood transfusions of 5 units or more of packed red blood cells (PRBCs) in the first 4 h were included in this study. Mortality was the primary endpoint with length of hospital stay, ICU hours and mechanically ventilated hours secondary endpoints.
Results: There were 331 patients included in this study with a median Injury Severity Score (ISS) of 36 (25–50) and a mortality of 29.9%. There was little change in the ratio of FFP:PRBC transfused per patient from 2005 to 2008. A low FFP:PRBC ratio in the first 4 h of resuscitation, older age, low initial GCS and coagulopathy on presentation were significant independent factors associated with mortality. When deaths in the first 24 h were excluded, the FFP:PRBC ratio had no association with mortality.
Discussion: This study has shown increased initial survival in association with higher FFP:PRBC ratios during massive transfusion in a population with a high proportion of blunt injuries. The association is difficult to interpret because of an inherent survival bias. The optimal ratio of FFP:PRBC during massive transfusion may be different to 1:1 and further prospective research is required. There is now an increasing need for well designed randomised controlled trials to determine the best FFP:PRBC ratio for the resuscitation of blunt multi-trauma patients.

Introduction

Uncontrolled haemorrhage is a leading cause of early mortality and remains a major challenge in trauma resuscitation.[15,17] Inadequate evidence has hampered attempts to establish transfusion guidelines in major trauma. The sub-group of patients requiring massive transfusions during trauma resuscitation depletes even well resourced centres of blood products. Because of the high mortality rate there has been considerable interest worldwide in establishing massive transfusion guidelines for trauma resuscitation.[12,13] An important component of massive transfusion guidelines is the amount of fresh frozen plasma (FFP) transfused.

Since military studies were published suggesting improved outcomes,[2,6] there have been multiple recent retrospective reviews on the benefits of high volumes of FFP transfusion.[3–5,7,8,11,18–20,22] A change of practice from the traditional administration of 1 unit of FFP for 4 units of packed red blood cells (PRBCs) to a 1:1 ratio has been advocated, but the optimal ratio during resuscitation has also been questioned.[9,18] Most of these studies did not focus on trauma reception and resuscitation. Furthermore, our civilian trauma epidemiology differs from the military

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experience and most international studies, with a relatively low percentage of patients with penetrating and blast injuries.[16]

The aims of this study were to retrospectively review the administration of FFP in patients undergoing massive transfusion during trauma resuscitation in a Level 1 civilian trauma centre. Current transfusion practice was examined to study any change in transfusion practice in light of the abovementioned literature. This was performed to add to the evidence base for the development of massive transfusion guidelines and identify areas requiring further research and practice change.

Materials and methods

Setting

The state of Victoria, Australia has one paediatric and two adult Major Trauma Services (MTS) located within metropolitan Melbourne. Major trauma triage guidelines are in place and intended to increase the proportion of major trauma patients treated at a MTS. Ambulance services triage adult major trauma patients and suspected adult major trauma patients directly to an adult MTS when the travel time is less than 30 min. There are no current provisions for the administration of blood products during transit.

The Alfred Hospital, Melbourne, Victoria is the largest adult MTS in Australia. There are more than 1930 trauma team activations per year. In 2008, 1007 patients had an Injury Severity Score[1] of greater than 15 (unpublished data, The Alfred Trauma Registry). In October 2008, a massive transfusion guideline had been drafted which commences resuscitation with 4 units of PRBCs and 4 units (600 mL) of FFP (1:1 ratio). This guideline had not been audited or formalised during the study period.

Patients

All trauma patients who presented to The Alfred Emergency & Trauma Centre between July 2004 and August 2008 and received a massive transfusion were included in this study. Patients transferred from other centres were excluded. We defined massive transfusions as the infusion of 5 units or more of PRBCs in the first 4 h to highlight transfusion practice in the initial trauma resuscitation phase.[14] The volumes of FFP and PRBC transfused to each patient at 4 h post-presentation were used to determine a FFP:PRBC ratio. As this was a continuous variable, these were sub-grouped into a range of ratios which best reflected the clinical practice of using whole number ratios. For example, the range of ratios across 1:2 (>1:2.5 to 1:1.5) was considered to reflect a transfusion practice of 1:2.

Study design

Patients who received blood transfusions were identified from the blood bank database and their records retrospectively reviewed. Data on initial vital signs, injuries and outcome were collected from The Alfred Hospital trauma database. All body regions injured were included, irrespective of their Injury Severity Scores. Pathology results were obtained from The Alfred pathology service. Demographic features, injuries and initial signs as listed in Tables 1 and 2 were analysed and entered into multivariate models. Mortality was the primary endpoint, whilst length of hospital stay, length of Intensive Care Unit (ICU) stay and mechanically ventilated hours were secondary endpoints. A sub-group analysis of patients surviving beyond the initial 24 h of hospital presentation was performed to minimise the impact of patients in whom resuscitation may have been ceased due to futility.

Table 1
Demographics, vital signs, investigations and management with univariate association with mortality.

		OR	95% CI	*p*
Demographics				
Age (years)	42.1 ± 19.3	1.01	1.00–1.02	0.045
Blunt trauma, *n* (%)	286 (86.4)	2.57	1.11–5.98	0.028
ISS	36 (25–50)	1.05	1.03–1.07	<0.001
Vital signs on presentation				
GCS	13 (5–15)	0.80	0.76–0.85	<0.001
SBP (mmHg)	112.1 ± 38.2	0.99	0.98–0.99	0.0.33
HR (b/min)	111.0 ± 28.5	0.99	0.98–0.99	0.042
RR (b/min)	20.0 ± 7.8	0.97	0.94–1.01	0.094
Temperature (°C)	34.8 ± 1.5	0.61	0.52–0.72	<0.001
Investigations on presentation				
FAST +ve, *n* (%)	125 (37.8)	1.1	0.68–1.79	0.690
Hb (g/dL)	101.7 ± 27.9	0.98	0.97–0.99	<0.001
Plat ($\times 10^9 L^{-1}$)	209.7 ± 103.5	0.99	0.98–0.99	<0.001
INR	2.1 ± 1.8	2.38	1.78–3.20	<0.001
APTT (s)	77.5 ± 67.8	1.28	0.77–2.13	0.333
Fibrinogen (g/L)	1.8 ± 2.4	0.62	0.45–0.87	0.005
pH	7.18 ± 0.21	0.02	0.01–0.07	<0.001
HCO_3^- (mmol/L)	19.1 ± 4.7	0.88	0.83–0.93	<0.001
Lactate (mmol/L)	4.9 ± 3.8	1.16	1.09–1.24	<0.001
Management				
Urgent surgery, *n* (%)	244 (73.7)	0.38	0.22–0.63	<0.001
PRBC transfused in first 4 h (units)	12 (8–23)	1.02	1.01–1.04	<0.001
FFP transfused in first 4 h (units)	6 (3–12)	1.03	1.01–1.06	0.016
FFP:blood ratio	0.43 ± 0.33	0.89	0.44–1.82	0.756

This study was approved by the Alfred Hospital Research and Ethics Committee.

Statistical analysis

All analysis was performed using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA). Endpoints were log transformed if not normally distributed. Univariate and multivariate analysis for the mortality was determined using logistic regression whilst other endpoints were assessed using linear and multiple linear regression. Multivariate models were developed using a stepwise selection procedure and a backwards elimination procedure before undergoing assessment for clinical and biological plausibility. Results from logistic regression models are reported as odds ratios with 95% confidence intervals, whilst results from the linear regression are reported as parameter estimates (PE) with standard errors (SE). Survival between different FFP:PRBC ratios was estimated by the Kaplan–Meier method and the curves were analysed by use of the log-rank test. A two-sided *p*-value of 0.05 was considered to be statistically significant. Continuous data were reported as mean ± standard deviation. Ordinal data were reported as median ± interquartile range. The *t*-test was used to test difference between means, whilst the Mann–Whitney *U* test was used to test differences between ranked ordinal data.

Results

There were 331 patients included in this study from January 2005 to August 2008. The transfusion practice of PRBC and FFP in the first 4 h over this time is presented in Fig. 1. Demographics, ED vital signs, initial investigations and management are presented in Table 1 together with univariate associations with mortality. Head injuries were present in 226 (68.3%) of patients and were significantly associated with mortality (OR 3.9, CI: 2.9–7.3; $p < 0.001$). There were no other body regions injured significantly associated with mortality. Demographics, clinical signs and investigations in