Short report

Ionised calcium levels in major trauma patients who received blood in the Emergency Department

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ABSTRACT

Background Exsanguination and coagulopathy remain one of the leading causes of preventable trauma related death. Low ionised calcium levels have been associated with hypotension and increased mortality and may inhibit clot formation. Blood product contains citrate that acts as a chelating agent. We hypothesised that trauma patients who have bled are at risk of hypocalcaemia and that receiving any amount of blood product can exacerbate this state.

Methods A retrospective cohort analysis was performed on all trauma patients who had received early blood product in the ED of a single urban major trauma centre in the UK between 2013 and 2014. Ionised calcium levels were taken from venous blood gases from before and after blood product had been transfused.

Results The study included 55 patients; 36 male (65%), age 33 (16–92) years, median injury severity score (ISS) 24 (4–50), units of blood product received 2 (1–16), overall mortality 18%. Fifty-five per cent patients were hypocalcaemic on arrival, 89% patients were hypocalcaemic after receiving any amount of blood product. There was a statistically significant difference in ionised calcium levels after receiving blood product, pretransfusion 1.11 mmol/L (95% CI 1.09 to 1.14), post-transfusion 0.98 mmol/L (95% CI 0.93 to 1.02) (p<0.001). A fall in calcium was seen after receiving just one unit and the more units of blood product received the greater the fall seen.

Conclusions Trauma patients that have sustained blood loss are at risk of hypocalcaemia. Ionised calcium levels fall significantly further even after receiving a small amount of blood product. Prompt recognition and early targeted treatment is needed from arrival.

BACKGROUND

Calcium is critical to the bleeding trauma patient. It plays a significant role in many cellular processes and is a vital cofactor to several components of the clotting cascade. Low calcium levels cause many pathophysiological effects detrimental to the trauma patient, primarily coagulopathy and hypotension through decreased cardiac contractility and decreased vasomotor tone.[1–3] Citrate phosphate dextrose adenine is used in many blood components to chelate calcium.[1 4] Hypocalcaemia is a common finding in critically ill patients.[2] Previous studies in trauma have shown that admission hypocalcaemia is associated with hypotension and significantly increased mortality.[2 5]

Haemorrhage remains the leading cause of trauma related death accounting for around 40% of trauma deaths in the UK.[1] Recent advances in trauma care have focused on haemostatic control and, understanding and treatment of coagulopathy.[6 7] Early aggressive recognition and treatment of haemorrhage and coagulopathy is key to improving survival.[8]

Blood product is increasingly being given much earlier, with great success, to aggressively resuscitate the severely injured trauma patient.[9] We aimed to investigate the effect that receiving early blood product had on ionised calcium levels and postulate that calcium correction should be considered much earlier during the resuscitation of trauma patients, even after just a small transfusion.

METHODS

A retrospective cohort analysis was performed from January 2013 to January 2014. The Trauma Audit Research Network (TARN) was used to identify all major trauma patients who received blood product in the ED of a London Major Trauma Centre. All patients, adult and paediatric, were included. Blood product was primarily packed red blood cells but also included fresh frozen plasma and cryoprecipitate. Patients with no documented blood product administration time, no documented ionised calcium level or no ionised calcium level before receiving blood in the ED were excluded (figure 1). Some patients received blood in the prehospital environment as well as in the ED and these were analysed separately. Electronic medical records were interrogated to review ED documentation using Symphony (V.2.29.3 Ascribe). Precise timings on blood product administration were taken from these records. Ionised calcium levels were taken from venous blood gas results that had been measured as part of routine care. Where these had not been documented they were collected from the internal memory of the blood gas machine. Hypocalcaemia was defined as ionised calcium of <1.1 mmol/L.

RESULTS

Of the 885 major trauma patients seen during the study period, 87 were identified by TARN as having received blood product in the ED. Twelve were excluded because blood product timing was not documented or there was no ionised calcium level obtained. Eight patients received blood in the prehospital environment and 12 patients received blood product in the ED prior to initial calcium level being taken (figure 1). This left a cohort of 55 patients who received transfusion in the ED and for whom data was available. Thirty-seven of these had calcium levels measured before and after receiving blood product in the ED. Demographics and results are shown in table 1.

Fifty-five per cent (30/55) of patients were hypocalcaemic on arrival before receiving blood rising

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Figure 1 Consort diagram. TARN, Trauma Audit Research Network.
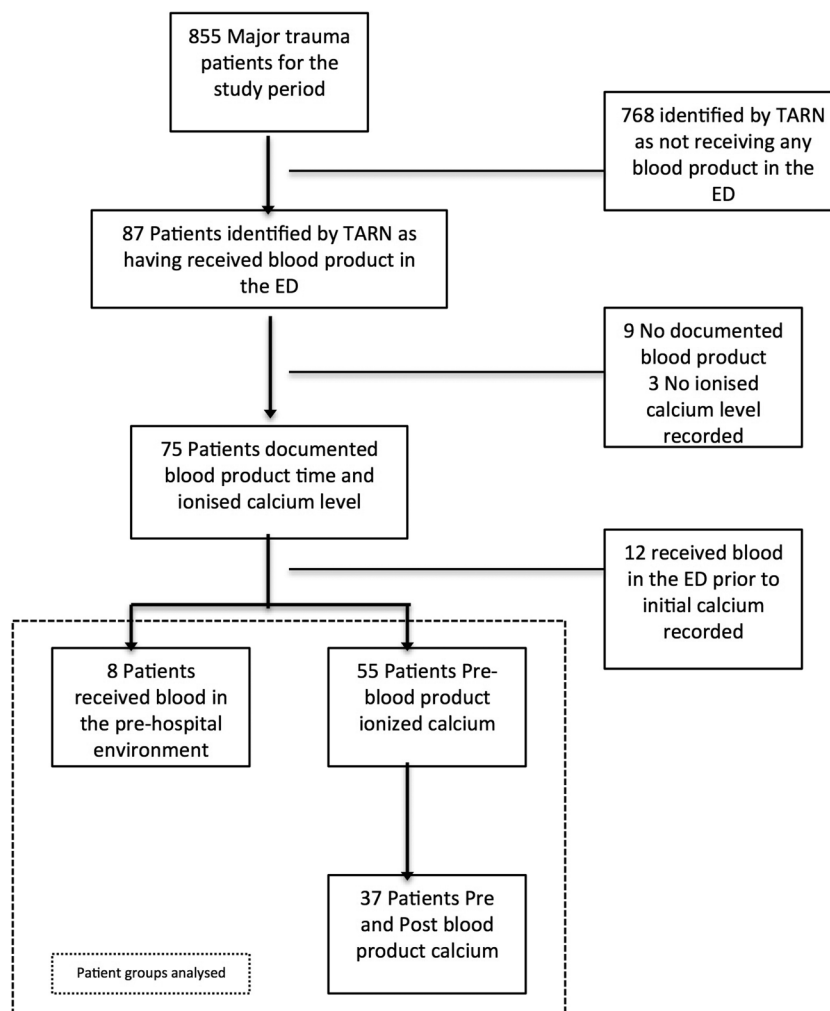
to 89% (33/37) after receiving any amount of blood product. Ionised calcium levels fell in 95% (35/37) regardless of how many units of blood product had been received. A fall was seen after receiving just one unit and the more the units received the greater the fall (figure 2). The initial ionised calcium level was 1.11 mmol/L (95% CI 1.09 to 1.14) and the post-ED blood product transfusion level 0.98 (95% CI 0.93 to 1.02) (p<0.001). Ionised calcium levels were significantly lower after receiving blood product (figure 3A).

The majority of patients 48% (18/37) received a two-unit blood product transfusion between calcium measurements and we demonstrated a statistically significant difference (p<0.001) after this small amount (figure 3B). Patients received a range of 1–16 units prior to their calcium being measured again (Median 2) and 13 patients subsequently went on to receive a massive transfusion. Two patients were documented to have received calcium in the ED, one of which was after the repeat calcium reading and the other as part of a massive transfusion; both were included in the data set.

Eight patients received prehospital blood product and these were analysed separately. Of these, 88% (7/8) were hypocalcaemic on arrival and calcium fell further for all for which there was subsequent data after further blood product transfusion (6/8). The initial calcium and post-ED blood product calcium were lower than the average for the cohort but not significantly so (table 2).

DISCUSSION

This paper demonstrates that trauma patients are at significant risk of being hypocalcaemic and adds that receiving any amount of blood product worsens this state.

Evidence in recent literature suggests that an ionised calcium of <1 significantly increases patient mortality

Table 1 Demographics and results

	Patients with pretransfusion ionised calcium level (n=55)	Patients also with post-transfusion ionised calcium level (n=37)
Male	36 (65%)	27 (73%)
Age range (median)	16–92 (33)	16–89 (33)
ISS range (median)	4–50 (24)	5–50 (25)
30 day mortality	10 (18%)	5 (14%)
Penetrating/blunt mechanism	10/45 (18%/82%)	7/30 (19%/81%)
%Hypocalcaemic on arrival	30/55 (55%)	20/37 (54%)
%Hypocalcaemic post ED transfusion	–	33/37 (89%)
Mean calcium level on arrival (mmol/L)	1.12	1.11
Mean calcium level post ED transfusion (mmol/L)	–	0.98

Figure 2 Change in ionised calcium compared with units of blood product received.
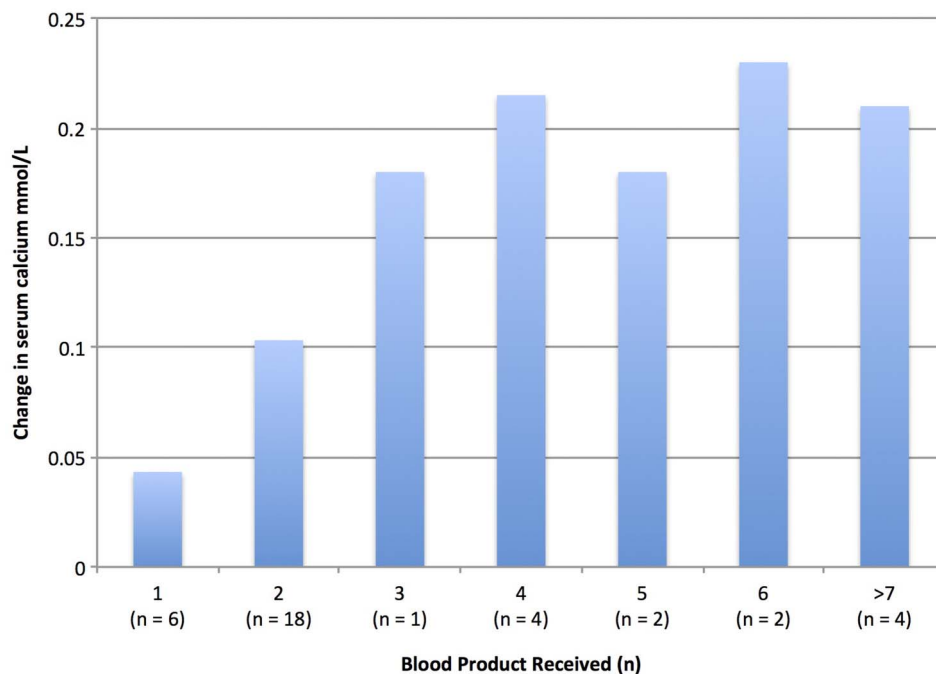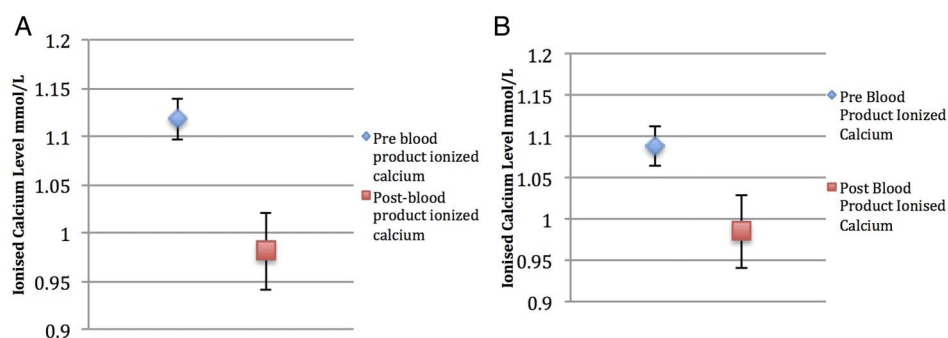

Figure 3 (A) Mean ionised calcium levels and 95% CIs. (B) Mean ionised calcium levels and 95% CIs in patients after receiving 2 units of blood product.

regardless of age and ISS[5] and calcium <0.88 increases mortality threefold.[10]

The current practice is to maintain calcium levels >1 mmol/L.[8] Many massive transfusion protocols advocate the use of calcium, however, it is not routinely considered in trauma patients before they receive blood, or if they have not yet met the massive transfusion criteria. While patients in our study may well have gone on to subsequently require further blood product, very few actually met the massive transfusion criteria while in the ED.

The majority of patients received a two-unit blood product transfusion (n=18) and a statistically significant difference in ionised calcium level were seen after receiving this small amount (figure 3B). This may have a clinical as well as statistical significance. With over half of the patients being already hypocalcaemic on arrival this raises the question of whether calcium correction should be considered at a much earlier stage in the management of the bleeding trauma patient.

Table 2 Demographics and results of patients that received prehospital blood

	Received blood product prehospital (n=8)
Male	6 (75%)
Age range (median)	23–50 (28)
ISS range (median)	14–50 (29)
30 day mortality	1 (12.5%)
Penetrating/blunt mechanism	2/6 (25%/75%)
%Hypocalcaemic on arrival	7/8 (88%)
%Hypocalcaemic post ED transfusion	6/6 (100%)
Mean calcium level on arrival (mmol/L)	1.07
Mean calcium level post ED transfusion (mmol/L)	0.89

LIMITATIONS

This paper was a retrospective, single centre observational study and was therefore reliant on good documentation and venous blood sampling pre and post blood product administration; this limited the data set. Possible confounding factors include pH, which may affect the availability of ionised calcium levels. It is possible that there is a dilutional element to the fall in calcium, however, evidence in the literature found no significant correlation between ionised calcium and amount of infused crystalloid.[11] Future research should look at whether correcting calcium early improves mortality.

CONCLUSION

Exsanguination and coagulopathy remain one of the leading causes of potentially preventable trauma related death. Calcium plays a critical role to many processes and hypocalcaemia is associated with increased mortality. With increasing early blood product use, trauma victims being at risk of hypocalcaemia and receiving any amount of blood product further worsening this state, prompt recognition of hypocalcaemia and early targeted therapy is needed from arrival.

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Contributors All authors contributed substantially to the creation of this paper.

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