Critical care in emergency department: massive haemorrhage in trauma

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Accepted 14 January 2012
Published Online First
10 February 2012

ABSTRACT

Inadequate resuscitation of major haemorrhage is an important cause of avoidable death in severely injured patients. Early recognition of blood loss, control of bleeding and restoration of circulating volume are critical to the management of trauma shock, and transfusion of blood components is a key intervention. Vital signs may be inadequate to determine the need for transfusion, and resuscitation regimens targeting vital signs may be harmful in the context of uncontrolled bleeding. This article addresses current concepts in haemostatic resuscitation. Recent guidelines on the diagnosis and treatment of coagulopathy in major trauma, and the role of component and adjuvant therapies, are considered. Finally, the potential role of thromboelastography and rotational thromboelastometry are discussed.

INTRODUCTION

Haemorrhage is a common cause of death within 6 h of traumatic injury and is responsible for 30–40% of all trauma deaths. The majority of preventable deaths occur from unrecognised and untreated haemorrhage, particularly within the abdominal cavity, making it the most important reversible cause of death in the trauma population.[1] A Canadian study reviewed 558 consecutive trauma fatalities and found that 16% of haemorrhagic deaths could have been prevented by earlier identification and treatment of blood loss from abdominal organs and the bony pelvis.[2] Treatment should focus on early recognition of blood loss, rapid control of the source of bleeding and restoration of circulating blood volume. Allogeneic blood transfusion (ABT) plays an important role in trauma resuscitation, and there have been recent developments in the safe and effective use of blood products. The contemporary approach to the management of trauma shock is discussed in the following paragraphs.

ILLUSTRATIVE CASE REPORT

A 62-year-old pedestrian is struck by a car that was travelling at an estimated 40 mph. He is brought to the emergency department (ED) by paramedics and receives initial assessment on a long spine board in the resuscitation room. He is awake and talking but looks pale. He has bruising around the right lower chest and right hypochondrium. His respiratory rate is 32/min, oxygen saturation 93% on high flow oxygen via a reservoir mask. Heart rate is 140/min and blood pressure 80/55 mm Hg. There is no open wound, and no clinical signs of pneumothorax or haemothorax. Two large bore cannulae are sited in the anterior cubital fossae. Blood samples are sent for full blood count, cross match, clotting screen (including fibrinogen), glucose, urea and electrolytes, and venous gases. Two litres of Hartmann's solution are in progress. Blood pressure responds only transiently and the patient receives 2 units of group O-RhD negative blood from the ED blood refrigerator. The patient receives tranexamic acid 1 g over 10 min by slow intravenous injection followed by 1 g over 8 h by intravenous infusion.

Supine chest film shows hazy right lower zone shadowing, while the pelvis radiograph is unremarkable. There is free fluid in Morrison's pouch on focused assessment with sonography (FAST) scan, and a whole body CT scan shows a complex laceration of the liver with significant haemoperitoneum. The surgical team is called to assess the patient for emergency laparotomy.

Questions

i. How are volume status and need for blood transfusion assessed in a bleeding patient?
ii. Define massive haemorrhage.
iii. What is meant by the term acute coagulopathy of trauma shock?

Discussion

i. Vital signs are routinely recorded but are not sufficiently sensitive or specific to allow an accurate determination of hypovolaemia in trauma shock. Hypotension is a late sign. A retrospective review of 115 000 patients from the US National Trauma Data Bank found evidence of inadequate tissue oxygenation in many patients, despite a normal blood pressure. By the time hypotension occurred, the base deficit was >20, and mortality was 65%.[3]

Various methods are available for measuring the state of the circulation, providing global measures of preload, cardiac output, organ perfusion and tissue oxygenation. The best method depends on the clinical setting; in the prehospital arena one may have to rely on pulse, blood pressure and capillary return time. In the ED and operating theatre, there is access to monitored data, fluid balance charts, and arterial and venous blood gases. In the ICU, the clinician may use echocardiographic and ultrasound techniques, as well as invasive monitoring, allowing measurement of stroke volume (and variation), cardiac index, mixed venous and central venous oxygen saturation and the response of these parameters to a fluid challenge.

One must take account of the injury mechanism and the anatomical injuries, providing an

indication of potential blood loss. In the modern ED setting, patients with multiple injuries receive FAST and, increasingly, a whole body CT scan. The pan scan may identify clinically significant injuries in up to 20% of trauma patients who may have no other sign of the index injury.[4]

Base deficit from an arterial or venous blood gas correlates well with shock severity and mortality risk in trauma patients, while lactate clearance, rather than initial lactate, predicts outcome.[5] International consensus guidelines on shock management were published in 2007. They emphasise the importance of the clinical assessment and vital signs in shock, suggesting that an arterial line is more reliable than non-invasive blood pressure. They recommend a fluid challenge, using crystalloid or colloid and targeting central venous pressure, to assess intravascular volume. Regular monitoring of mixed venous or central venous oxygen saturation, as well as pH, base excess and lactate are also recommended.[6] European guidelines on the management of bleeding following major trauma advise crystalloid or colloid for initial resuscitation, targeting a systolic blood pressure of 80–100 mm Hg, and blood transfusion to a target haemoglobin (Hb) of 7–9 g/dl.[7]

ii. Normal blood volume is approximately 70 ml/kg in the adult. Massive blood loss has been variously defined as loss of 50% blood volume within 3 h, blood loss at a rate of 150 ml/min or 1.5 ml/kg/min for more than 20 min. More recently the term critical bleeding has been coined to describe life threatening haemorrhage that is likely to result in the need for massive transfusion; half of one blood volume (5 units) in 4 h, or more than one blood volume in 24 h in adults. Massive transfusion is relatively uncommon in UK trauma practice, and is associated with a very high mortality.

iii. A quarter of severely injured patients are coagulopathic at initial assessment due to a process called acute coagulopathy of trauma shock. The endothelium is central to the response. Exsanguination and tissue injury lead to thrombomodulin release which sequesters thrombin and leads to widespread generation of activated protein C. This inactivates factors V and VIIIa causing systemic anticoagulation. The endothelium also releases tissue plasminogen activator which lyses fibrin. These anticoagulant and fibrinolytic pathways promote further bleeding, exacerbated by excessive volume resuscitation which dilutes clotting factors as well as increasing wall tension and extravasation.[8] The lethal interaction of trauma shock comprises hypothermia, coagulopathy and acidosis. Untreated, the condition rapidly leads to death. Recognition of these mechanisms has prompted a re-evaluation of resuscitation strategies in trauma:

   a. *Balanced resuscitation* is the administration of controlled volumes of fluid, sufficient to maintain organ perfusion, without disrupting clot and worsening extravasation. This approach is recommended in the current Advanced Trauma Life Support programme.[9]

   b. *Damage control resuscitation (DCR)* is discussed below.

CASE PROGRESSION

After stabilisation in the ED, the patient is transferred to the operating theatre. At laparotomy he is found to have numerous mesenteric tears, diffuse thickening and oedema of the small bowel wall and a complex liver laceration which the surgeon manages with packing. The patient receives massive haemorrhage packs 1 and 2 in theatre. He is then transferred to the intensive care unit, intubated and ventilated, and with an open abdomen covered with a Bogota bag. He receives continued resuscitation during the next 24 h, including rewarming and correction of coagulopathy and acidosis.

Questions

i. Distinguish DCR, haemostatic resuscitation and permissive hypotension.

ii. Discuss the available adjuncts to DCR.

iii. What are the challenges for the blood bank in responding to massive haemorrhage?

Discussion

i. Management of massive haemorrhage should focus on early recognition of blood loss, rapid control of the source of bleeding and restoration of circulating blood volume. Overly aggressive volume resuscitation can cause serious problems, including exacerbation of bleeding due to clot disruption, haemodilution, thrombocytopenia and coagulopathy, as well as later complications such as peripheral oedema, compartment syndrome, acute lung injury and immunomodulation leading to multiple organ failure.

DCR involves targeting a lower than normal blood pressure, haemostatic transfusion of red blood cells (RBC), fresh frozen plasma (FFP) and platelets, appropriate use of coagulation factors such as fibrinogen containing products, and abbreviated surgery to arrest bleeding and clear contamination. Permissive hypotension and minimal volume resuscitation are strategies in which a systolic blood pressure of 80–100 mm Hg is accepted until definitive control of bleeding. It is contraindicated in patients with traumatic brain injury because reduced perfusion pressure can worsen the brain injury.

The contemporary approach to trauma shock resuscitation involves the use of FFP earlier and in greater quantity than previously recommended in order to treat the coagulopathy of trauma. This is haemostatic resuscitation, and new guidelines on massive haemorrhage management reflect this approach.[7] The evidence comes mainly from the military; studies showing improved mortality when the ratio of FFP to RBC approaches 1:1.[10] A study of 1250 patients from a civilian German Trauma Registry showed that a ratio of at least 1 pack of FFP to 2 units of RBC conferred a survival advantage in brain injured and non-brain injured adults.[11] A number of retrospective studies have shown improved outcomes with high FFP to RBC ratios. Three studies also looked at platelets, and found survival benefit when platelets were transfused at a ratio of 1 dose of platelets to fewer than 5 RBC units.[12] A recent systematic review recommends ratios close to 1:1:1 in massive traumatic bleeding. However, the evidence is weaker for platelets than for FFP.[13] Survivor bias is a regular criticism of the various retrospective studies. In other words, only those patients who were bound to survive in any event lived long enough to receive the products. In one study, when timing of delivery of product was taken into account, the survival benefit from plasma disappeared.[14] Prospective studies are needed to provide higher levels of evidence.

Fibrinogen is the first factor that reaches critically low levels in trauma haemorrhage. Fibrinogen is an essential component of the coagulation system due to its role in initial platelet aggregation and formation of a stable fibrin clot. FFP contains some fibrinogen (0.5–1.3 g/unit of plasma). A typical adult dose of 4 units would contain 2–5 g in approximately 1000 ml. Cryoprecipitate is the preferred source of fibrinogen if the levels of fibrinogen are low (<1.5 g/l). Cryoprecipitate contains factor VIII, von-Willebrand factor, fibronectin and factor XIII as well as fibrinogen. One dose (2×5 donor pools of

cryoprecipitate, equivalent to 10 single donor units) contains 3–6 g of fibrinogen in a volume of 200–500 ml. This would be expected to increase fibrinogen by about 1 g/l. Fibrinogen concentrate (3–4 g) is currently not licensed in the UK but is used extensively in Europe as an alternative to cryoprecipitate. It has been used in military trauma surgery, but in UK hospital practice it should be used only in the context of clinical studies.

ii. Adjuncts to DCR include tranexamic acid, calcium, recombinant factor VIIa and prothrombin complex concentrate (PCC).
   a. *Tranexamic acid*
      Tranexamic acid is an antifibrinolytic drug which works by blocking the lysine binding site on plasmin. A major international prospective randomised controlled trial, including more than 20 000 adult trauma patients at risk of bleeding, found a significant reduction in all-cause mortality versus placebo when the drug was given within 3 h of the injury. The study collaborators concluded that tranexamic acid (1 g intravenously over 10 min, then 1 g infusion over 8 h) should be given as early as possible to bleeding trauma patients.[15] Prehospital administration by ambulance personnel will be rolled out in the UK during 2012.
   b. *Calcium*
      RBC for transfusion were previously suspended in citrate–phosphate–dextrose. Transfusion of multiple units was associated with the risk of hypocalcaemia, reducing myocardial contractility and worsening the shock state. Calcium is a cofactor for many constituents of the coagulation cascade but hypocalcaemia does not impair coagulation. RBC are nowadays preserved in sodium chloride, adenine, glucose and D-mannitol (SAG-M). Calcium chloride (10 ml of 10%) is given by slow intravenous injection to patients during resuscitation with blood, FFP and platelets only if there is clinical or biochemical evidence of hypocalcaemia. The objective is to maintain ionised calcium levels >1 mmol/l.
   c. *Recombinant factor VIIa*
      Recombinant factor VIIa (rVIIa) is used for patients with critical bleeding unresponsive to surgery and component therapy. It promotes coagulation by its interaction with tissue factor, the tissue factor: VIIa complex activating factors IX and X. Before treating patients with rVIIa, clotting factors must be adequately replaced using blood components. This includes fibrinogen, which stabilises the platelet plug at the site of vascular injury, and platelets. Correction of acidosis is also recommended. A recent systematic review found no evidence of improved survival when rVIIa was used for off-label indications, including trauma.[16]
   d. *Prothrombin complex concentrate*
      Prothrombin complex concentrate (PCC) is a concentrate of vitamin K dependent coagulation factors derived from pooled human plasma. The two proprietary formulations, Beriplex and Octaplex, also contain protein C and protein S. PCC is used for the rapid reversal of the international normalised ratio (INR) in patients on oral anticoagulants. The concentrate is reconstituted from powder in 10 or 20 ml sterile water (provided) and the volume injected (at 1–3 ml/min) depends on the initial INR and weight of the patient.

iii. The early recognition of major blood loss and the institution of effective resuscitation are essential to avoid unnecessary trauma deaths. A key element is the effective communication between all staff involved in the provision and transportation of blood components. A 2010 National Patient Safety Agency Rapid Response Report showed that delays to transfusion adversely affects outcome.[17] Over a 4 year period (October 2006–September 2010), the agency was made aware of 11 deaths and 83 incidents of patient harm as a result of a delay in the provision of blood components in emergencies. According to the National Reporting and Learning Service, the system fails due to misunderstandings at every point in the process. This includes lack of understanding of urgency, overzealous application of rules aimed at non-urgent situations and poor communication.
   The logistical challenges of providing blood products to support DCR are considerable. Massive haemorrhage pathways enable the delivery of haemostatic, plasma rich resuscitation. Major haemorrhage packs contain RBC, FFP and platelets, often in the ratio 4:4:1. Pathways also set out the indications for tranexamic acid, cryoprecipitate and calcium. Protocols are not just for traumatic haemorrhage; massive haemorrhage in the ED setting usually originates from the upper gastrointestinal tract and ruptured aortic aneurysm. It remains to be seen whether widespread uptake of protocolised resuscitation will impact on survival in trauma and non-traumatic massive haemorrhage (figure 1).

CASE CONCLUSION

The immediate postoperative Hb, recorded in the ICU, is 9 g/dl. Five hours later the patient remains inadequately resuscitated. He is cold (core temperature 35.6°C) and acidaemic (arterial blood pH 7.28). Hb has fallen to 7 g/dl. Surgical review is requested and the patient is given 2 units of cross matched RBC. On the second postoperative day he is taken back to theatre for removal of packs and definitive surgery, with closure of the abdomen. A further 3 units of cross matched RBC are given in theatre. The patient is extubated in the ICU on the third postoperative day.

Thromboprophylaxis with low molecular weight heparin is instituted on day 4. He is transferred to a surgical ward on day 6 and is discharged home 14 days after admission.

Questions

i. How safe is blood transfusion in trauma?
ii. What is the role of thromboelastometry/thromboelastography?
iii. What is the most appropriate target Hb concentration for a trauma patient in the ICU setting?
iv. What are the headline conclusions of the most recent consensus guidelines on massive transfusion in trauma?

Discussion

i. The early and late complications of ABT are listed in table 1. The role of ABT in the treatment of haemorrhagic shock is established while transfusion of stored RBC in the subsequent treatment of euvolaemic anaemia is not recommended when Hb is >7 g/dl.[18]
   Modern transfusion practice makes the risk of transfusion transmitted infections remote; none was reported in the UK in 2010.[19] Major transfusion reactions are also rare. However, aggressive volume and blood transfusion may lead to transfusion associated circulatory overload.
   Blood transfusion is safe in the UK. And yet, in critically ill trauma patients, ABT is identified as an independent risk factor for adverse outcomes, including infections, organ dysfunction, prolonged lengths of stay and mortality. The

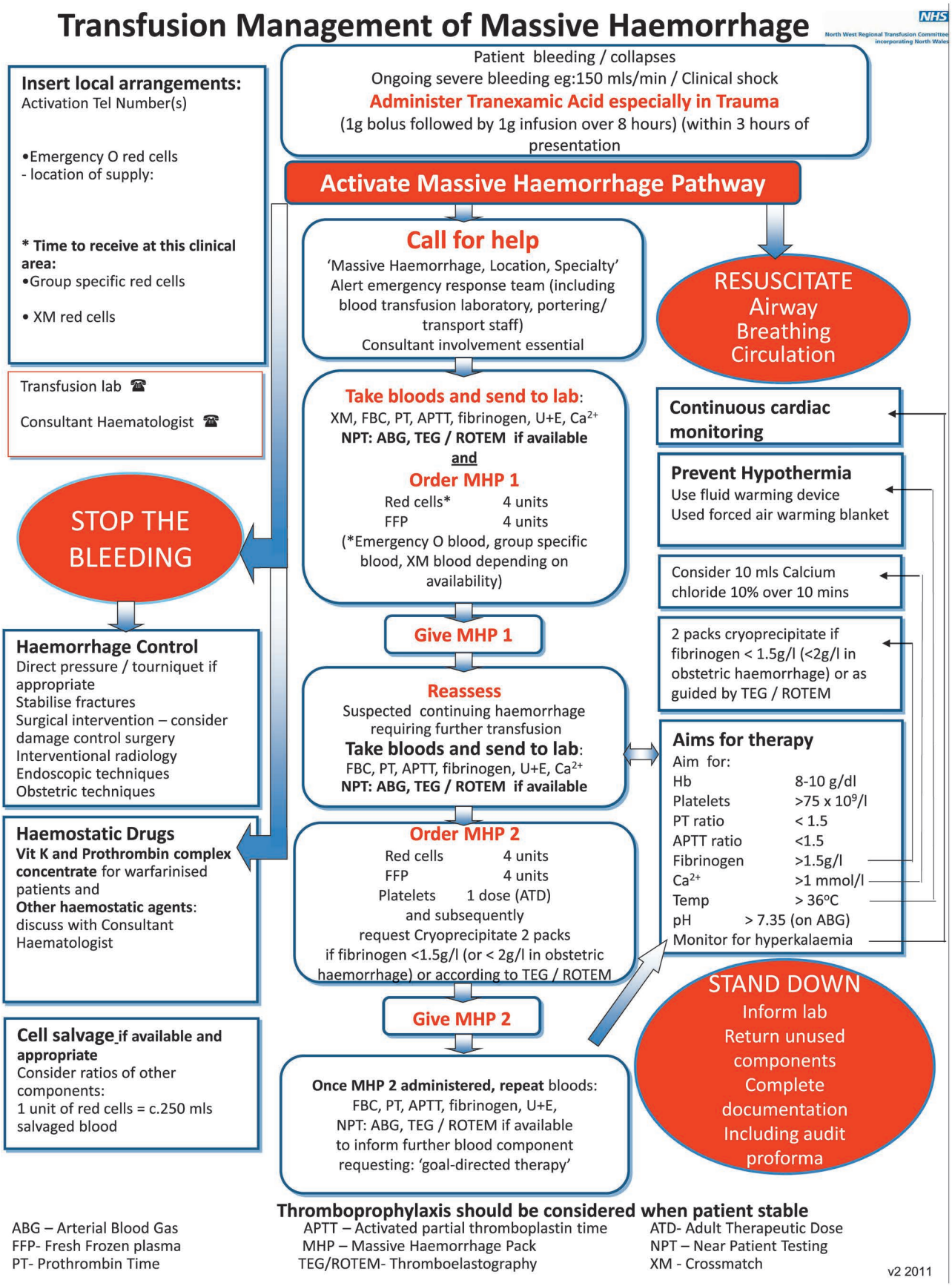

Figure 1 NHS Northwest Regional guideline for transfusion management of massive haemorrhage (reproduced with permission).

Table 1 Early and late complications of allogeneic blood transfusion in adults

Early	Late
Haemolytic reactions	Transmission of infection:
Non-haemolytic febrile reactions	Viral (hepatitis B, C, HIV, HTLV1)
Circulatory overload	Bacterial (gram negative and gram positive organisms)
Transfusion related acute lung injury	Parasites (malaria, toxoplasma)
Air embolism	Graft versus host disease
Hyperkalaemia	Iron overload (after chronic transfusion)
Hypothermia	Immune sensitisation
Coagulopathy (after massive blood transfusion)	
Thrombophlebitis	
Reactions secondary to bacterial contamination	
Anaphylaxis	

effect is dose dependent and has prevailed even after universal leucodepletion. Interpretation of published outcome studies is made difficult by the fact that the sickest patients are more likely to have required a transfusion, and to have endured a period of prolonged hypoperfusion. However, there is evidence that stored RBC are associated with immunomodulatory effects that promote organ failure and increase mortality, even in less severely injured patients.[20] Transfusion risks are higher in plasma rich products, such as FFP and platelets. The 2010 SHOT report showed that allergic and anaphylactic reactions were more common in patients transfused with FFP and platelets than with RBC. Transfusion related acute lung injury is more frequent when transfusing plasma rich products, due to the accumulation of inflammatory mediators in stored platelets and the presence of antileucoctye antibodies. In addition, the risk of bacterial contamination is higher with platelets than with other components because of room temperature storage conditions although the risk should be reduced following the recent introduction of bacterial screening of platelets in the UK.

ii. The value of laboratory based coagulation tests (prothrombin time/INR, activated partial thromboplastin time, fibrinogen, platelet count) in the acute situation is limited because of delays to obtaining results of 45–60 min. Moreover, coagulation tests measure only the initial 20–60 s of the coagulation process and, as tests are determined in plasma, they do not assess the interaction with red cells and platelets. Tests provide no information on platelet function and, because analysis is performed at 37°C, results do not accurately represent the hypothermic patient. Finally, the laboratory tests are relatively insensitive; by the time the INR is >2, levels of vitamin K dependent clotting factors are only 15–20% of normal. Recently, the viscoelastic properties of fresh clot assessed by thromboelastography/thromboelastometry (TEG/TEM) have been used to provide information on the speed of coagulation initiation, the kinetics of clot growth, stability of the fibrin clot and its breakdown by fibrinolysis.[21] Such measures of clot strength and lysis may be used to inform interventions. Preliminary results can be obtained as early as 5 min at the bedside, while full results follow 10–20 min later.

Point of care TEG/TEM devices are in widespread use in the UK, principally in the operating theatres of liver and cardiac centres. Use of such devices in other settings, such as the ED, is beginning to be tested. In a 2009 study, TEG guided platelet and FFP transfusions were associated with improved 30 day mortality from 31.5% to 20.4%.[22] Disadvantages include a relatively high coefficient of variation, poorly standardised methodologies and limitations on the specimen stability of native whole blood samples.

iii. Anaemia is common in critical illness, including trauma patients, and leads to adverse effects such as impaired recovery of consciousness, delayed respiratory wean and worsening renal and gut function. Transfusion is commonly required in the ICU setting but stored blood may be ineffective in improving oxygen delivery to the tissues[23] and may have a deleterious effect on immune function; worsening acute lung injury and prolonging length of stay. Transfusion triggers, targeting Hb concentration, have been investigated in a number of studies.

In the Transfusion Requirements in Critical Care study,[24] normovolaemic patients transfused at Hb <7.0 g/dl (restrictive strategy) received approximately 3 fewer RBC units than those transfused at Hb <10.0 g/dl (liberal strategy). One-third of the former group avoided transfusion. Thirty day mortality was 18.7% in the restrictive strategy arm compared with 23.3% in the liberal strategy arm (p=0.11).

iv. A Canadian consensus conference reported in December 2011.[25] They concluded that there was insufficient evidence to support a policy of 1:1:1 (RBC:FFP: platelets) formula driven resuscitation. There was unanimous support for an alternative approach, based on immediate administration of a foundation ratio of components, such as 6 RBC to 3 FFP. Thereafter, therapy should be individually tailored and not driven by rigid protocols. Platelets should be reserved for counts $<100\times10^9$/l or based on TEG/TEM. The panel did not favour TEG/TEM over laboratory tests. Cryoprecipitate or fibrinogen concentrate should be given to maintain levels above 1.5 g/l and rVIIa should not be used in traumatic bleeding. Tranexamic acid must be given as soon as possible after injury.

SUMMARY OF CONCLUSIONS

Delayed and inadequate treatment of haemorrhagic shock is a major cause of avoidable death in trauma. Early recognition of massive haemorrhage enables the use of transfusion protocols and the rapid provision of blood components to the resuscitation room. A coordinated approach involving emergency medicine, intensive care medicine, surgical, anaesthetic and transfusion professionals is required to optimise outcomes. It is essential to record vital signs, even though they may not reflect the extent of blood loss. The mechanism of injury, and data from the accident scene, should be taken into account. Resuscitation to normal vital signs should not be targeted until exsanguinating bleeding has been controlled. The acute coagulation of trauma shock should be anticipated and, where indicated, the patient should be transfused with a haemostatic regimen including RBC, platelets and FFP. The trauma shock patient should be kept warm and fibrinogen or cryoprecipitate should be given if levels fall to <1.5 g/l. Tranexamic acid should be given as quickly as possible, certainly within 3 h of injury. There is no evidence for the use of rFVIIa or PCC outside of the licensed indications. TEG/TEM has the potential to improve the safety and clinical and cost effectiveness of blood products in traumatic bleeding but its use in the ED setting has yet to be established.

Contributors TM and PAN wrote the original draft, based on their participation in the North West Regional Guideline Development Group on critical bleeding and massive transfusion. KP chaired that group and updated numerous sections following very recent Canadian Consensus Guidelines on massive transfusion. SB wrote the sections related to laboratory science and transfusion practice. AN checked all references for accuracy and assisted with the final draft of the manuscript.

Competing interests None.

Provenance and peer review Commissioned; not externally peer reviewed.

REFERENCES

1. http://www.ncepod.org.uk/2007report2/Downloads/SIP_report.pdf (accessed 21 Sep 2011).
2. **Tien HC,** Fernando S, Tremblay LN, *et al*. Preventable deaths from hemorrhage at a level I Canadian trauma center. *J Trauma* 2007;**62**:142—6.
3. **Parks JK,** Elliot AC, Gentilello LM, *et al*. Systemic hypotension is a late marker of shock after trauma: a validation study of Advanced Trauma Life Support principles in a large national sample. *Am J Surg* 2006;**192**:727—31.
4. **Salim A,** Sangthong B, Martin M, *et al*. Whole body imaging in blunt multisystem trauma patients without obvious signs of injury: results of a prospective study. *Arch Surg* 2006;**141**:468—75.
5. **Husain FA,** Martin MJ, Mullenix PS, *et al*. Serum lactate and base deficit as predictors of mortality and morbidity. *Am J Surg* 2003;**185**:485—91.
6. **Antonelli M,** Levy M, Andrews PJ, *et al*. Hemodynamic monitoring in shock and implications for management. International Consensus Conference, Paris, France, 27—28 April 2006. *Intensive Care Med* 2007;**33**:575—90.
7. **Rossaint R,** Bouillon B, Cerny V, *et al*; Task Force for Advanced Bleeding Care in Trauma. Management of bleeding following major trauma: an updated European guideline. *Crit Care* 2010;**14**:R52.
8. **Brohi K,** Cohen MJ, Ganter MT, *et al*. Acute coagulopathy of trauma: hypoperfusion induces systemic anticoagulation and hyperfibrinolysis. *J Trauma* 2008;**64**:1211—17.
9. **American College of Surgeons Committee on Trauma.** *Advanced trauma life support for doctors*. 8th edn. Chicago: American College of Surgeons Committee on Trauma, 2008.
10. **Borgman MA,** Spinella PC, Perkins JG, *et al*. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. *J Trauma* 2007;**63**:805—13.
11. **Peiniger S,** Nienaber U, Lefering R, *et al*; Trauma Registry of the Deutsche Gesellschaft für Unfallchirurgie (TR-DGU). Balanced massive transfusion ratios in multiple injury patients with traumatic brain injury. *Crit Care* 2011;**15**:R68.
12. **Munro AR,** Ferguson C. Blood component therapy in trauma patients requiring transfusion. *Emerg Med J* 2010;**27**:53—5.
13. **Phan HN.** Should we increase the ratio of plasma/platelets to red cells in massive transfusion: what is the evidence? *Vox Sang* 2010;**98**:395—402.
14. **Snyder CW,** Weinberg JA, McGwin G Jr, *et al*. The relationship of blood product ratio to mortality: survival benefit or survival bias? *J Trauma* 2009;**66**:358—62.
15. **Shakur H,** Roberts I, Bautista R, *et al*; CRASH-2 trial collaborators. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet* 2010;**376**:23—32.
16. **Yank V,** Tuohy CV, Logan AC. Systematic review: benefits and harms of in-hospital use of recombinant factor VIIa for off-label indications. *Ann Intern Med* 2011;**154**:529—40.
17. http://www.transfusionguidelines.org.uk/docs/pdfs/nbtc(npsa) rapid_response_report.pdf (accessed 13 Dec 2011).
18. **Napolitano LM,** Kurek S, Luchette FA, *et al*; American College of critical care Medicine of the Society of critical care Medicine; Eastern Association for the surgery of trauma practice management Workgroup. Clinical practice guideline: red blood cell transfusion in adult trauma and critical care. *Crit Care Med* 2009;**37**:3124—57.
19. **Serious Hazards of Transfusion Steering Committee.** Serious hazards of transfusion: annual report 2010. Manchester, SHOT, 2010.
20. **Weinberg JA,** McGwin G Jr, Marques MB, *et al*. Transfusions in the less severely injured: does age of transfused blood affect outcomes? *J Trauma* 2008;**65**:794—8.
21. **Lang T,** Bauters A, Braun SL. Multi-centre investigation on reference ranges for ROTEM thromboelastometry. *Blood Coagul Fibrinolysis* 2005;**16**:301—10.
22. **Johansson PI,** Stensballe J. Effect of haemostatic control resuscitation on mortality in massively bleeding patients: a before and after study. *Vox Sang* 2009;**96**:111—18.
23. **Nee PA,** Bonney SC, Madden P, *et al*. Transfusion of stored red blood cells in critical illness: impact on tissue oxygenation. *JICS* 2010;**4**:240—4.
24. **Herbert PC.** Transfusion requirements in critical care (TRICC): a multicentre, randomized, controlled clinical study. Transfusion Requirements in Critical Care Investigators and the Canadian Critical Care Trials Group. *Br J Anaesth* 1998;**81** (Suppl 1):25—33.
25. **Dzik WH,** Blajchman MA, Fergusson D, *et al*. Clinical review: Canadian National Advisory Committee on Blood and Blood Products—Massive Transfusion Consensus Conference 2011: report of the panel. *Crit Care* 2011;**15**:242.

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Emerg Med J 2013 30: 9-14 originally published online February 10, 2012
doi: 10.1136/emermed-2011-201061