Fresh frozen plasma for correction of the international normalized ratio: safe practice?

Plasma forms about 55% of the total blood volume. It contains, among others, proteins such as fibrinogen, globulin and albumin, mineral ions and glucose, as well as clotting factors.

Fresh frozen plasma was first produced in 1941. From the outset plasma had wide-ranging uses, from a volume expander to replacement of products in clotting defects. It is now used mainly for correction of clotting defects before or during surgery, prophylactic transfusion before invasive procedures on intensive care such as central line insertion or removal, or epidural catheter removal. This treatment is usually guided by derangement in classical tests of coagulation such as prothrombin time or the international normalized ratio (INR).

The case for use of fresh frozen plasma

There are some circumstances where coagulopathy leading to bleeding may have catastrophic consequences, e.g. significant intracranial or intraocular surgery. Likewise epidural haematoma, although rare, can be a devastating complication. The 3rd national audit project showed that patients with epidural haematoma had a poor prognosis and were left with significant complications (Cook et al, 2009). Although cases were not stated to have been associated with coagulopathy, clinicians are likely to be cautious when removing an epidural catheter from a patient with coagulopathy. Additionally there are specific settings, such as trauma, where patients having massive transfusion have improved survival when high fresh frozen plasma:red blood cell ratios have been used (Stinger et al, 2008). However, one should be cautious about extrapolating these findings to other situations.

Dr Matthew Henley *is Specialist Registrar in Anaesthetics and* **Dr Susan Mallett** *is Consultant Anaesthetist in the Department of Anaesthesia, Royal Free London NHS Foundation Trust, London NW3 2QG*

Correspondence to: Dr M Henley (matthenley@nhs.net)

The case against use of fresh frozen plasma

Why do people administer fresh frozen plasma? A number of assumptions are made, namely that elevation of the prothrombin time or INR will predict bleeding in the setting of a procedure, that pre-procedure administration of fresh frozen plasma will correct prolonged clotting times, that prophylactic transfusion results in fewer bleeding events (Segal et al, 2005) and that potential for benefit outweighs the risk. Are these assumptions correct? Segal et al (2005) showed that across a variety of procedures, including liver and kidney biopsy, prothrombin time or INR did not predict bleeding. Despite being widely used as a 'clotting screen' classical coagulation tests are not validated in bleeding patients. INR is only validated for monitoring of vitamin K antagonists, prothrombin time is sensitive to deficiencies in procoagulants but insensitive to deficiencies in anticoagulants. A linear relationship of clotting factor deficiency to INR is generally assumed but this is not correct (Gulati et al, 2011).

In a prospective audit of 121 patients with mild to moderate derangement of prothrombin time (13.1–17 sec) and INR (1.1–1.85), a total of 324 units of fresh frozen plasma being transfused (median transfusion 2 units) resulted in a median decrease in prothrombin time by 0.2 s and INR by 0.07 (Abdel-Wahab et al, 2006). Only in 15% of patients did the INR improve by 50%. In a UK-wide study of transfusion practice Stanworth et al (2010) showed a median reduction in INR of -0.2 using a median dose of 11 ml/kg fresh frozen plasma in patients with mild (<1.5) to moderate (2.6–2.9) derangement of INR.

Transfusion of fresh frozen plasma is not a benign act; it can result in transfusion-related lung injury or associated cardiac overload, haemodilution, allergic reactions, viral and bacterial contamination, and potential procedural delays.

Conclusions

The limitations of classical coagulation tests (prothrombin time and INR) must be both understood and recognized. Coagulation tests demonstrate in-vitro abnormality, but this does not necessarily equate with an in-vivo failure of clinical haemostasis and the presence of clinical coagulopathy. Clinicians should consider the use of global tests of haemostasis, such as the thromboelastogram or rotational thromboelastometry viscoelastic tests.

The clinician also has to bear in mind what his/her objective is – is it the treatment of coagulopathy or is it avoidance of medicolegal complications? The correction of a mild derangement of coagulation before central line removal is a very different scenario to a coagulopathy in a massive transfusion trauma patient. BJHM

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Anaesthetic and critical care dilemmas are coordinated by Dr Steven Cone and Dr Matthew Henley, Specialist Registrars in Anaesthetics, Royal Free Hospital, London

Ideas for future dilemmas can be sent to Rebecca Linssen rebecca.linssen@markallengroup.com