TxMD™ Myths and Realities of Plasma Use

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Patient Blood Management Strategies

Optimize Your Patient	Minimize Blood Loss	Adopt Best Practices
• Identify & correct anemia • Assess & treat bleeding disorders • Review prescription & over the counter medications that may increase patient's bleeding risk • Engage patient in treatment plan	• Control surgical bleeding with intraoperative techniques & fluid management • Consider blood salvage/ blood recovery • Utilize pharmacalogical agents to maintain hemostasis • Reduce frequency of lab testing & minimize sample volumes	• Follow restrictive transfusion thresholds based on clinical signs & symptoms • Give one unit of RBC then reassess • Transfuse plasma & platelets per evidence-based guidelines

Myths and Realities of Plasma Use

Recent advancements in alternative treatments, awareness of risks, and ongoing improvements in patient blood management have brought to light the risks of some longstanding myths regarding plasma use. Plasma has traditionally been used for the management of patients on warfarin undergoing invasive procedures; yet the low cost and availability of plasma have made it attractive for use when not indicated.

The myths surrounding plasma use can be allocated to three categories:

1) Indications and dosing
2) Relevance of International Normalized Ratio (INR) in plasma use
3) Efficacy of plasma transfusion – balancing risks and benefits

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Indications & Dosing

1 Myth 1: One unit of plasma is an adequate dose to lower INR

Reality: An appropriate dose of plasma is 10-20mL/kg or 3-4 units in a 70-80 kg adult, which is expected to raise the level of coagulation factors by about 20-30% immediately after the infusion. In the absence of bleeding, one unit of plasma will raise coagulation factors by only 4-5% in an average-sized adult.

Appropriate dose for urgent warfarin-reversal

2 Myth 2: Patients need coagulation factor levels of 100% for adequate hemostasis

Reality: Satisfactory hemostasis may be achieved when coagulation factors are at least 30-40% of normal and when fibrinogen level is >100-125 mg/dL. Factor levels that are 40-50% of normal, which is adequate for hemostasis, may still result in a mildly prolonged PT or a PTT.[1]

3 Myth 3: Plasma is indicated when a patient is bleeding but has no significant coagulopathy

Reality: Plasma use should be guided by results of coagulation tests when time allows. Coagulopathy may develop due to massive bleeding, but often the cause is multifactorial. Plasma may be considered for temporary correction, but investigation of the underlying cause of bleeding is required for correct management. Routine use of plasma when INR is 1.7 or less is not recommended.[1] (See Myth 7)

4 Myth 4: Fixed ratios of plasma to RBC should be given during all episodes of major blood loss

Reality: In a trauma-related massive transfusion, time is of the essence, and waiting for lab values is not feasible. As such, early delivery and 1:1 or 1:2 ratios of plasma to RBC have become accepted by many trauma centers for preventing trauma-related disseminated intravascular coagulopathy (DIC). In non-trauma patients, however, such an approach is not indicated – for example, in the patient with surgical blood loss or GI bleeding. For these patients, when bleeding is controlled, use of plasma should be guided by timely monitoring of coagulation assays. A "formula" to guide plasma replacement should not be used outside of massive trauma.[2,3,4]

Relevance of INR to Plasma Use

5 Myth 5: INR can predict the risk of bleeding

Reality: Coagulation tests such as PT/INR and aPTT were originally developed to diagnose isolated coagulation factor deficiencies and to monitor warfarin therapy. A 2005 meta-analysis of 25 studies of patients with abnormalities in PT/INR (INR <2.0) and undergoing a variety of minor invasive procedures[5] showed:

- Elevated pre-procedure PT/INR did not predict a greater risk for bleeding.
- There was no increased risk of bleeding in patients with mild coagulopathy compared to those without coagulopathy in those studies with a control group.

In a prospective audit of plasma transfusions in patients who had mild coagulopathy (INR 1.1 to 1.85), the INR did not correlate with estimated RBC loss.[6]

6 Myth 6: Plasma is always indicated to correct an INR >1.7

Reality: American College of Chest Physician guidelines recommend management of non-bleeding patients on warfarin by withholding warfarin and, depending on the elevation of the INR, administration of Vitamin K. Use of plasma transfusions is not indicated in the non-bleeding patient.

In patients with EITHER serious life-threatening bleeding (e.g. CNS bleed) OR emergent surgery associated with substantial blood loss AND elevated INR, the following approaches are recommended: [7]

- 4-factor Prothrombin Complex Concentrate (4F-PCC) to urgently reverse the effects of warfarin and supplement Vitamin K dependent factors
- Halting warfarin therapy
- Giving vitamin K (5-10 mg slow IV infusion)

7 Myth 7: Plasma transfusions are effective when the INR is 1.7 or less

Reality: BloodCenter of Wisconsin (a part of Versiti™) guidelines recommend transfusing plasma only when the patient has active bleeding (or imminent surgery) AND a coagulopathy reflected by INR > 1.7. The INR of donated plasma is typically between 1.1 – 1.3. Therefore, patients with an INR ≤ 1.7 would have minimal change in their INR with plasma infusion at an appropriate dose.

Several studies have shown the following:

Mild coagulopathy (INR<2.0) + plasma transfusion

NOT SUCCESSFUL INR REDUCTION
in 3 out of 4 patients

And increasing the number of units of plasma did not result in a larger reduction of the INR. For as few as 1 in 6 patients, plasma will only partially correct a mildly elevated INR.[8, 9] Instead, vitamin K can create the desired effect.

8 Myth 8: Patients with liver disease who have elevated INRs are at risk for bleeding

Reality: While the PT/INR is frequently prolonged in patients with liver disease, reflecting decreased production of procoagulant factors; there is a parallel decrease in the anticoagulant proteins which results in a "rebalanced hemostasis". The bleeding tendency in patients with liver disease is therefore complex and multifactorial, confounding traditional modes of measuring and re-establishing hemostasis. There can be alterations in all the components for hemostasis (procoagulants, anticoagulants, platelets and antifibrinolytic system) within a patient with liver disease. As such, PT/INR is not a reliable indicator for the risk of bleeding in patients with liver disease.[10]

Efficacy of Plasma Transfusion

9 Myth 9: Correction of coagulation factors by plasma is long-lasting

Reality: For patients on warfarin who have received an adequate dose of plasma (>10 mL/kg) the INR returns to pre-transfusion level approximately 10-12 hours post transfusion. The half-life of various coagulation factors ranges from 2-3 hours to 4 days. So, large volumes of plasma at a constant rate would be needed to sustain high levels of coagulation factors. If correction is truly required before an invasive procedure, the plasma products should be given shortly before the procedure, or preferably during the procedure for optimal effect.[11]

10 Myth 10: Plasma transfusions are risk-free

Reality: Allergic reactions are common, occurring in 1% of plasma transfusions. Plasma is also associated with significant risk for respiratory complications, in particular Transfusion Associated Circulatory Overload (TACO) and Transfusion-Related Acute Lung Injury (TRALI), both of which are leading causes of transfusion-associated deaths.[12, 13]

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References

1. Callum JL, Dzik WH. The use of blood components prior to invasive bedside procedures: a critical appraisal. In: Mintz PD. Ed. Transfusion Therapy: Clinical Principles and Practice 3rd ed. Bethesda, MD: AABB Press, 2011:1-36

2. Holcomb JB, delJunco DJ, Fox EE, et al. The prospective, observational, multicenter, major trauma transfusion (PROMMTT) study. Comparative effectiveness of a time-varying treatment with competing risks. JAMA Surg 2013;148(2):127-136

3. Mitra P, Cameron PA, Gruen RL. Aggressive fresh frozen plasma (FFP) with massive blood transfusion in the absence of acute traumatic coagulopathy. Injury 2012;43(1):33-7

4. Sambasivan CN, Kunio NR, Nair PV, et al. High ratios of plasma and platelets to packed red blood cells do not affect mortality in nonmassively transfused patients. J Trauma 2011;71(2 Suppl 3):S329-36

5. Segal JB, Dzik WH. Paucity of studies to support the abnormal coagulation test results predict bleeding in the setting of invasive procedures. Transfusion 2005;45(9):1413-1425

6. Abdel-Wahab OI et al. Effect of fresh frozen plasma transfusion on prothrombin time and bleeding in patients with mild coagulation abnormalities. Transfusion 2006;46(8):1279-85

7. Holbrook A, Schulman S, Witt DM, et al. Evidence-based management of anticoagulant therapy. Antithrombotic therapy and prevention of thrombosis, 9th ed. American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2012;141(Suppl):e152S-e184S

8. Abdel-Wahab OI et al. Effect of fresh frozen plasma transfusion on prothrombin time and bleeding in patients with mild coagulation abnormalities. Transfusion 2006;46(8):1279-85

9. Holland LL, Foster TM, Marlar RA, Brooks JP. Fresh frozen plasma is ineffective for correcting minimally elevated international normalized ratios. Transfusion 2005;45:1234-5

10. Lisman T, Porte RJ. Understanding and managing the coagulopathy of liver disease. In: Kitchens CS, Kessler CM, Konkle BA, eds. Consultative hemostasis and thrombosis. 3rd ed. Philadelphia PA: Elsevier Saunders, 2013:688-697

11. Hambleton J et al. Pharmacokinetic study of FFP photochemically treated with amotosalen (S-59) and UV light compared to FFP in healthy volunteers anticoagulated with warfarin. Transfusion 2002;42:1302-7

12. Murad MH, Stubbs JR, Gandhi MJ, et al. The effect of plasma transfusion on morbidity and mortality: A systematic review and meta-analysis. Transfusion 2010;50:1370-83

13. Fatalities Reported to FDA Following Blood Collection and Transfusion: Annual Summary for Fiscal Year 2013, accessed June 9, 2015

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