PLASMA TRANSFUSION
Current Evidence and Future Directions

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At the conclusion of this educational activity, participants will be able to:

- Understand preparation, types and content of plasma products
- Gain knowledge as to appropriate dose, volume, timing and monitoring of plasma transfusion
- Review current evidence-based guidelines for plasma transfusion
- Discuss adverse reactions/complications of plasma transfusion
OUTLINE

- General comments
- Content and preparation of plasma products
- Dosing, timing and monitoring
- Indications for plasma transfusion
- Adverse reactions and complications of plasma transfusion
- Final comments
• Transfusion of plasma in the U.S. is growing & exceeds use in other developing countries
• General lack of education exists for healthcare professionals
• Need to examine the risk:benefit ratio for plasma transfusion
• Blood resources are not indefinite or assured
PREPARATION & TYPES OF PLASMA PRODUCTS

- Plasma separated from WBD requires centrifugation processes
- FFP = plasma frozen within 8 hrs., expiration 1 yr.
- Plasma 24 = plasma from WBD frozen within 24 hrs.
- Thawed plasma = plasma thawed, then stored @ 1-6 degrees C. for 5 days
PREPARATION & TYPES OF PLASMA PRODUCTS

- Cryo-poor plasma = plasma with cryoprecipitate removed (vWF)
- Solvent detergent treated plasma = plasma specially treated to eliminate lipid enveloped viruses
• Plasma contains the protein fractions of whole blood including albumin, Ig, fibrinogen & coagulation factors
• Volume of each prepared unit of plasma = 200 – 300 mls.
• Typical dose = 10 – 15 mls./kg body weight
• Roughly 2 – 4 unit dose for adults
• Each unit should increase factor activity by roughly 20%
• Plasma should be ABO compatible
• Transfuse using standard administration set within 4-6 hrs. of planned procedure
• Follow-up testing within 15 min. to 1 hr.
• Testing may include PT/INR, aPTT, & fibrinogen
CAVEATS

- Normal coagulation is maintained if factor concentrations > 25-30% and fibrinogen > 100

- Absence of either exogenous or endogenous inhibitors (e.g. heparin, coumadin, acquired inhibitor Abs)
INDICATIONS FOR PLASMA TRANSFUSION

• British Committee for Standards in Haematology
• College of American Pathologists
• American Association of Blood Banks
• American Society of Anesthesiologists
• Circular of Information
INDICATIONS FOR PLASMA TRANSFUSION

• Management of patients with coagulopathy or acquired coagulation factor deficiency for which specific factors are not available
• Management of bleeding patients who require replacement of multiple coagulation factors (e.g. DIC, liver failure)
• During massive transfusion protocol
INDICATIONS FOR PLASMA TRANSFUSION

- Bleeding patients on warfarin who need invasive procedures before Vitamin K can reverse effect
- Therapeutic plasma exchange in TTP
- Rare plasma protein deficiencies (e.g. C1 esterase inhibitor)
CONTRAINDICATIONS FOR PLASMA TRANSFUSION

- Volume expansion or nutrition
- DIC without bleeding
- Reverse Vitamin K antagonist without bleeding
- TPE not associated with TTP
CONTRAINDICATIONS FOR PLASMA TRANSFUSION

• To prevent periventricular hemorrhage in premature neonates
• By formula in massive transfusion
• Mild to moderate elevations of PT/INR or aPTT without bleeding
Throughout the 1990s to current years multiple studies point to a LACK of evidence that perioperative patients with slight increases in PT/INR confers an increased incidence of bleeding than those with “normal” studies.
Transfusion of small quantities of plasma in these perioperative patients confers little benefit and actually increases the risks of adverse events resulting from the use of plasma products.

Brit. Comm. for Std. in Haematol., 2004
• Donor plasma units from WBD may have distribution of INR just < 1.4 (Holland et. al., Transfusion, 2005)

• Subsequent study by same group (AJCP, 2006) showed little to no change in INR with plasma transfusion if the initial patient INR was < 1.7.
• Retrospective study (Abdel-Wahab et. al., Transfusion, 2006) with greater than 300 units of plasma transfused to 121 patients with initial INR 1.1-1.85, showed little change in post transfusion INR (0.07-0.2)

• Two additional studies mirrored these findings (Youssef et. al., Am. J. Gastroenterology, 2003 & Cheng et. al., Can. Transf., 2007)
• Welsh study (Chowdhury et. al., Brit. J. Haem, 2004) found correction of INR with doses 30 mls/kg; this is twice current dosing recommendation

• No assessment of clinical outcomes or adverse reactions
PLASMA TRANSFUSION: CURRENT EVIDENCE

• Meta-analysis by Dzik and Segal (Transfusion, 2005) of 25 studies addressing this issue
• Studies included clinical outcomes (i.e. bleeding episodes)
• Procedures included liver/kidney biopsy, venous catheter placement, paracentesis, bronchoscopy
• Correlated INR with % coagulation factors
• This meta-analysis found NO significant difference in bleeding risks with these procedures between those with normal INR vs. mild to moderate elevations.

• Stanworth (Brit J Haem, 2004) similar meta-analysis that revealed NO decrease in EBL or transfusion requirement when those with mild increase INR were compared to controls.
• Patients with ESLD given plasma transfusion will only infrequently correct INR as a reflection of coagulopathy (Youssef et. al.)

• This was described in the early 1990s in several studies (McVay & Toy, Transfusion; Foster et al., Arch of Surg; Docaflur et al., Chest)
Editorial, Transfusion, 2006, (Triulzi): “Taken as a whole, the data...do not support the efficacy in treating bleeding or as prophylaxis for invasive procedures in patients with mild coagulopathy defined as an INR < 2.0.”
2010 studies, Mayo & Emory – questioned the benefit of high plasma ratios in MTPs and association of plasma transfusion with ALI respectively.

“Evidence-based Guidelines for Plasma Transfusion”, (Roback, JD et al., Transfusion, 2010) GRADE method to evaluate six questions surrounding plasma transfusion including MTP, ratios, ICH etc.
• AABB Commission – data not available to correlate plasma transfusion with degree of coagulopathy

• AABB Technical Manual - comment on target INR of 1.3-1.5 is without factual basis
Exponential relationship of INR to percentages of factor levels. (Used with permission Wayne Chandler, MD, University of Washington Department of laboratory Medicine.)
The multitude of evidence points to the clinical inefficacy of plasma transfusion in patients with mild to moderate increases in INR even in the face of invasive procedures.

This calls into question the clinical utility of coagulation testing in the assessment of bleeding risk.
COAGULATION TESTING

- Used to aid in the diagnosis of coagulation disorders
- To monitor therapeutic effect of anticoagulation therapy or after plasma transfusion
- NOT used to predict bleeding risk
COAGULATION TESTING

• Results of coagulation tests (triggers) are NOT to be used to predict risk of bleeding or to solely or absolutely define the need for plasma transfusion

• TREAT PATIENTS NOT LABORATORY VALUES

• True need for plasma transfusion MUST be based on clinical assessment, evaluation of risk:benefit in conjunction with lab testing
• PT/INR instituted to standardize reporting of PT results between labs
• Utilized as a therapeutic monitor NOT as a diagnostic tool to predict bleeding risk
• Coagulation testing does not predict who WILL bleed nor who WILL NOT bleed
In 2008, the British Commission for Standards in Haematology proposed guidelines on assessment of bleeding risk prior to surgery or invasive procedures and determined that coagulation screening in most instances is inefficient, costly, and may delay surgery as well as causing unnecessary patient concern.

Clinical & family history are key
• Wide variation in practice is seen with plasma transfusion

• Study in UK, 2010, showed in over 2500 admissions to 29 ICUs, 34% plasma txns were for INR <1.5 with no bleeding & 29 episodes had NO documented INR (Walsh, TS et al. Crit Care Med)
• 2009 data, INR level associated with plasma transfusion: 54% for INR < 1.7, (correlates w/Cheng, Transfusion, 2007)

• Liver transplant algorithm begun in 2002 utilizes INR > 1.9 as indication for plasma transfusion; avg. plasma use <10 units for cases over past 9 yrs.

• Current shift to INR >1.9 for fulminant liver failure patients needing ICP monitor (Jl Neurosurg, 2010)
INR/PLASMA TXN - JH

FFP TRANSFUSION COMPARISON TO PATIENT INR RESULT
2009 YEAR-TO-DATE
TOTAL NUMBER OF PATIENTS MONITORED = 198 (THRU DECEMBER)

INR RESULT

- <1.7: 107
- 1.7-3.0: 49
- 3: 15
- 4: 6
- 5: 7
- 6: 5
- >7.00: 9
FFP TRANSFUSION COMPARISON TO PATIENT INR RESULT
2011 JANUARY-JULY
TOTAL NUMBER OF PATIENTS MONITORS-223
72% TRANSFUSED AT INR>1.7
LIVER TRANSPLANT ALGORITHM

Component shortages (ALERT SYSTEM) will be communicated to the Transplant Coordinator

- PT/PTT with INR ≤ 2.0
  - Fibrinogen > 100 mg/dl → No FFP
  - TEG < 15 min reaction time

- PT/PTT with INR > 2.0
  - Fibrinogen > 100 mg/dl
  - TEG > 15 min reaction time
  - Platelet count < 75,000/μL
  - TEG MA < 40 mm
  - Platelet Aggregation < 50% (Platelet Works)

- Fibrinogen < 100 mg/dl
  - Active bleeding/fibrinolysis

  1. 4 units FFP
  2. Wait 10 - 15 mins
  1. 1 Single donor pheresis platelet
  2. Consider Amicar

WATCH PRESSOR AGENTS
REPEAT LABS, TEG’s prn
RECORD ALL PRODUCTS, TIMES GIVEN LABS, (sent and rec’d results)
INCLUDE CELLSAVER AND RAPID INFUSION COMPONENTS
PLASMA IN LIVER TX

* = p<0.0001

Blood Product Usage

\[ ^\wedge = p = 0.019 \]

- Average PRBC
  - Before protocol: 19
  - After protocol: 8

- Average FFP
  - Before protocol: 49
  - After protocol: 7

- Average PLT
  - Before protocol: 34
  - After protocol: 5

- Average Cryo
  - Before protocol: 4
  - After protocol: 2
• EDUCATION AND INTERACTION IS KEY!

• Studies from UTSW, Providence and Italy, found that PROSPECTIVE review using guidelines can decrease use, M&M, and cost without increases in bleeding events
Allergic
Anaphylactic
ABO mismatch
Transfusion transmitted diseases
Transfusion related acute lung injury (TRALI)
Transfusion associated circulatory overload (TACO)
Transfusion related immune modulation (TRIM)
TRALI

- Acute lung injury associated w/all blood products esp. plasma-containing components
- Sxs of respiratory distress, hypoxia, fever, hypotension (ARDS)
- Incidence 1:400-50,000 units transfused
- HLA and granulocyte Abs/cytokines implicated
- Supportive care usually resolves w/in 72 hrs
- Still w/significant mortality rate
• Circulatory overload associated with high volume transfusion
• Estimated incidence 1:200 – 10,000 units transfused
• Adjust volume for size of patient and consider comorbid cardiopulmonary disease
• Slower rates of transfusion, O2, diuretics
• Difficult to separate from TRALI (BNP?)
• Numerous articles re: TRIM with RBC transfusion
• Increase in infections, LOS, CA recurrence
• Sarani et. al. (Crit Care Med, 2008) found increased infectious complications in patients receiving plasma transfusion
• Watson et al. (Jl of Trauma, 2009) found increase risk of MOF and ARDS in those who received plasma transfusion
Figure 1-7. Zones of response to bleeding risk at the time of invasive procedures. The x-axis is meant to depict the product of both platelet number and functional activity. Patients with normal laboratory values are represented by the smallest rectangle. A large number of patients with mild-to-moderate abnormalities of preprocedure laboratory tests are in the zone of physiologic reserve and are not likely to derive any benefit from preprocedure transfusion therapy.
• Better assessment of bleeding risk
• Correction of drug-induced coagulopathy or other bleeding abnormalities
• In-house efforts to limit plasma transfusion
• Education!!!!
• RCTs for prophylactic plasma transfusion (NHLBI/TMH Network, SHIP Study)
Current evidence and risk:benefit assessment in a significant number of clinical situations suggests a more restrictive practice for plasma transfusion (mirrors TRICC Trial for RBC transfusion)

Continued effort to provide quality and safe transfusion practice across all areas of component therapy
THE 4 R’s

TRANSFUSION MUST REPRESENT:

- THE RIGHT PRODUCT for
- THE RIGHT PATIENT @
- THE RIGHT TIME for
- THE RIGHT REASON
Questions?
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