The Trends of Fresh Frozen Plasma Usage in Adults at a Tertiary Care Hospital with an Insight into Transfusion Guidelines



Medical Science

KEYWORDS: Fresh Frozen plasma, appropriate, guidelines

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ABSTRACT

Aim: The aim of this study is to look into the trends of Fresh Frozen Plasma(FFP) usage with an insight into various guidelines.

Material and Methods: Blood Bank records of FFP usage in adults admitted in our tertiary hospital were retrospectively reviewed for one year. It was analysed for usage of FFP in various departments and evaluated for appropriateness of usage based on various criterias. The guidelines published by College of American Pathologists(CAP), National Health and Medical Research Council (NHMRC) and Australasian Society for Blood Transfusion (ASBT) were used as standards.

Results: A total of 1682 units of FFP were issued for 377 adult patients in one year study which included 248 (65.5 %) males and 129 (34.5 %) females with a mean age of 51 years. The most predominant usage of FFP was seen in Medicine Intensive Care Unit followed by Surgery Intensive Care Unit.

Conclusion: This study highlights the non adherance to guidelines among clinicians.

INTRODUCTION

There is shortage of blood and blood components in most of the developing world. Appropriate use of blood components is required to ensure their availability for needy patients and to avoid risk of transfusion transmitted diseases. Fresh Frozen Plasma (FFP) is a blood product extracted from plasma and frozen to -30 degree C or below within 6 hrs of collection. FFP from a standard donation of whole blood(450 ml) usually measures 175-250 ml and it contains 70-80 units of factors VIII , IX, VWF and other clotting factors.

FFP is widely used in clinical practice³ despite its indications being limited to a few conditions⁴⁻⁵ such as the treatment of bleeding with an abnormal coagulation test result, patients having a bleeding tendency combined with disseminated intravascular coagulation, clotting factor deficiencies and some rare bleeding disorders. Various adverse effects including non hemolytic febrile reaction, allergic reaction due to plasma protein incompatibility and transfusion related acute lung injury may occur during or after FFP transfusion.6-7It is also capable of transmitting viruses like human immunodeficiency virus, hepatitis B virus and hepatitis C virus.1 In certain situations like specific factor or fibrinogen deficiency FFP is not indicated.8 The National Health and Medical Research Council and Australian Society of blood Transfusion, the College of American Pathologists and the British Committee for Standards in Haematology have published guidelines to highlight these issues and to minimize the misuse of FFP.9

Literature search revealed audits of FFP usage in India are scarce. 9

The aim of this study is to evaluate the trends of FFP usage in various departments of our hospital.

MATERIAL AND METHODS

Blood Bank records of FFP usage were retrospectively reviewed for 1year during 1 st January 2012 to 31st December 2012. Patients who received FFP along with other supplements such as Whole blood, Packed red cell, Platelet were also incuded in this study. Patients of age group below 18 are excluded from this study. The following data was collected: demographic data including age, gender and blood group of the patient, date, department of the requesting clinician, number of the units transfused. The guidelines published by CAP, National Health and Medical Research Council (NHMRC) and Australasian Society for Blood Transfusion (ASBT) were used as standards 10-11.

RESULTS:

A total of 1682 units of FFP were issued for 377 adult patients in one year study which included 248 (65.5 %) males and 129 (34.5 %) females with a mean age of 51 years (range 18-84 years).FFP was most commonly transfused in the patients with age group of 18 to 50 years (53%). Medical and Surgical ICU requested most units of FFP followed by Cardiac Care Unit & Burns department. Out of 377 patients who received FFP transfusion 227 patients received only FFP and 150 patients received FFP along with other supplements such as Whole blood, packed cell, platelets and cryoprecipitate.Maximum patients (121) have O+ Blood group followed by B+ Blood group (120) patients. 96 patients had A+ Blood group followed by 23 patients with AB+ blood group. Patients with Rh-ve blood group were rare. Only 8 patients with A- Blood group, 6 with O- Blood group and 3 with B- Blood group were there.

DEPARTMENTS	Total Percentage of Patients received FFP per Department	Total Units of FFP Transfused Per Department	Total Percentage of FFP transfused Per Department
Medicine Intensive Care Unit	20.95%	382	23.01%
Surgical Intensive Care Unit	20.15%	307	18.4%
OBG	10.6%	158	9.51%
CCU	9.5%	215	12.95%
Burns	12.2%	197	11.8%
Medicine	6.3%	77	4.6%
Post Operative Ward	4.77%	79	4.7%
Surgery	3.71%	88	5.3%
Ortho	3.44%	27	1.6%
Intensive Care Unit	3.44%	46	2.77%
Neurosurgical Intensive Care Unit	2.65%	80	4.8%
ENT	2.12%	26	1.56%

Table 1: Distribution of FFP Transfused in different departments

The indications for which patients were given blood group were mentioned in only 70% cases in the data collected from the blood bank. The most common reason was disseminated intravascular coagulation (25%) followed by prolonged coagulation factors and surgery(19%), anemia(11%),Hypovolemic replacement(6%), snake bite(5%), Liver disease(3%), Warfarin reversal(1%).

The most common reasons for FFP usage is sepsis with disseminated intravascular coagulation (DIC), Bleeding and patients undergoing invasive procedures. In our study the use of FFP is clearly appropriate in DIC where there is activation of the coagulation system with consumption of coagulation factors leading to a generalized coagulopathy but according to CAP guidelines, FFP should be given only in setting of bleeding in these patients.¹

In our study for Surgical specialties, FFP is being requested for correction of only mild prolongation of clotting times. For other indications like Liver disease and warfarin reversal, requests are being made in absence of bleeding or planned surgery respectively.

DISCUSSION:

In our study we observed that a total of 1682 units of FFP was used in a year which is only 15 % of all the blood components being used in a year. FFP is a frequently prescribed blood product; its use continues to rise, despite the fact that the supply of plasma derived from allogeneic blood donation is limited. Unfortunately this product is commonly overused or inappropriately used. Many studies have shown a high incidence of inappropriate use of FFP. Significant efforts during the last 20 years have been focused on developing rational criteria for the transfusion of

FFP.(Table 2)¹⁴ Most guidelines use the lab criteria of PT and/or aPTT greater than 1.5 times normal paired with the presence of bleeding or anticipated bleeding. The threshold of PT and aPTT prolongation of > 1-1.5 times normal was based on retrospective studies and PT and aPTT themselves are poor predictors of perioperative bleeding especially in patients with negative bleeding history. Therefore the utility of routine preoperative coagulation testing has been questioned.¹⁵ A bibliographic search of databases , websites revealed 11 guidelines for FFP usage of which 5 were evaluated using standardized criteria.¹⁶ None of the guidelines were complete and well structured in all their parts.

Regardless of how appropriately it is defined , it is readily apparent that physicians do not trust the recommendations offered by these guidelines.14There may be several reasons for this. First, guidelines are old and many doctors may not be aware of their existence. Second, physicians may not be aware of changes in transfusion practice and are relying on outdated knowledge. Junior doctors are taught these outdated practice and the problem is thus perpetuated. Third, in a litigious society, precautionary attitude prevails resulting in overtreatment especially in acute bleeding situations or patients going for invasive procedures when there is the slightest coagulation defect. Lastly, in the age of evidence-based medicine, guidelines for FFP usage are not based on Grade A evidence.

In this study most common and appropriate usage was from the department of Obstetrics & Gynecology for DIC, Antepartum and Postpartum haemorrhage with coagulation defects.

In our study FFP is being used in burns unit to replace massive protein loss as the synthetic albumin is either unavailable or unaffordable by the patients in our country due to its high cost. However the use of FFP should be done judiciously and curtailed as much as possible as it carries many risks.

The next most common misuse was circulatory volume replacement. The use of FFP for the purpose of volume expansion is totally unwarranted. In massive bleeding it has been shown that there is no indication for FFP unless the blood loss is in excess.¹⁸

Grey areas exist. For example, Is prophylactic FFP required for patients with coagulopathy due to DIC and liver disease in the absence of bleeding and invasive procedures? If so, what should be the threshold for transfusion? Is FFP indicated for patients who are bleeding or going for invasive procedure with only mildly prolonged clotting time (less than 1.5 times normal)? Again if so, is there a threshold below which FFP transfusion will not make a clinical difference? These are questions that require studies to answer.¹

Previous studies have shown widespread deficiencies in physicians knowledge regarding transfusion indications and risks 9,13 . Interventions such as educational conferences or multifaceted interventions are considered most effective in changing physicians behavior. 7,19

There are other situations where products more effective and safer than FFP are available for correction of coagulopathy such as recombinant or virally inactivated specific clotting factor concentrates for treatment of hemophilia, von Willebrands disease and hypofibrinogenemic states and prothrombin complex concentrates and Vit K for warfarin reversal. ²⁰⁻²¹

Year 1985 1990	Laboratory criteria None given PT/INR> 1.5 times normal	Dose (ml/kg) None given 10-15
1990	PT/INR> 1.5 times	
		10-15
		,
1992	PT/PTT>1.5 times normal; PT> 1.8 times normal with liver disease	12-15
1994	PT/PTT>1.5 times normal	15
1994	PT> 1.5 times midpoint of normal; PTT > 1.5 times upper normal	6-7
1994	PT/INR > 1.5 times normal	10-15
1994	PT/INR> 1.5 times normal	6-7
1997	Significant increase in coagulation time; PT> 2 with liver disease	10-15
1999	PT/PTT>1.5 times normal	8-12
2001	PT/PTT>1.5 times normal	12-15
2001	Abnormal coagulation	5-20
2002	PT/PTT>1.5 times normal	None given
2003	Disturbed coagulation	15-20
2004	Multiple factor deficiencies	10-15
2004	PT/PTT>1.5 times normal	10-20
	1994 1994 1994 1997 1999 2001 2002 2003 2004	normal; PT> 1.8 times normal with liver disease 1994 PT/PTT>1.5 times normal 1994 PT/PTT>1.5 times midpoint of normal; PTT > 1.5 times upper normal 1994 PT/INR > 1.5 times normal 1994 PT/INR > 1.5 times normal 1994 PT/INR > 1.5 times normal 1997 Coagulation time; PT> 2 with liver disease 1999 PT/PTT>1.5 times normal 2001 PT/PTT>1.5 times normal 2001 Disturbed coagulation 2003 Disturbed coagulation 2004 Multiple factor deficiencies

Table 2: FFP Transfusion Guidelines 14

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Conclusion:

This study highlights the generalized and widespread irrational use of FFP among specialists. To reduce the inappropriate usage of FFP the following strategies may be used:

- 1. Hospital Transfusion guidelines should be established based on existing international guidelines.
- Awareness programmes should be conducted for clinicians regularly.
- 3. Appropriate indications should be incorporated in the request forms to remind doctors.
- 4. Regular evaluation may reduce the inappropriate usage.
- Computerized Transfusion Decision Support System should be designed to be more powerful and effective enough for transfusion practices.

REFERENCE

1. Chng WJ, Tan MK, Kuperan P. An audit of FFP usage in an acute general hospital in Singapore. Singapore Med J. 2003;44:574-8 | 2. Kulkarni N. Evaluation of Fresh frozen plasma usage at a medical college hospital- A two year study.IJBTI.2012;2:16-20 | 3. Triulzi DJ. The art of plasma transfusion therapy. Transfusion. 2006; 46:1268-70 | 4. Crosby E , Ferguson D , Hume HA , et al. Guidelines for red blood cell and plasma transfusion for adults and children. Can Med Assoc J.1997;156(Suppl);S1-12 | 5. O'Shaughnessy DF, Atterbury C, Bolton MP. Guidelines for the use of fresh frozen plasma, cryoprecipitate and cryosupernatant. Br J Haematol. 2004;126:11-28 | 6. Alter HJ, Klein HG. The hazards of blood transfusion in historical perspective. Blood. 2008;112:2617-26 | 7. Chang CS, Lin YC, Wu YC, Yeh CJ, Lin YC. The $effects of computerized Transfusion decision support and its appropriateness for Fresh Frozen Plasma use in a Medical Centre. Am J Clin Pathol. 2011;135:417-22 \mid 8. Bjerrum OS, and the properties of the prope$ Jersild C. Class specific anti-1g A associated with severe anaphylactic Transfusion reactions in a patient with pernicious anaemia. Vox Sang.1971;21:411 | 9. Shinagare SA, Angarkar NN, Desai SR, Naniwadekar MR. An audit of fresh frozen plasma usage and effect of fresh frozen plasma on the pre-transfusion International Normalized Ratio. Asian J Transfus Sci. 2010;4(2):128-32 | 10. Practice parameter for the use of fresh frozen plasma, cryoprecipitate, and platelets. Fresh Frozen Plasma, Cryoprecipitate, and Platelets Administration Practice Guidelines Development Task Force of the College American Pathologists. JAMA. 1994;271 (10):777-81. | 11. National Health and Medical Research Council. Clinical Practise guidelines on the use of blood components (red blood cells, platelets, fresh frozen plasma,cryoprecipitate) 2001. Available at http://www.nhmrc.gov.au/publications/_files/ cp78.pdf.Accessed November 1, 2005. | 12. Parvez A, Naseem L. The Trends of use of Fresh Frozen Plasma at a tertiary care Hospital. International Journal of Pathology.2009; 7(2):88-93. | 13. IorioA, Basileo M, Marchesini E, Palazzesi GP, Materazzi M, | Marchesi M, et al. Audit of the clinical use of fresh frozen plasma in Umbria:Study design and results of the pilot phase. Blood Transfus. 2008;6:211-9. | 14. Holland LL, Brooks JP. Towards Rational Fresh Frozen Plasma Transfusion: The Effect of Plasma Transfusion on Coagulation Test Results.Am | Clin Pathol.2006; 126:133-39. | 15. Ewe K. Bleeding after liver biopsy does not correlate with indices of peripheral coagulation. Dig Dis Sci. 1981;26:388-93. | 16. IorioA, Basileo M, Marchesini E, Palazzesi GP, Materazzi M, Marchesi M , et al. The good use of plasma: A critical analysis of five international Guidelines. Blood Transfus. 2008;6: 18-24. | 17. Critical care of the Burn Patient: The First 48 Hours, Barbara A. Latenser, MD, FACS Critical Care Med. 2009;37 (10):2819-26. | 18. British Committee for Standards in Haematology. Stainsby D, MacLennan S, Thomas D, Issac J, Hamilton PJ. Guidelines on the management of massive blood loss. Br J Haematol. 2006; 135(5):634-4. | 19. Eisenstaed RS. Modifying physicians' transfusion practice. Transfusion Med. 1997; 11:27-37. | 20. Haslindawani WW, Zaidah AW. Coagulation parameters as a guide for fresh frozen plasma transfusion practice: A tertiary hospital Experience. Asian J Transfus Sci. 2010; 4:25-7. 21. Wilson K, MacDougall L, Fergusson D, Graham I, Tinmouth A, Hebert PC. The effectiveness of interventions to reduce physicians levels of inappropriate transfusion: What can be learned from a | systematic review of the literature. Transfusion.2002; 42:1224-9. |