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Evaluation of fresh frozen plasma usage at a medical college hospital - A two year study

Nagarekha Kulkarni

ABSTRACT

Aims: The aim of this is study was to evaluate the usage of fresh frozen plasma (FFP) according to indications and to reduce inappropriate usage. Methods: A two year retrospective study was conducted in Medical College Hospital blood bank. Based on the guidelines published by College of American Pathologists, National Health and Medical Research Council and Australasian Society for Blood Transfusion FFP usage were categorized into appropriate and inappropriate. Pre and post-transfusion INR/PT were recorded and the effect of FFP were studied in patients who received FFP. Results: During two years 1884 units of FFP were used for 945 patients. Only 454 (48%) requests were appropriate and 491 (52%) were inappropriate requests. Absence of bleeding or surgical intervention was the commonest reasons for inappropriate FFP use. Mean improvement in the pre-transfusion INR per unit of FFP was 0.75 (median 0.56, range 0–3.7) of which 33% showed significant improvement in the pre-transfusion INR. Conclusion: Our results showed a 48% appropriate and 52% inappropriate use of FFP in patients. Inappropriate FFP use could be reduced by educating the staff, by establishing the hospital transfusion guidelines, by regular evaluation of requistions and by conducting awareness programme among clinicians.

Keywords: Appropriate, Inappropriate, Fresh frozen plasma

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INTRODUCTION

There is shortage of blood and blood components in most of the developing world. The resources are inadequate in terms of meeting the ever growing demand of blood components especially platelets. Appropriate use of blood components is required to ensure their availability for needy patients as well as to avoid the unnecessary risk of transfusion transmitted diseases [6]. Each donation of whole blood can be used to create as many as four different products (packed red cell concentrate, platelet concentrate, fresh frozen plasma and cryopreciptate) that can be transfused to patients. If plasma unit is isolated from the unit of whole blood and frozen within eight hours from donation, the unit is termed fresh frozen plasma (FFP). FFP from a standard donation of whole blood (450 ml) usually measures 175–250 ml and it contains 70–80 units of factor VIII, IX, VWF and other clotting factors. The use of FFP has significantly increased in the past 10

years. There are certain situations where FFP is clearly indicated such as coagulation deficiency secondary to liver disease, DIC, dilutional coagulopathy due to massive blood transfusion, in infants with secondary immunodeficiency, antithrombin deficiency and open heart surgery [1] .

FFP contains antibodies against ABO antigens and is capable of causing complications like hemolytic transfusion reactions and transfusion related acute lung injury. It is also capable of transmitting transfusion transmissible infections. Other complications like allergic reaction and fluid overload associated with blood transfusion can also occur with plasma infusion. Hence, the use of FFP is not without potential damage. In certain situations like specific factor or fibrinogen deficiency FFP is not indicated [2].

In spite of improvement in quality control, standardization and available guidelines about use of FFP, there are many studies around the world which report a high frequency of inappropriate use of this blood component. The appropriate use of FFP requires an understanding of the properties of FFP and its inadequacies as well as an appreciation of the complications. The college of American Pathologist (CAP) and British committee for standards in hematology have published guidelines to highlight these issues and minimize the misuse [3, 4]. Literature search revealed only few audits from India [2].

The aim of this is study was to evaluate the usage of FFP according to indications and to reduce inappropriate usage.

MATERIALS AND METHODS

A two years restrospective study was conducted in a Medical College Hospital, blood bank during the period Janaury 2010 to December 2011. Case records of all the patients were reviewed. The patients in whom FFP was requested and transfused were included in this study. In order to study the effect of FFP transfusion on international normalized ratio (INR), patients who received FFP along with other supplements such as whole blood (WB) and packed red cell concentrate (PRC) were excluded from this calculation except for five patients who received vitamin K along with FFP. The following data was collected: demographic data including age and gender of the patient, provisional clinical diagnosis, indications for FFP, department of the requesting clinician, date of transfusion, number of units transfused and coagulation profile of the patient. The guidelines published by CAP, National Health and Medical Research Council (NHMRC) and Australasian Society for Blood Transfusion (ASBT) were used as standards as shown in tables 1 and 2 [3, 5]. Fresh from plasma infusion of 10–15 ml/kg body weight of the patient were considered as adequate dose. If FFP infusion was according to the above mentioned guidelines it was categoried as appropriate transfusion otherwise as inappropriate transfusion. Patients were screened for bleeding disorder, vitamin K deficiency and haematological malignancies. Requisition for FFP and transfusion was based on decision of the clinicians. The PT (prothrombin time) was assayed and INR calculated on a single test coagulometer. The pre and post –transfusion PT/INR were calculated in order to study the effect of FFP. The post-transfusion PT/INR was done within one hour of completion of transfusion. The improvement in the INR per unit of FFP was calculated. Appropriateness and inappropriateness was calculated for each transfusion.

Table 1: FFP Transfusion guidelines, college of american pathologist, 1994 [3].

1. History or clinical course suggestive of a coagulopathy due to a congenital or acquired deficiency of coagulation factors with active bleeding or other invasive procedures. This must be documented by at least one of the following: a. Prothrombin time (PT) greater than 1.5 times mid point of normal range. b. Activated partial thromboplastin time (APTT) greater than 1.5 times the top of normal. c. Coagulation assay of less than 25% activity.
2. Massive blood transfusion :replacement of more than one blood unit within several hour's with evidence of a coagulation deficiency as above with continued bleeding.
3. Reversal of warfarin effect: If immediate haemostasis is required to stop active bleeding or prior to emergency surgery or an invasive procedure (PT>18 seconds or INR>1.6).
4. Prophylactically for surgery or invasive procedures in cases of documented congential or acquired coagulation factor deficiency.
5. Deficiency of antithrombin, heparin cofactor 11 protein C or protein S.
6. Plasma exchange for thrombotic thrombocytopenic purpura or haemolytic uraemic syndrome.

Table 2: National Health and Medical Research Council and the Austrralasian Society for Blood Transfusion guidelines for transfusing fresh frozen plasma, 2002 [5].

Appropriate if any one of the following applicable, likely to be inappropriate if none applicable
1. INR or APTT high and liver disease before major surgery or invasive procedure
2. INR or APTT high and liver failure
3. INR or APTT high and acute disseminated intravascular coagulation
4. INR or APTT high and excessive bleeding
5. INR or APTT high before an invasive procedure
6. INR or APTT high before, during or major surgery
7. INR high and warfarin effect present and massive blood loss or emergency surgery
8. Correction of single factor deficiency when a specific factor was not available
9. Treatment of thrombotic thrombocytopenic purpuras

RESULTS

A total of 1884 units of FFP were issued for 945 patients in our study group. There were 542 (57.35%) males and 423 (42.65 %) females with a mean age of 20 years (range 1–55 years). FFP was most commonly transfused in the patient age group of 12–22 years. Most number of FFP units requested were from obstetrics and gynaecology department (23.28%) followed by paediatrics (19.25%) and general medicine (16.08%) as shown in table 3. The most common indication was DIC (27.38%) followed by surgical bleeding (19.95%), chronic liver disease (19.74%), accidents and emergencies (9.17%), protein energy malnutrition (8.81%), coagulation factor deficiency (7.43%), hypovolaemic replacement (6.36%) as shown in table 4. FFP was transfused to 945 patients out of which 454 (48%) were appropriate and 491 (52%) were inappropriate transfusions as per published guidlines. Highest appropriate request were from obstetrics and gynaecology department (31.71%) followed by general medicine (18.06). Highest inappropriate request was from the department of paediatrics (20.57%).

Out of the 454 patients who received appropriate FFP transfusions, 331 patients reecieved only FFP and 123 received FFP along with other supplements such as WB, PRC or vitamin K. In order to study the effect of FFP transfusion on INR, patient who received other supplements were excuded, except for five patients who received vitamin K along with FFP. Vitamin K requires four to eight hours to exert its effect and the post transfusion PT/INR assay was done within one hour of transfusion. Pre- and post-transfusion INRs were compared in 336 patients. In this group of patients INR or PT was recorded prior to FFP transfusion 292 (87%) cases and <24 hours after FFP transfusion in 183 (54%) cases as shown in table 5. Mean pre- transfusion INR was 3.2 (median 2.4, range 1.4–12). Mean post-transfusion INR was 1.8 (median 1.5, range 0.8–7). The effect of FFP was measured by the difference between the pre-transfusion result and the first recorded post-transfusion INR. The improvement of INR was 0.75 (median 0.56, range 0–3.5) as shown in figure 1. Out of 336 cases, 112 (33%) showed significant improvement in the pre-transfusion INR. Thirty percent cases, received additional units of FFP within 24 hours, following the initial FFP transfusion.

DISCUSSION

Blood components have been in use since many years. To meet patient needs for blood and blood components, our blood bank requires more than 600 donors per month. FFP is a frequently used blood product and evaluation of FFP usage is very important. Inspite of clear guidelines regarding the use of FFP, many studies have shown a high incidence of inappropriate use of FFP [5–8]. Inappropriate use of FFP has a significant impact upon the patient's as well as the hospital staff in the form of healthcare cost, wastage of resources, depriving more needy patient and transmission of infections with unnecessary allergic reactions leading to mortality and morbidity in patients. The blood bank has to evaluate the exisiting trend of utility of FFP to prevent misuse which may lead to shortage and thus deny this blood product to someone in a life threatening situation. Unlike red cell transfusion, where the traditional threshold of 10 g/dl has been found to be unnecessarily high in some settings like surgery and intensive care by prospective randomized studies, such studies do not exists for FFP [9]. According to British Committee for Standards in Haematology guidelines, bleeding history including family history, details of prior surgeries and anticoagulant treatment should be taken prior to surgery. Patient with negative bleeding history do not require routine preoperative coagulation testing [4]. However, some recent papers still recommend routinely performing PT, APTT and platelet count prior to surgery and invasive procedures in adults and children. In the present study, after evaluation of all the requisition

Table 3: Distribution of FFP requests according to different departments.

Sl. No.	Department	No. of requests (n, %)	Units of FFP supplied (n, %)	Appropriate requests (n, %)	Inappropriate request (n, %)
1.	General Medicine	152 (16.08)	400 (21.23)	82 (18.06)	70 (14.25)
2.	Medicine ICU	70 (7.45)	92 (4.88)	25 (5.50)	45 (9.16)
3.	Surgery	112 (11.85)	256 (13.58)	34 (7.48)	78 (15.88)
4.	Surgery ICU	82 (8.67)	102 (5.41)	32 (7.04)	50 (10.18)
5.	Obs & Gynaec	220 (23.28)	432 (22.92)	144 (31.71)	76 (15.47)
6.	Accidents & Emergencies	65 (6.87)	172 (9.12)	25 (6.0)	40 (8.14)
7.	Paediatrics	182 (19.25)	320 (16.98)	81 (17.84)	101 (20.57)
8.	Orthopaedics	12 (1.26)	12 (0.63)	04 (0.88)	08 (1.67)
9.	Neurosurgery	50 (5.29)	98 (5.25)	27 (5.94)	23 (4.68)
Total		945	1884	454	491

Table 4: Use of FFP as pre disease indication

Sl. No.	Diseases	No. of bags used	Percentage
1.	DIC	516	27.38
2.	Chronic liver disease	372	19.74
3.	Coagulation factor deficiency	140	7.43
4.	Protein energy malnutrition	166	8.81
5.	Hypovolemic replacement	120	6.36
6.	Accidents & Emergency	172	9.17
7.	TTP	22	1.16
8.	Surgical bleeding	376	19.95
Total		1884	100

Table 5: Reporting of coagulation screen tests

Either INR or PT test reported	No. of cases (n = 336)
Before FFP was given	292 (87%)
24 hours after FFP given	183 (54%)

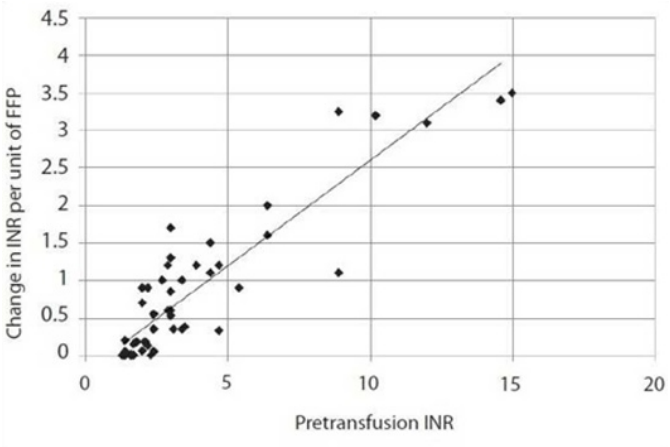

Figure 1: A linear relationship was scan between pretransfusion INR and change in INR per unit of FFP

forms 52% did not fulfill the conditions that constitute appropriate FFP usage. One inappropriate usage was for volume expansion in which other alternatives like plasma expanders should have been used instead of FFP. For coagulation factor deficiency at least 5–6 units of FFP must be transfused to correct the haemostatic defect, however many times only 1–2 units were transfused.

Various published articles also show a high proportion of inappropriate usage and which range from 10–83% [7, 8]. Yeh et al. carried audit on FFP usage and followed it by five sessions of education on transfusion guidelines which resulted in 30% decrease in inappropriate FFP usage [9].

FFP transfusion is appropriate in bleeding patients; patients undergoing invasive procedures with coagulopathy resulting from DIC, massive blood transfusion or liver failure and plasma exchange for thrombotic thrombocytopenic purpura [10–12]. In the present study the appropriate usage of FFP was 48% which is more than the study conducted by Bhat et al. which showed 32.6% appropriate FFP usage [13]. In liver diseases, complete correction of coagulation defect is often impossible and there is no aggrement on the levels of coagulation factors. FFP is considered appropriate in patients with excessive warfarin effect only if they have a massive bleeding or are undergoing emergency surgery. In massive transfusion, there is no evidence that prophylactic replacement of FFP prevents the onset of abnormal bleeding or reduce transfusion requirements. Lastly, there are situations in which FFP is clearly not indicated like volume resuscitation, nutritional support in protein losing states like burns and plasma exchange procedures for conditions other than TTP [12, 14]. In the present study the most common and appropriate FFP usage was from the department of Obstetrics and Gynaeco for DIC, antepartum and postpartum haemorrhage.

As mentioned earlier, the effect of FFP on the pre-transfusion INR was considered in a group of 336 patients. In this group 33% patients showed a significant improvement in the INR per unit of FFP. Shinagare et al. found 64.9% improvement in the INR per unit of FFP and the improvement in the INR was more in those patients who had a high pre-transfusion INR and improvement in the INR was less likely in patients who had a low pre-transfusion INR [15].

CONCLUSION

After evaluating the usages of FFP, it was found that there is a generalized and widespread irrational use of FFP among specialists. To reduce the inappropriate usage of FFP the following strategies may be used:

1. The hospital transfusion guidelines should be established based on exisiting internatonal guidelines.
2. Awareness program for the clinician should be conducted regularly.
3. In the requisition forms the appropriate indication for FFP transfusion should be mentioned to serve as a reminder.
4. Regular evaluation may help to reduce inappropriate use and plays a vital role in overseeing transfusion practives to ensure optimal use of blood and component therapy.

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Author Contributions

Nagarekha Kulkarni – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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