An Audit of Fresh Frozen Plasma Usage in a Tertiary Trauma Care Centre in North India

Neha Agarwal · Arulselvi Subramanian ·
Ravindra Mohan Pandey · Venencia Albert ·
Sulekha Karjee · Vedanand Arya

Received: 19 April 2011 / Accepted: 19 April 2013 / Published online: 15 May 2013
© Indian Society of Haematology & Transfusion Medicine 2013

Abstract Fresh frozen plasma (FFP) transfusion is a crucial part of management of trauma patients. There is a paucity of literature about the audit of appropriateness of FFP use in trauma patients. To evaluate and analyze the appropriateness of FFP transfusion practices for trauma patients. Prospectively compiled blood bank records of FFP transfusion practices over a period of 4 months from Augusts'08 through Deember'08 were retrospectively analyzed for 207 patients. The number of FFP units used in all these trauma patients were evaluated a propos the cause of injury, departments, type of surgery, presence of coagulopathy, bleeding, massive transfusion, length of hospital stay and patient outcome. Trauma scores such as Glasgow coma score and injury severity score were also calculated to estimate the severity of injury. The appropriateness of FFP transfusion was assessed according to the guidelines drafted by the College of American Pathologists. FFP transfusion for patients experiencing active bleeding, micro vascular bleeding, coagulopathy and/or massive transfusion, was deemed appropriate. Patients receiving FFP were

categorized and individually correlated with the outcome. The influences of other variables which affect patient outcome were excluded using stepwise multivariate logistic regression analysis. *p* value < 0.05 were considered to be statistically significant. A total of 207 trauma patients were included in the study, 183 (88.4 %) males and 24 (11.6 %) females. The FFP use among neurosurgery patients was 46.9 %, general surgery patients 40.6 % and orthopedics 12.6 %. Appropriate use of FFP was 49.5 % according to the CAP guidelines. Trauma patients who required FFP as a part of treatment were categorized as; Patients who had bleeding alone (*n* = 40), bleeding with coagulopathy (*n* = 16), and coagulopathy alone (*n* = 43), and further correlated with the outcome and were found statistically insignificant. The prevalence of appropriate use of FFP at trauma centre was 49.5 %. The FFP use by neurosurgery:orthopedics:general surgery was 5:1:4. The highest appropriate FFP use was by Neurosurgery department (50.5 %). Assessing the pattern of usage and rate of misuse of FFP units, allows us to establish required strategies to improve the state of affairs.

Presentation at a meeting: Presented as a paper presentation in trauma conference November,2009 In JPNATC, AIIMS received 2nd prize for best paper.

N. Agarwal · A. Subramanian (✉) · V. Albert
Department of Laboratory Medicine, Jai Prakash Narayan Apex
Trauma centre, AIIMS, New Delhi, India
e-mail: arulselvi.jpnatc@gmail.com

A. Subramanian · S. Karjee · V. Arya
Department of Blood Bank, Jai Prakash Narayan Apex Trauma
centre, AIIMS, New Delhi, India

R. M. Pandey
Department of Biostatistics, Jai Prakash Narayan Apex Trauma
Centre, AIIMS, New Delhi, India

Keywords FFP · Appropriateness · Guidelines · Coagulopathy

Introduction

Trauma is a serious global health problem. Uncontrolled bleeding is a major reason for around 40 % of trauma-related deaths [1–3]. Life-threatening bleeding in trauma patients is usually caused by a combination of vascular injury and coagulopathy causes of which are multifactorial and interrelated, including consumption and dilution of coagulation factors and platelets, dysfunction of platelets

and the coagulation system, increased fibrinolysis, compromise of the coagulation system by the infusion of colloid, hypocalcaemia, and disseminated intravascular coagulation (DIC) like syndrome [4–9].

Since trauma patients often develop coagulopathy and bleeding, Fresh frozen plasma (FFP) forms an indispensable part of trauma patient management. FFP contains significant amounts of all of the coagulation proteins, both pro coagulant and anticoagulant.

Although guidelines for FFP usage are available, inappropriate employment continues to be significant problem. Furthermore excessive usage can lead to shortage in times of need as well as reduced availability for the production of albumin and immunoglobulins. Therefore, there is a need to use FFP only for specific indications. Hence, scrutinizing FFP consumption is important to lessen its associated misuse and risk.

The present study was done to improve the quality of care provided to patients by ensuring the appropriate use of FFP in patients

Materials and Methods

Retrospective analysis of the Blood Bank records of patients admitted at a level I trauma centre for duration of 4 months (August–December 2008) was carried out. A total number of 207 trauma patients benefitted from FFP transfusion with available clinical and laboratory data were considered for the duration and purpose of the study.

Patients with coagulation disorders, liver disease and those on anticoagulants prior to attaining injury were excluded from the study cohort. Patients with missing clinical or laboratory records were also excluded from the study ($n = 80$).

Clinical records of patients who were admitted with trauma and their corresponding demographics, clinical and transfusion data such as age, sex, Glasgow coma score (GCS), injury severity score (ISS), and indication for FFP transfusion and FAST (focussed abdominal sonography) were recorded. Laboratory investigations namely complete hemogram (Hb, TLC, and DLC) and coagulation profile (PT, APTT) were performed on the Sysmex XE-2100 hematology analyzer and STA Compact coagulation analyzer, respectively. The total number of FFP units transfused during the hospital stay and adverse effects of transfusion were noted from the blood bank records. The presence of coagulopathy was diagnosed if any of the PT or APTT was >1.5 times normal and the INR value was >1.6 . Immediate outcome was assessed in terms of hospital length of stay and mortality. We used the CAP guidelines [10], to assess the appropriateness of each request in relation to the clinical indication.

According to CAP guidelines, patients should be given FFP in case of (a) active bleeding, PT/APTT $> 1.5 \times$ normal, coagulation assay of $<25\%$ activity, (b) microvascular bleeding, massive transfusion, deteriorating status, (c) emergent reversal of warfarin, (d) prophylactically for surgery or invasive procedure in cases of documented congenital or acquired coagulation factor deficiency, (e) deficiency of antithrombin III, heparin cofactor 11, protein C or protein S, (f) hypoglobulinemic states in rare instances, (g) plasma exchange for thrombotic thrombocytopenic purpura or hemolytic uremic syndrome.

Recommended dosage of FFP is 10–15 mL/kg, i.e. up to 3–4 units.

Data Analysis

Data was recorded on a predesigned proforma and managed on an excel spread sheet. Statistical analysis was done using SPSS 15.0 (SPSS Inc. Chicago, IL, USA) statistical software. The statistical significance and association of FFP transfused with the patients immediate outcome was studied according to the patient's variables using Chi square and two way ANOVA tests. The influences of other variables which affect patient outcome such as Glasgow coma and ISSs, length of stay and age were excluded using stepwise multivariate logistic regression analysis. In this study p -values <0.05 has been considered statistically significant.

Results

Among two hundred and seven patients during the study period, 34 were (12 %) females and 183 (88 %) males. The median age was 28.5 years. A total of 1,104 units of FFP were issued during the period of study. The mean FFP used was 4 units (range 1–29 units). 97 (46.9 %) of FFP requests were for neurosurgery patients, 26 (12.6 %) were for orthopedics and 84 (40.6 %) were for General surgery patients. Neurosurgery department requested the most numbers of FFP units (46.9 %) followed by general surgery department (40.6 %).

It was considered appropriate FFP use according to CAP guidelines if the patient had presence of active bleeding, microvascular bleeding, coagulopathy and/or massive transfusion. 16 (16 %) patients had bleeding with coagulopathy, 40 (40 %) had only bleeding and 43 (44 %) patients had coagulopathy with no bleeding. Only 4 patients in the study had massive transfusion (0.01 %). The appropriateness of FFP use at trauma centre was 49.5 %. The highest percentage of inappropriate usage was for orthopedic patients (69.3 %) (Fig. 1).

Fig. 1 The incidence of appropriate use of FFP in various departments of trauma centre

No immediate transfusion reaction was reported on FFP transfusion which could be due to the patient being on ventilator or under sedation.

Trauma patients who required FFP as a part of treatment were categorized broadly under 3 categories: Patients who had bleeding alone ($n = 40$), bleeding and coagulopathy ($n = 16$) and coagulopathy alone ($n = 43$). Massive transfusion was removed from being a separate category due to its reduced sample size ($n = 4$). Figure 2 depicts the mean FFP issued according to indications for FFP transfusion and immediate outcome at the end of the hospital stay. All categories receiving FFP transfusion were further individually correlated with the outcome and found statistically insignificant.

Fig. 2 Mean FFP issued according to the indications for FFP transfusion and immediate outcome at the end of the hospital stay

Multivariate analysis was done after excluding the effects of variables like age, ISS, GCS and hospital length of stay on the outcome of the trauma patients (Table 1). It revealed that FFP transfusion did not have any independent influence on the immediate outcome of trauma patients (dead/discharged).

Discussion

The administration of FFP has increased dramatically in recent years despite the paucity of definitive indications for its use, and the evidence of its potential risks, such as viral hepatitis and possibly acquired immunodeficiency syndrome. Many patients who receive FFP can be managed more effectively and safely with alternative modalities.

Several indications of FFP transfusion given by expert consensus have been reported in the literature since 1985 [11–14]; however there exists discrepancy. First, these guidelines were published a decade or more ago. Second, they were mainly expert consensus rather than recommendations derived from well-conducted prospective randomized controlled studies [15].

Various studies have reported a high incidence of inappropriate use of FFP [16–22]. Appropriate use of FFP must be justified on clinical grounds until better evidence is available. A systematic review by Stanworth et al. [23], to identify and analyze all RCTs examining the clinical effectiveness of FFP, reported that the strongest RCT evidence indicates that the prophylactic use of FFP is not significantly or consistently effective across a range of different selected clinical settings. Recently similar review by Kozek-Langenecker et al. [24], concluded that the published evidence does not appear to support the clinical

Table 1 Statistical significance (*p* value) of Fresh Frozen Plasma issued according to the patients variables and indications of FFP Transfusion

Variables	Indication for FFP transfusion in trauma patients		
	Bleeding alone	Bleeding and coagulopathy	Only coagulopathy
Age	0.14	0.10	0.47
Length of stay	0.23	0.59	0.69
Injury severity score	0.37	0.13	0.69
Glasgow coma score	0.45	0.70	0.29

effectiveness of FFP in many situations, and even suggests that it can be detrimental.

In this study we retrospectively analyzed transfusion requests in a tertiary care trauma centre to ascertain their appropriateness according to CAP guidelines. A total of 1,104 units of FFP were mostly given to patients of average age 28.5 years. Neurosurgery department requested the most numbers of FFP units (46.9 %); the highest percentage of inappropriate usage was for orthopedic patients (69.3 %). In a similar retrospective study by Shinagare et al. [25], FFP was most often used in patients of age range 16–30 years, the obstetrics and gynecology department requested the most units of FFP (40 patients, 115 units).

This retrospective study reports an appropriateness of FFP to be 49.5 %, concordantly appropriateness of 47 %, probable appropriateness of 9 % and inappropriateness of 45 % for FFP usage was reported by Luk et al. [18], in 2002. Similarly Pratibha et al. [26] conducted a study in which they demonstrated 40 % appropriate use. Another retrospective study by Iorio et al. for 221 FFP requests showed that indication was appropriate in 31.5 % of the requests and inappropriate in 68.5 % [27]. A recent prospective analysis by Akkaş M et al. [28] reported inappropriate use of FFP in 137 (67 %) of 204 patients.

Similar to our study Chng [15] applied the criteria set by the College of American Pathologists in 1994, only 27 % of the FFP transfusion episodes of nine hundred and thirty-two units of FFP were deemed appropriate.

Our study differs from all others since it exclusively studied only trauma patients in North India. Other published Indian FFP audits have been conducted on a broad range of medical and surgical patients. Two studies have deemed the FFP usage appropriate using guidelines by the National Health and Medical Research Council and The Australasian Society for Blood Transfusion. First reported that 60 % of the patients were appropriately transfused and 40 % were inappropriately transfused [25], and 48 % appropriate and 52 % inappropriate use of FFP in patients was reported by the second in 2012 [29].

A prospective audit by Kakkar et al. [30] identified 304 (60.3 %) prescriptions as inappropriate according to the British Committee for Standardization in Hematology (BCSH) guidelines. The re-audit performed after an educational campaign among clinicians showed a reduction in inappropriate requests by 26.6 %. The specific areas of misuse were FFP transfusions in patients with hypoproteinaemic states (40.5 %), anaemia (36.5 %), bleeding without coagulation factor deficiency (10.2 %) and volume depletion (9.2 %). Another prospective study by Chaudhary [31] using the same guidelines has shown appropriate FFP use of 29.5 % for indications that primarily included chronic liver disease, disseminated intravascular coagulopathy and prolonged bleeding with abnormal coagulation profile. While Makroo [32] in his study showed appropriateness of 69.8 % and deemed 30.2 % of inappropriate FFP requests using the CAP guidelines.

The high rate of inappropriate use reflects the uncertainty among clinicians about appropriate FFP usage. FFP misuse results in wastage and subjecting recipients to unnecessary risk.

Bochicchio [33] studied 1,172 trauma patients during a 2 year period including transfusion rate of blood products (PRBCs, FFP and platelets), and compared the transfusion group of patients with non transfused group. Their univariate analysis revealed that blood product transfusion (any type) is associated with a significantly greater infection rate (34 % vs. 9.4 %, $p < 0.001$), hospital length of stay (18.6 vs. 9 days), $p < 0.001$, ICU length of stay (13.7 vs. 7.4 days) and mortality (19 % vs. 8.3 %). Risk of death was observed to increase by 3.5 % for every unit of FFP transfused [34]. However in the present study no association of FFP transfusion to immediate patient mortality was seen.

Conclusions

The appropriate use of FFP requires an understanding of the properties of FFP and its inadequacies, as well as the appreciation of the complications of its usage. We observed a prevalence of 49.5 % appropriate use of FFP in our hospital. The FFP use by neurosurgery: orthopedics: general surgery department was 5:1:4. FFP was mostly used among neurosurgery patients (46.9 %) followed by general surgery trauma patients (40.6 %). The highest appropriate FFP use was by neurosurgery department (50.5 %). More studies on definite clinical indications of FFP transfusion, including the clinical presentation of emergency trauma patients with shock, arterial blood gas and serum electrolyte results which help in identifying patients with subtle shock changes.

FFP transfusion does not have any independent influence on the immediate hospital outcome of trauma patients (dead/discharged). The present study is the first step in the formulation of a FFP transfusion protocol and guidelines for our institute. Assessing the pattern of usage and rate of misuse of FFP units, allows us to establish required strategies to improve the state of affairs. Further studies are required to assess the causes of inappropriate FFP usage by the individual departments of our center. Unnecessary transfusions should be avoided by better decision-making with regard to the use of blood components based on defined guidelines. A continual system of staff education and administrative intervention a propos FFP usage is recommended. Transfusion guidelines should be included in all junior doctor handbooks and included in all new doctors' hospital orientation program

References

- Holcomb JB (2004) Methods for improved hemorrhage control. *Crit Care* 8(Suppl 2):S57–S60
- Hoyt DB (2004) A clinical review of bleeding dilemmas in trauma. *Semin Hematol* 41:40–43
- Sauaia A, Moore FA, Moore EE et al (1995) Epidemiology of trauma deaths: a reassessment. *J Trauma* 38:185–193
- Gando S, Nanzaki S, Sasaki S, Kemmotsu O (1998) Significant correlations between tissue factor and thrombin markers in trauma and septic patients with disseminated intravascular coagulation. *Thromb Haemost* 79:1111–1115
- Gando S, Tede I, Kubota M (1992) Posttrauma coagulation and fibrinolysis. *Crit Care Med* 20:594–600
- Kapsch DN, Metzler M, Harrington M, Mitchell FL, Silver D (1984) Fibrinolytic response to trauma. *Surgery* 95:473–478
- Miller RD, Robbins TO, Tong MJ, Barton SL (1971) Coagulation defects associated with massive blood transfusions. *Ann Surg* 174:794–801
- Reiss RF (2000) Hemostatic defects in massive transfusion: rapid diagnosis and management. *Am J Crit Care* 9:158–165
- Risberg B, Medegard A, Heideman M et al (1986) Early activation of humoral proteolytic systems in patients with multiple trauma. *Crit Care Med* 14:917–925
- College of American Pathologists (1994) Practice parameter for the use of fresh-frozen plasma, cryoprecipitate, and platelets. *JAMA* 271:777–781
- O'Shaughnessy DF, Atterbury C, Bolton Maggs P, Murphy M, Thomas D, Yates S (2005) Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. *Br J Haematol* 126:11–28
- Office of Medical Applications of Research (1985) National Institutes of Health: Fresh-frozen plasma: indications and risks. *JAMA* 253:551–553
- American College of Obstetricians and Gynecologists (1984) Blood component therapy, Technical Bulletin No. 78. American College of Obstetricians and Gynecologists, Washington
- British Committee for Standards in Haematology (1992) Guidelines for the use of fresh frozen plasma. *Transfus Med* 2:57–63
- Chng WJ, Tan MK, Kuperan P (2003) An audit of fresh frozen plasma usage in an acute general hospital in Singapore. *Singapore Med J* 44(11):574–578
- Beloeil H, Brosseau M, Benhamoud D (2001) Transfusion of fresh frozen plasma (FFP): audit of prescriptions. *Ann Fr Anesth Reanim* 20:686–692
- Schofield WN, Rubin GL, Dean MG (2003) Appropriateness of platelet, fresh frozen plasma and cryoprecipitate transfusion in New South Wales public hospitals. *MJA* 178:117–121
- Luk C, Eckert KM, Barr RM, Chin-Yee IH (2002) Prospective audit of the use of fresh-frozen plasma based on Canadian Medical Association transfusion guidelines. *Can Med Assoc J* 166:1539–1540
- Blumberg N, Laczin J, McMican A et al (1986) A critical survey of fresh-frozen plasma use. *Transfusion* 26:511–513
- Brien WF, Butler RJ, Inwood MJ (1989) An audit of blood component therapy in a Canadian general teaching hospital. *Can Med Assoc J* 140:812–815
- Jones P, Jones A, Al-Ismail SS (1998) Clinical use of FFP: results of retrospective process and outcome audit. *Transfus Med* 8:37–41
- Mozes B, Epstein M, Bassat BI et al (1989) Evaluation of the appropriateness of blood product transfusion using present criteria. *Transfusion* 29:473–476
- Stanworth SJ, Brunskill SJ, Hyde CJ, McClelland DB, Murphy MF (2004) Is fresh frozen plasma clinically effective? A systematic review of randomized controlled trials. *Br J Haematol* 126(1):139–152
- Kozek-Langenecker S, Sørensen B, Hess JR, Spahn DR (2011) Clinical effectiveness of fresh frozen plasma compared with fibrinogen concentrate: a systematic review. *Crit Care* 15(5):R239
- Shinagare SA, Angarkar NN, Desai SR, Naniwadekar MR (2010) An audit of fresh frozen plasma usage and effect of fresh frozen plasma on the pre-transfusion international normalized ratio. *Asian J Transfus Sci* 4(2):128–132
- Pratibha R, Jayarane S, Ramesh JC, Lopez CG, Vasanthi N (2001) An audit of fresh frozen plasma usage in a tertiary referral centre in a developing country. *Malaysian J Pathol* 22(2):41–46
- Iorio A, Basileo M, Marchesini E, Palazzesi GP, Materazzi M, Marchesi M et al (2008) Audit of the clinical use of fresh-frozen plasma in Umbria: study design and results of the pilot phase. *Blood Transfus* 6:211–219
- Akkaş M, Kömür Ataman D, Akman C, Metin Aksu N, Karaca MA, Aksu S, Özmen MM (2011) Inappropriate Fresh Frozen Plasma use in coagulation disorder. *Eur J Surg Sci* 2(2):38–41
- Kulkarni N (2012) Evaluation of fresh frozen plasma usage at a medical college hospital—a two year study. *Int J Blood Transfus Immunohem* 2:16–20
- Kakkar N, Kaur R, Dhanoa J (2004) Improvement in fresh frozen plasma transfusion practice: results of an outcome audit. *Transfus Med* 14:231R–235R.
- Chaudhary R, Singh H, Verma A, Ray V (2005) Evaluation of fresh frozen plasma usage at a tertiary care hospital in North India. *ANZ J Surg* 75:573–576
- Makroo RN, Raina V, Kumar P, Thakur UK (2007) A prospective audit of transfusion requests in a tertiary care hospital for the use of fresh frozen plasma. *Asian J Transf Sci* 1(2):59–61
- Bochicchio GV, Napolitano L, Joshi M, Bochicchio K, Meyer W, Scalea TM (2008) Outcome analysis of blood product transfusion in trauma patients: a prospective, risk-adjusted study. *World J Surg* 32:2185–2189
- Schots J, Steenssens L (1994) Blood usage review in a Belgian university hospital. *Int J Qual Health Care* 6(1):41–45