TERUMO PENPOL REVIEW
ON BLOOD MANAGEMENT SYSTEMS

JUL-SEP 18 NUMBER 95

Desai P, Navkudkar A, Rajadhyaksha SB. Evaluation of utilization pattern of fresh frozen plasma in a tertiary care oncology center. Glob J Transfus Med 2018;3109-12.

Published in every quarter by TERUMO PENPOL Private Limited

TERUMO PENPOL ®

Evaluation of Utilization Pattern of Fresh Frozen Plasma in a Tertiary Care Oncology Center

Priti Desai, Anisha Navkudkar, Sunil B Rajadhyaksha

Department of Transfusion Medicine, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India

Abstract

Introduction :

Blood component therapy is widely used in an oncology center. Fresh frozen plasma (FFP) transfusions are mainly used for the treatment of certain clinical conditions such as coagulation derangements. Transfusion audits are important to understand clinical transfusion practices. This study evaluates the utilization pattern of FFP in a tertiary care oncology center.

Materials and Methods: Retrospective analysis of 1338 FFP transfusions in 216 patients was done for 3 months. Analysis according to age, sex, clinical indications, requesting clinical unit, time of requisition and pre- and post-transfusion prothrombin time (PT), activated plasma thromboplastin time (aPTT), and international normalized ratio (INR) was carried out.

Results: Of 1338 FFP transfusions, 63% transfusions were in males and 37% in females. Adult patients received 75% while pediatrics received 25% of all transfusions. Surgical oncology patients received maximum transfusions (56%), followed by medical oncology (41%) and least by radiation

oncology (3%). Based on clinical indications, patients with deranged coagulation profile required maximum transfusions (55%) followed by bleeding patients (43%) and least for patients with disseminated intravascular coagulation (2%). Mean pre- and post-transfusion PT, aPTT, and INR values were 25.6 s, 36.8 s, 2.1 and 20.56 s, 31.9 s, and 1.6 respectively; it was statistically significant ($P < 0.05$).

Conclusion :

FFP transfusion plays a significant role in oncology patients as many of them experience deranged coagulation during the course of treatment. Evaluation of utilization pattern would help in better understanding of clinical transfusion practices.

Keywords :

Clinical transfusion practices, coagulation derangements, fresh frozen plasma transfusions, transfusion audit

Introduction

Blood component therapy is an important aspect of patient blood management in various clinical conditions. Each unit of donated whole blood can be separated into red cells, platelet concentrate, and plasma. Plasma is prepared from whole blood donations (platelet-rich plasma or buffy coat methods) or is collected by plasmapheresis. Fresh frozen plasma (FFP) is fresh plasma separated from the whole blood not later than 6–8 h of collection and frozen solid at -30°C or lower as early as possible.[1,2] FFP contains factor VII, IX, von Willebrand factor, and other clotting factors along with plasma proteins. As compared to packed red cells and platelet concentrates, FFP usage is less, but its use has increased over the past two decades.[3] General indications for plasma transfusion include coagulation factor deficiency, consumptive coagulopathy such as disseminated intravascular coagulation (DIC), dilutional coagulopathy due to massive transfusion, coagulopathy of liver disease, thrombotic microangiopathic hemolytic anemia including thrombocytopenic purpura, hemolytic uremic syndrome, and reversal of warfarin anticoagulation.[4-6] In addition to Vitamin K, guidelines recommend plasma for reversal of over-anticoagulation but only in patients with major bleeding (BL). However, in the absence of major BL associated with over-anticoagulation, primary treatment should be initiated

with oral/intravenous Vitamin K.[7]

Plasma transfusion is not without risk, and certain complications are more likely with plasma than other blood components. Risks commonly associated with FFP include transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload, and allergic/anaphylactic reactions. Other less common risks include transmission of infections, febrile nonhemolytic transfusion reactions, and hemolytic transfusion reactions.[3] Despite various available national and international guidelines for FFP transfusion, sometimes FFP transfusion is given inappropriately.[6] Inappropriate use of FFP affects the safety of the recipients as well as workload of transfusion services. Hence, transfusion audits are important to understand ordering and utilization pattern of blood components in any institute. Majority of the transfusion audits are done to study the clinical transfusion practices for packed red cells and platelets, and very few studies are available for FFP usage.[8-14] Our institute is a tertiary care oncology center in an urban part of India. Consistent with the global trend, FFP usage has been increasing in our institute since past few years. This study was taken up to understand the utilization pattern of FFP in a tertiary care oncology center where FFP transfusions are mainly indicated for various coagulation derangement conditions arising in patients suffering with malignancies. The objective of this study is to evaluate the utilization pattern of FFP and to correlate its effect by comparing the pre- and post-transfusion laboratory parameters such as prothrombin time (PT), activated plasma thromboplastin time (aPTT), and international normalized ratio (INR). This may help in anticipating the requirement of FFP to improve the coagulation derangement. It may also help formulate policy to improve utility and reduce wastage of this important blood component by utilizing excess plasma instead for fractionation.

Materials and Methods

To evaluate the utilization pattern of FFP usage, a retrospective analysis of 1338 FFP transfusions in 216 patients was done at tertiary care oncology center from May 2015 to July 2015. Requisition for FFP transfusion was based on the decision of

the clinicians. Following details were collected from the patient's requisition records: demographic data including age and gender, clinical diagnosis, indication for FFP transfusion, time of requisition, and specialty of requesting clinical unit. Institute's guidelines were used as standards for transfusion. A usual dose of plasma of 10–20 mL/kg was considered for transfusion. To study the effect of FFP, atient's laboratory parameters of pre- and posttransfusion PT, aPTT, and INR were analyzed. The improvement in the INR per dose of FFP was calculated. Pretransfusion INR was correlated with the improvement in INR per dose of FFP, using Pearson's linear correlation. Kruskal–Wallis test and Wilcoxon signed rank test were the test of significance applied for comparison between pre- and post-transfusion PT, aPTT, and INR. SPSS software was used for statistical analysis.

Results

A total of 1338 units of FFP were transfused in 216 patients over 3 months which included 131 (61%) males and 85 (39%) females. The mean age for transfusion was 37 years (range: 1–79 years). FFP was most commonly transfused in the patient age group of 25–45 years (30%). FFP transfusions were maximum (56%) in surgical oncology patients (751) followed by 41% in medical oncology patients (544) and least (3%) in radiation oncology patients (43). Of the 751 FFP transfusions of surgical oncology, maximum (50%) were in patients of gastrointestinal surgeries followed by 22% in patients of bone and soft-tissue surgeries, 13% in gynecology patients, 11% in head-and-neck surgeries, 3% in breast surgeries, and 2% in other surgeries [Table 1]. Of the 544 FFP transfusions inhemato-oncology, maximum (51%) were in leukemia patients (especially acute

Table 1: Fresh frozen plasma transfusions in surgical oncology unit

Units	Gastro-intestinal (%)	Bone soft tissue (%)	Gynecology (%)	Head and neck (%)	Breast (%)	Others (%)
DCP	210	103	38	35	14	8
BL	158	59	61	47	12	6
DIC	0	0	0	0	0	0
Total = 751	368 (50)	162 (22)	99 (13)	82 (11)	26 (3)	14 (2)

DCP : Deranged coagulation profile, BL: Bleeding, DIC: Disseminated intravascular coagulation

promyelocytic leukemia [APML]), 17% in lymphoma patients, and 32% in other patients [Table 2]. FFP transfusions were also classified based on clinical indications. Of the total 1338 FFP transfusions, 55% were in patients with deranged coagulation profile (DCP), 43% in BL patients, and 2% in patients with DIC [Figure 1]. Vitamin K was administered in five patients with DCP, but it did not restore the coagulation factors and subsequent FFP transfusion proved fruitful. FFP transfusion was not used as a volume expander in any patient.

Mean pretransfusion PT, aPTT, and INR values were 25.6 s, 36.8 s, and 2.1, respectively, while the posttransfusion values were 20.56 s, 31.9 s, and 1.6, respectively [Table 3]. Difference in pre- and post-FFP transfusion in patients of DCP, BL, and DIC was significant ($P < 0.5$), indicating FFP transfusion showed a significant improvement in posttransfusion PT, aPTT, and INR.

Discussion

Blood is a scarce product obtained only from human beings; hence, it should be

Table 2 : Fresh frozen plasma transfusions in medical oncology units

	Leukemia (%)	Lymphoma (%)	Others (%)
DCP	166	19	110
BL	81	74	66
DIC	28	0	0
Total = 544	275 (51)	93 (17)	176 (32)

DCP: Deranged coagulation profile, BL: Bleeding, DIC : Disseminated intravascular coagulation

Table 3: Mean pre- and post-transfusion prothrombin time, activated plasma thromboplastin time, and international normalized ratio values

Comparison of pre- and post-transfusion PT, aPTT, INR			
Parameter	**DCP**	**BL**	**DIC**
Pretransfusion PT	33.15	24.28	30.36
Posttransfusion PT	26.16	18.55	28.32
P	0	0	0.001
Pretransfusion aPTT	36.78	36.52	34.71
Posttransfusion aPTT	32.46	30.6	32.41
P	0	0	0.021
Pretransfusion INR	2.49	1.92	2.49
Posttransfusion INR	1.74	1.36	2.27
P	0	0	0.002

PT : Prothrombin time, aPTT : Activated plasma thromboplastin time, INR: International normalized ratio, DCP : Deranged coagulation profile, BL: Bleeding, DIC: Disseminated intravascular coagulation

used with caution. It is very essential that blood and its components should be used appropriately and judiciously. Each requisition for blood transfusion should have clinical indication supporting it and should not be based only on laboratory parameters. In spite of having local and national guidelines for FFP usage, a few studies mention high incidence of inappropriate use.[13,15] Inappropriate use of FFP can have an impact on patients' safety as plasma transfusion may lead to transmission of transfusion-transmissible infections, allergic reactions, TRALI, volume overload, etc. It is also necessary to rationalize plasma therapy, as many important products of fractionation such as albumin, globulin, and factor VIII and IX are prepared from plasma. Most of the audits related to FFP transfusions were conducted in general hospital, while the present audit is one of its kinds which evaluates utilization pattern of FFP transfusions in an oncology center. Hence, only a few parameters were comparable with the general hospital FFP usage. It was observed in the present study that patients of surgical oncology required maximum transfusions followed by hemato-oncology and least by radiation oncology. In surgical oncology unit, patients with gastrointestinal cancers required maximum FFP transfusions. This was probably due to underlying hepatic function derangements causing DCP and BL. A study by Moiz et al. showed that patients with maximum FFP transfusions had DCP due to hepatic dysfunction.[16] Study by Jayanthi et al. observed that patients with liver disease had maximum FFP transfusions.[17] From Hemat-oncology, patients with leukemia especially APML required maximum FFP transfusions due to DCP.

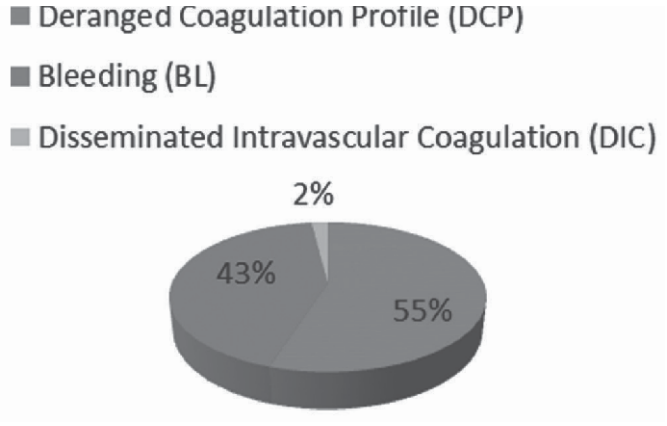

Figure 1 : Transfusions based on clinical indications

There is evidence that APML blasts express tissue factor and secrete interleukin 1, inducing activation of the coagulation cascade.[18,19] Rafael et al. showed that coagulation activation, fibrinolysis, and proteolysis are three major mechanisms leading to DCP in such patients.[20] Hence, once APML is suspected, an aggressive treatment along with transfusion support is the key to reduce morbidity and mortality. Based on clinical indications, patients with DCP required maximum FFP transfusions followed by surgical BL patients and least by DIC. Study by Moiz et al. showed 54% FFP transfusions in patients due to DCP.[16] P values of patients with DCP and BL in pre- and post-transfusion PT, aPTT, and INR were 0 ($P < 0.5$, significant) and P value of DIC in pre- and post-transfusion PT, aPTT, and INR was 0.001, 0.021, and 0.002, respectively, indicating FFP transfusion showed a significant improvement in posttransfusion PT, aPTT, and INR. Although the posttransfusion PT, aPTT, and INR values did not reach the normal range, it showed a significant reduction in those values ($P < 0.05$). Vitamin K was administered in five patients with DCP, but it did not restore the coagulation factors and subsequent FFP transfusion proved fruitful. In our study, FFP was not transfused at all as a volume expander. Unlike the study by Shinagare et al. showed that FFP was transfused in 16/100 patients for volume expansion.[21] In these cases, other alternatives such as plasma expanders should have been ideally used instead of FFP. Transfusion audits are important to monitor clinical transfusion practices. This facilitates better inventory management and also improves patient safety.

Limitation

The present study is a single-centered, retrospective study. There is a possibility of having missing information from the requisitions or records of the patients, which was conducted retrospectively.

Conclusion

FFP transfusion plays a significant role in oncology patients as many of them experience deranged coagulation during the course of treatment. Request forms for blood transfusion should mention appropriate clinical indication which aids transfusion therapy.

Regular evaluation of utilization pattern would help in better understanding of

clinical transfusion practices and will ensure optimal use of the blood components.

Furthermore, awareness program for the clinicians should be conducted regularly to help better understanding of transfusion practices.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Brecher ME. Technical Manual. 17th ed. Bethesda, MD: AABB Press; 2011.
2. Ministry of Health and Family Welfare Government of India. Standards for Blood Banks and Blood Transfusion Services, National Aids Control Organisation (NACO). Ministry of Health and Family Welfare Government of India; 2007.
3. Pandey S, Vyas GN. Adverse effects of plasma transfusion. Transfusion 2012;52 Suppl 1:65S-79S.
4. Gurevitz SA. Update and utilization of component therapy in blood transfusions. Lab Med 2010;41:739-44.
5. Stehling L, Luban NL, Anderson KC, Sayers MH, Long A, Attar S, et al. Guidelines for blood utilization review. Transfusion 1994;34:438-48.
6. Wong MP, Droubatchevskaia N, Chipperfield KM, Wadsworth LD, Ferguson DJ. Guidelines for frozen plasma transfusion. BCMJ 2007;49:311-9.
7. Simon TL, McCullough J, Snyder EL, Solheim BG, Strauss RG. Rossi's Principles of Transfusion Medicine. 5th ed. Hoboken (NJ):Willey-Blackwell. 2016. p. 300.
8. Chng WJ, Tan MK, Kuperan P. An audit of fresh frozen plasma usage in an acute general hospital in Singapore. Singapore Med J 2003;44:574-8.
9. Apfelroth S. Standard terminology for plasma products. Transfusion 2003;43:983.
10. Bowden R, Sayers M. The risk of transmitting cytomegalovirus infection by fresh frozen plasma. Transfusion 1990;30:762-3.
11. Walker RH. Special report: Transfusion risks. Am J Clin Pathol 1987;88:374-8.
12. O'Shaughnessy DF, Atterbury C, Bolton Maggs P, Murphy M, Thomas D, Yates S, et al. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. Br J Haematol 2004;126:11-28.
13. Shariff MM, Maqbool S, Butt TK, Iqbal S, Mumtaz A. Justifying the clinical use of fresh frozen plasma – An audit. J Coll Physicians Surg Pak 2007;17:207-10.
14. Kakkar N, Kaur R, Dhanoa J. Improvement in fresh frozen plasma transfusion practice: Results of an outcome audit. Transfus Med 2004;14:231-5.
15. Palo R, Capraro L, Hovilehto S, Koivuranta M, Krusius T, Loponen E, et

al. Population-based audit of fresh-frozen plasma transfusion practices. Transfusion 2006;46:1921-5.

16. Moiz B, Arif FM, Hashmi KZ. Appropriate and inappropriate use of fresh frozen plasma. J Pak Med Assoc 2006;56:356-9.

17. Jayanthi N, Pitchai R. Audit of fresh frozen plasma usage and study the effect of fresh frozen plasma on the pre-transfusion and post – Transfusion international normalized ratio. Int J Curr Med Appl Sci 2015;7:34-9.

18. Zhu J, Guo WM, Yao YY, Zhao WL, Pan L, Cai X, et al. Tissue factors on acute promyelocytic leukemia and endothelial cells are differently regulated by retinoic acid, arsenic trioxide and chemotherapeutic agents. Leukemia 1999;13:1062-70.

19. Cozzolino F, Torcia M, Miliani A, Carossino AM, Giordani R, Cinotti S, et al. Potential role of interleukin-1 as the trigger for diffuse intravascular coagulation in acute nonlymphoblastic leukemia. Am J Med 1988;84:240-50.

20. Rafael HJ, Eduardo MR. Coagulation abnormalities in acute promyelocytic leukemia. Rev Bras Hematol Hemoter 2009;31 Suppl 2:48-50. Available from: http:// www.scielo.br/scielo.php?script=sci_arttext&pid=S1516-84842009000800013&lng=en. [Last accessed on 2017 Oct 02].

21. 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;4:128-32

REGISTERED OFFICE

TERUMO PENPOL Private Limited
I-2 , Jawahar Nagar, Kowdiar P.O,
Thiruvananthapuram - 695003, Kerala, India.
Ph.No : 0471-3015500 / 501
Fax : 0471-2721519
CIN : U33112KL1985PTC004531

www.terumopenpol.com
www.terumobct.com

MARKETING OFFICE

TERUMO PENPOL Private Limited
YGRA-12, TC 4/1399(3),
Kuravankonam, Kowdiar Post,
Thiruvananthapuram - 695003, Kerala, India
Tel : 0471-3015647/649

TERUMO PENPOL®