

An audit of fresh frozen plasma usage in a tertiary referral centre in a developing country

Prathiba R, MBBS, Jayaranee S, MPath, *Ramesh JC, FRCS, Lopez CG, FRCPA and Vasanthi N, DFM.

Unit of Transfusion Medicine, University of Malaya Medical Centre and *Unit of Paediatric Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia.

Abstract

This paper evaluates the practice of fresh frozen plasma (FFP) transfusion at the University Hospital, Kuala Lumpur, and analyses its usage by the various clinical departments. The aim of this study is to identify where it is inappropriately used and the clinical indications in which such misuse is common. A retrospective analysis of the blood bank request forms and work sheets during a 6-month period between January 1998 and June 1998 formed the basis of this study. Overall, 40% of 2665 units transfused were considered appropriate. However, out of the 931 episodes of FFP transfusions only 31% were for appropriate indications. The average FFP requirement when used for appropriate indication was about 4 units per episode, whereas for inappropriate indication it was 2.5 units per episode. Inappropriate use in terms of the number of units was highest by the surgical services (68%) and Orthopaedics (64%), while the Department of Paediatrics had the lowest incidence of inappropriate use (40%). When Paediatrics was used as the benchmark, the incidence of inappropriate use by other departments was significantly higher ($p < 0.01$). As for FFP usage in common clinical indications, there was a high incidence of inappropriate use in burns (82%), perioperative period (73%), cardiac surgery (68%), massive bleeding (62%) and trauma (60%). The findings in this study, specifically the use of FFP for volume support in trauma, massive bleeding and burns, routine requests without identified indication in cardiac bypass surgery, and prophylactic use in the perioperative period can be the basis for recommendations to minimize the inappropriate use of FFP in the future.

Key words: fresh frozen plasma, transfusion, clinical audit

INTRODUCTION

Inappropriate use of fresh frozen plasma (FFP) exposes patients to risk of transfusion transmissible diseases, allergic and haemolytic reactions caused by A and B antibodies. Rarely, antibodies against the patient's granulocytes may cause leukocyte aggregation in pulmonary vessels leading to transfusion related acute lung injury (TRALI Syndrome).¹ Moreover 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. Monitoring FFP utilization is important to reduce not only all the above-mentioned risks and disadvantages but also wastage and cost.

Guidelines for the use of FFP have been developed by several expert groups. The "Practice Parameters for the use of FFP" by the Task Force of the College of American Pathologists in 1994 was used in this study to provide the basis for appropriate use of FFP (Table 1).²

Several studies from the developed countries have identified the magnitude of inappropriate use of FFP along with recommendations to reduce such practices. However, there are very few published reports from the developing countries critically analyzing the practice of FFP transfusion. This study presents an analysis of the practice of FFP transfusion at a tertiary referral centre in a developing country.

MATERIALS AND METHODS

During a 6-month period from January 1998 to June 1998, 2665 units of FFP were provided for 931 transfusion episodes. A transfusion episode in this study was defined as one when FFP was transfused for each request. During the same period, 19,109 patients were admitted to the hospital and 7997 units of blood were provided. The Transfusion Unit records, data from the FFP request forms and work sheets were retrospectively analysed. The results of the coagulation profile for several cases were traced

TABLE 1: Practice parameters for FFP transfusion, College of American Pathologists, 1994

<ol style="list-style-type: none"> 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 procedure. This must be documented by at least one of the following: <ol style="list-style-type: none"> a) Prothrombin time (PT) greater than 1.5 times the mid point of the normal range. (usually greater than 18 seconds). b) Activated partial Thromboplastin time (aPTT) greater than 1.5 times the top of the normal range (usually > 55-60 seconds) (fibrinogen must be functionally normal with a level generally > 1.0 g/l, and the specimen must be free of heparin for the PT and PTT to be accurate). c) Coagulation factor assay of less than 25% activity. 2) Massive blood transfusion: Replacement of more than 1 blood volume (approximately 5000 ml in a 70 kg adult) within several hours with evidence of a coagulation deficiency as in (1) with continued bleeding. 3) Reversal of Warfarin effect: If immediate hemostasis is required to stop active bleeding or prior to emergency surgery or an invasive procedure (PT > 18 seconds; international normalized ratio > 1.6) 4) Documented congenital or acquired coagulation factor deficiency or prophylactically for surgery or invasive procedure. 5) Deficiency of antithrombin III (when a concentrate is not available), heparin cofactor 11, protein C, or protein S. 6) Hypoglobulinemic states in rare instances. 7) Plasmaexchange for thrombotic thrombocytopenic purpura or haemolytic uremic syndrome: 8) Because of all the alternatives available and the many hazards associated with FFP transfusion, the use of FFP as a volume expander or to enhance wound healing is contraindicated.

from the computer data retrospectively. We evaluated all FFP transfusions, classifying them as appropriate or inappropriate according to the recent FFP transfusion guidelines.² In this study, in accordance with practice parameters for the use of FFP, the transfusion was considered appropriate if the prothrombin time or activated partial thromboplastin time was 1.5 times the control values. A FFP transfusion was considered inappropriate if (a) clotting profile was not done / could not be traced and (b) the PT / PTT was < 1.5 times the normal range. Perioperative period in this study includes requests for FFP on the preoperative day, the day of operation and the first postoperative day.

RESULTS

Coagulation studies were done in 653 (70%) out of the 931 transfusion episodes. The PT/PTT was found to be >1.5 times the normal for 289 (31%) episodes and was <1.5 times normal in 364 (39%) episodes. Coagulation profile was not performed in 262 (28%) and could not be traced in 16 (2%) requests. Although, the diagnosis was stated in the request form, the actual indication for FFP transfusion was

mentioned in 381 requests (41%). Fifty-two units were thawed and never used and therefore wasted. This wastage was categorized as inappropriate use.

The major users were from the Departments of Surgery, Medicine and the Intensive Care Units. The use of FFP by the various departments is shown in Tables 2 and 3. The highest inappropriate use was by the Department of Surgery (68%) and the lowest by the Department of Paediatrics (41%) (Tables 2 and 3). Amongst the clinical indications, burns had the highest incidence (82%) of inappropriate use (Tables 4 and 5). Other clinical indications for which FFP was commonly misused were during the perioperative period (73%), cardiac surgery (68%), massive bleeding (62%) and trauma (60%) (Table 2).

DISCUSSION

The safety of FFP currently lies on donor selection, which is based on a questionnaire without confidential interview and screening tests. Both strategies are subject to errors. The inappropriate use of FFP reported in the literature ranges from as high as 96.23% to as low as

TABLE 2: Units of FFP utilised by various Departments

Departments	Units of FFP	Units with appropriate use	Units with inappropriate use
ICU/CCU	1024	404 (39%)	620 (61%)
Surgery	551	179 (32%)	372 (68%)
Medicine	428	196 (46%)	232 (54%)
Paediatrics	220	131 (60%)	89 (40%)
Orthopaedics	154	55 (36%)	99 (64%)
Obstetrics & Gynaecology	127	56 (44 %)	71 (56%)
Accident & emergency	87	35 (40%)	52 (60%)
Otorhinolaryngology	22	6 (27%)	16 (73%)
Others	52	–	52 (100%)
Total	2665	1062 (40%)	1603 (60%)

ICU= Intensive Care Unit; CCU = Coronary Care Unit

TABLE 3: Episodes of FFP utilisation by various Departments

Departments	Number of episodes	Episodes with appropriate use	Episodes with inappropriate use
ICU/CCU	300	99 (33%)	201 (67%)
Surgery	224	61 (27%)	163 (73%)
Medicine	157	48 (31%)	109 (69%)
Paediatrics	94	38 (40%)	56 (60%)
Orthopaedics	54	16 (30%)	38 (70%)
Obstetrics & Gynaecology	46	17 (37%)	29 (63%)
Accident & emergency	36	9 (25%)	27 (75%)
Otorhinolaryngology	5	1 (25%)	4 (75%)
Others	15	–	15 (100%)
Total	931	289 (31%)	642 (69%)

ICU= Intensive Care Unit; CCU = Coronary Care Unit

8.7%, even though guidelines were available in the late eighties.^{3,4} The incidence of inappropriate use in some of the series include; **Shaikh**⁵ (30%), **Snyder**⁶ (32%) and **Marti-Carvaja**¹⁷ (48.7%). The rate of 57% inappropriate use in our institution is similar to these studies. However as these studies highlighted, there is a need to minimize the misuse of FFP.

Although 40% of units of FFP transfused were considered appropriate, in terms of number of episodes, it accounts for only 31%. This shows that when used for appropriate indications, the number of units required per episode is

appreciably higher than when used inappropriately (3.7 units/episode to 2.5 units/episode respectively).

Our study shows several clinical situations where FFP was used inappropriately. Six units of FFP are routinely given at the end of the coronary bypass operation whether there was any excess bleeding or not. This routine practice of FFP transfusion is not justified as excess plasma load can increase antithrombin III availability leading to a **heparin rebound**.⁸ Another reason why FFP transfusion is unjustified is that non-surgical bleeding during

TABLE 4: Units of FFP utilised according to clinical indications

Clinical Indications	Number of units	Appropriate	Inappropriate
Bums	150	27 (18%)	123 (82%)
Surgical (Perioperative)	199	54 (27%)	145 (73%)
Cardiac Surgery	161	51 (32%)	110 (68%)
Trauma	87	35 (40%)	52 (60%)
Massive bleeding	303	114 (38%)	189 (62%)
Liver diseases	173	74 (43%)	99 (57%)
DIVC/ sepsis	229	109 (48%)	120 (52%)
Coagulopathy/ Bleeding tendencies	331	195 (59%)	136 (41%)
Haematological (malignancy)	228	97 (43%)	131 (57%)
Haematological (Paediatric malignancy)	147	61 (41%)	86 (59%)

DIVC = disseminated intravascular coagulation

TABLE 5: Episodes of FFP utilisation according to clinical indications

Clinical Indications	Number of episodes No. (%)	Appropriate episodes PT/ PTT >1.5 No. (%)	Inappropriate episodes PT / PTT < 1.5 No. (%)
Bums	49	6 (12%)	43 (88%)
Surgical- Perioperative	109	30 (28%)	79 (72%)
Cardiac Surgery	43	10 (23%)	33 (77%)
Trauma	36	9 (25%)	27 (75%)
Massive bleeding	119	29 (24%)	90 (76%)
Liver diseases	46	20 (43%)	26 (57%)
DIVC/ sepsis	52	27 (52%)	25 (48%)
Coagulopathy/ Bleeding tendencies	83	44 (53%)	39 (47%)
Haematological (malignancy)	51	14 (27%)	37 (73%)
Haematological (Paediatric malignancy)	57	18 (32%)	39 (68%)

DIVC = disseminated intravascular coagulation

cardiopulmonary bypass is due to platelet dysfunction rather than to deficiency of plasma coagulation factors.^{9,10}

The most common abuse was for circulatory volume replacement. The use of FFP for the purpose of volume expansion is totally unjustified.^{11,12,13} Most of the FFP requests from the accident and emergency services and for massive bleeding were made before the results of coagulation studies were available. As the indication for FFP use was not mentioned in

several of the request forms, it was assumed to be either for volume support or in anticipation of coagulopathy resulting from massive blood loss and/or transfusion. However, both are not valid indications for FFP transfusion. Such practice of FFP requests has also resulted on occasion in non-use of FFP after thawing and these therefore had to be discarded. In massive bleeding it has been shown that there is no indication for FFP unless the blood loss is in excess of 5000 ml.¹² There was a high incidence of misuse of FFP in

bums. Most of the requests in bums were for volume or nutritional support. Usage for such indications is unjustified.

The high rates of inappropriate transfusion may reflect the uncertainty among clinicians about the appropriate laboratory criteria as the basis for FFP usage for clotting support. This is exemplified by 39% of patients receiving transfusion with **PT/PTT** values of <1.5 times the normal range. FFP transfusions prophylactically for patients who do not have abnormal coagulation results, before or after procedures with the potential for haemorrhage is another area of inappropriate use. This was evident from the over utilization of FFP in the peri-operative period by the surgical services and in haematological malignancies requiring procedures such as insertion of central lines. This misuse is largely due to misconceptions regarding the haemostatic effectiveness of FFP.¹³ In the absence of consumption coagulopathy, it has been shown that FFP is unnecessary if whole blood is transfused.^{13,14,15}

Attempts to formulate guidelines for proper FFP use has been faced with controversy and lack of a firm scientific foundation. However, a programme of daily monitoring of FFP usage combined with continuous education had significantly reduced the usage of FFP by 77% at William Beaumont hospital.¹⁶ Systematic review of FFP requests may be more educational and beneficial in the long term compared to a retrospective review. Some centres have also modified the blood products request form to incorporate indications for transfusion, clinical and laboratory.

In conclusion, this study indicates the misuse of FFP to be relatively high in our hospital. By disseminating this information and data it will be possible to create awareness of the high incidence of inappropriate use, especially for volume support and other unidentified indications such as in cardiac bypass surgery, bums, and prophylactic use in the perioperative period. Our findings indicate a need for continuous monitoring and review of all requests for FFP, so as to ensure adherence to guidelines for every episode and clinical situation. In the long-term, limiting the use of blood components only for appropriate indications will result in patients receiving optimal treatment with the lowest risk of side effects, and transmission of infectious agents. This practice will prevent wastage of FFP, avoid shortages in times of crisis and minimise the treatment cost.

REFERENCES

1. Nordhagen R, Conradi M, Dromtorp SM. Pulmonary reaction associated with transfusion of plasma containing anti-5b. *Vox Sang* 1986; 5: 102-8.
2. Fresh-Frozen Plasma, Cryoprecipitate, and Platelets Administration Practice Guidelines Development Task Force of the College of American Pathologists. Practice parameter for the use of Fresh-Frozen Plasma, Cryoprecipitate and Platelets. *JAMA* 1994; 271: 777-81.
3. Pita-Ramirez L, Carbrera Carbajal BE, Ortega Zavala C. Reasons for fresh frozen plasma in a general hospital [abstract]. *Entrez-Pub Med Rev Invest Clin* 1999; 51 (2): 89-92.
4. Feng CS, Tsang SS. A survey of fresh frozen plasma use in a teaching hospital in Hongkong. *Entrez*. 1989; 21 (2): 85-7.
5. Shaikh BS, Wagar D, Lau PM, Campbell EW Jr. Transfusion pattern of fresh frozen plasma in a medical school hospital. *Vox Sang* 1985; 48: 366-9.
6. Synder AJ, Gottschall JL, Menitove JE. Why is fresh frozen plasma transfused? *Transfusion* 1986; 26: 107-12.
7. Marti-Carvajal AJ, Munoz-Navarro SR, Pena-Marti GE, Comunia G. An audit of appropriate use of blood products in adult patients in a Venezuela General University hospital. *Int J Qual Health Care* 1999; 11 (5): 391-5.
8. Shanberge JN, Murato M, Quattrociocchi-Longe T, Van Neste L. Heparin-protamine complexes in the production of heparin rebound and other complications of extracorporeal bypass procedures. *Am J Clin Pathol* 1987; 87:210-17.
9. Harker IA, Malpass TW, Branson HE, Hessel II EA, Slichter S J. Mechanism of abnormal bleeding in patients undergoing cardio-pulmonary by pass: acquired transient platelet dysfunction associated with selective alpha-granule release. *Blood* 1980; 56: 824-34.
10. Moriau M, Masure R, Hurlet A, et al. Haemostasis disorders in open-heart surgery with extracorporeal circulation. *Vox Sang* 1977; 32: 41-51.
11. Kurtz SR. Clinical Practice of Transfusion Medicine. In: Petz LD, editor. *Coagulation Factor Replacement for Patients with Acquired Coagulation Disorders*. 3rd ed. Churchill Livingstone; 1996. p. 433-8.
12. The Office of Medical Applications of Research, National Institute of Health, Bethesda, Md. Fresh Frozen Plasma: Indications and Risks. Proceedings of the Consensus Development Conference on FFP 1984 Sep 24-26. *JAMA* 1985; 253: 551-3.
13. Contreas M, Ala FA, Greaves M, Jones N, Levin M, Machin SJ et al. Guidelines for the use of Fresh Frozen Plasma. British Committee for standards in Haematology, Working party of the Blood Transfusion Task Force. *Transfusion Medicine* 1992; 2: 57-63.
14. Counts RB, Haisch C, Simon TL et al. Haemostasis in massively transfused trauma patients. *AM Surg* 1979; 190: 91-9.
15. Mannucci PM, Federici AB, Sirchia G. Haemostasis testing during massive blood replacement. A study

- of 172 cases. *Vox Sang* 1982; 42: 113-23
16. **Shanberge** JN, Quattrocioni-Longe T. Analysis of fresh frozen plasma usage with suggestion for ways to reduce usage. *Transfusion Medicine* 1992; 2: 189-94.