ORIGINAL RESEARCH PAPER

Volume-8 | Issue-1 | January-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

AN AUDIT OF FRESH FROZEN PLASMA USAGE IN A TERTIARY CARE TEACHING HOSPITAL IN SOUTHERN INDIA: A CROSS-SECTIONAL STUDY

Immunohematology

Suresh B — Assistant Professor, Department of Transfusion Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati.

Chaitanya Kumar IS* — Assistant Professor , Department of Transfusion Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati.*Corresponding Author

Arun R — Associate Professor, Department of Transfusion Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati.

Sreedhar Babu KV — Professor & Head, Department of Transfusion Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati.

ABSTRACT

Background: Fresh Frozen Plasma has been available since 1941. In this study we assessed the extent of usage of FFP and evaluated the appropriateness of usage of FFP and the outcome of patients treated with FFP.

Materials and Methods: A cross-sectional study has been undertaken to evaluate the usage of FFP; in a tertiary care hospital for a period of one year. The FFP transfusions were evaluated according to college of American pathologists guidelines-1994'.

Results: A total of 1746 FFP units have been transfused to 408 patients. The maximum numbers of FFP units, 67.8% were issued to surgical specialties and 32.2% to medical specialties. A total of 964 (55.2%) units were considered inappropriate.

Conclusion: We observed higher rate of inappropriate usage of FFP in our center. We suggest that continual education at regular intervals may help to prevent the inappropriate usage of FFP practices.

KEYWORDS

Fresh frozen plasma, audit, transfusion.

Introduction:

Fresh Frozen Plasma (FFP) is the plasma recovered from a unit of whole blood separated by centrifugation and frozen within six hours after collection and then stored, in a monitored deep freezer, typically -30°C, thawed at 30°C to 37°C before transfusion (1). It may be obtained from plasmapheresis also. Before the availability of specialized concentration products to replace specific clotting factor deficiency, patients with hemophilia were treated with whole blood and FFP. FFP contains near normal levels of most plasma contents including pro-coagulants and inhibitory components of coagulation factors, acute phase reactant proteins, immunoglobulins and albumin, although all levels are diluted by citrate anticoagulant. One unit of FFP prepared from 450 mL of whole blood contains on an average volume of 175-230mL with 1 IU/mL of each factor (including Factors V and VIII), 200 – 400 mg of fibrinogen. The dosage of FFP will be 10-20mL/kg body weight. FFP should be transfused as rapidly as tolerated by the patient. The frequency depends primarily on clinical response. In critically ill patients, higher dose (30mL/kg body weight) should be considered (2). Prothrombin Time (PT) / Activated Partial Thromboplastin Time (APTT) or coagulation assay should be determined before and also within 4 hours of transfusion to know the outcome. A coagulation factor unit is defined as the activity in 1mL of pooled normal plasma, so 100% activity is 1 unit/mL or 100 units/dL. About 30% activity of each of the coagulation factors is required for adequate hemostasis. On an average about 4-6 units of FFP are required to correct coagulation in liver disease/disseminated intra vascular coagulopathy (DIC). With continued hemorrhage, additional doses are needed, if PT is more than 1.5 times that of normal or international normalized ratio (INR) is greater than 1.8 to 2 (3). Because several key clotting factors such as factor VII (3-6 hrs), VIII (12 hours), IX (18-24 hours) have half lives < 24hours, repeated transfusions are required to maintain hemostasis in these situations.

In this study we assessed the extent of usage of FFP in various surgical and medical specialties, evaluated the appropriateness of usage, outcome of patients treated with FFP and noted any adverse reactions.

Materials and Methods

This is a cross-sectional study was carried out at the Department of Transfusion Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh. Blood bank records were reviewed for a period of one year and all FFP requests and transfusion episodes were studied. The case records of the patients for whom FFP was requested were retrieved and analyzed. The particulars of the disease, haemostatic status, coagulation profiles, particularly the PT, APTT and International Normalized Ratio (INR) were noted. The number of units of FFP transfused, the pre and post coagulation profiles of the patients, and the progress of the patients were noted. The guidelines published by CAP were used as standards (Table 1) (4) Usage outside of these indications was deemed inappropriate. Results were tabulated and analysed.

Table 1: College of American pathologists Guidelines-1994.

FFP transfusion guidelines, college of American pathologists, 1994
1) History of clinical course suggestive of a coagulopathy due to a congenital or acquired deficiency of coagulation factors, with active bleeding or invasive procedures. This must be documented by at least one of the following **a.** PT greater than 1.5 times the midpoint normal range **b.** APTT greater than 1.5 times the top of the normal range **c.** Coagulation assay of less than 25% activity.
2) Massive blood transfusion: Replacement of more than one blood volume within several hours with evidence of coagulation deficiency as in (1) 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 when PT > 18 seconds or INR > 1.6 .
4) Prophylactically for surgery or invasive procedure in cases of documented congenital or acquired coagulation factor deficiency.
5) Deficiency of antithrombin, heparin cofactor II, protein C or protein S.
6) Plasma exchange for thrombotic thrombocytopenic purpura or haemolytic uraemic syndrome

Results:

During the above period of one year, a total number of 2,136 FFP units had been transfused to 476 patients. Among these, 390 FFPs issued to 68 patients outside our hospital were not included in the study. Hence 1746 FFPs transfused to 408 patients were taken into our study. On an average each patient was given 3- 4 units of FFP, except for patients undergoing plasmapheresis for whom 15 to 20 units of FFP were used. In our study, out of 1746 FFPs transfused, 964 (55.2%) FFPs were transfused to patients, when INR was not more than 1.5 as stipulated in guidelines. In remaining 782 (44.8%) FFPs were transfused to patients with INR of more than 1.5, but in none it was more than INR 3.0. In these patients the transfusion was considered to be appropriate. Only

782(44.8%) of these transfused FFPs were deemed appropriate based on the CAP criteria. This also means that 964 (55.2%) FFPs may have been wasted. FFP is used by both medical and surgical specialties with cardio thoracic surgery (CT), surgical gastro enterology (SGE), neurology and medicine being the main users. In none of the 408 patients in the study, any adverse reaction during FFP administration was recorded. The case details of patients who were given FFP and expired at a later date were analyzed in particular. Table 2 and 3 shows department and specialty wise distribution of FFP usage and their appropriateness.

Table 2: Departmental wise distribution of FFP

Sr.No	Department	Number of patients took FFP (%)	Number of FFP taken (%)
1.	CT surgery	171 (41.9)	667(38.2)
2.	Surgical GE	70 (17.1)	304 (17.4)
3.	Medical GE	32 (7.8)	132 (7.6)
4.	Neuro surgery	27 (6.6)	98 (5.6)
5.	Neurology	25 (6.1)	358 (20.5)
6.	Casuality	35 (8.6)	79 (4.5)
7.	Cardiology	29 (7.2)	73 (4.2)
8.	Urology	19 (4.7)	35 (2)
	Total	408	1746

Table3: Specialty wise distribution of FFP and their appropriatenes

Sr. No	Specialties	Number of patients took FFP (%)	Number of FFP taken (%)	Appropriate (%)	Inappropriate (%)
1.	Medical	86 (21.1)	563 (32.2)	304 (38.9)	259 (26.9)
2.	Surgical	322 (78.9)	1183 (67.8)	478 (61.1)	705 (73.1)
	Total	408	1746	782 (44.8)	964 (55.2)

Out of 408 patients who received FFP, 44 (10.78%) patients died. Clinical diagnoses of these patients were enlisted in Table 4. But the fatality could not be attributed to FFP transfusion.

Table 4: Departmental wise distribution of fatality.

General Medicine (18)	C T Surgery cases (9)	Surgical GE cases (9)	Casuality (3)	Neurology(3)	Medical G E (2)
1.Snake bite with systemic envenomation – 7 2.OPC poisoning – 1 3.Supervasmol poisoning with ARF – 2 4.Leptospirosis with hepatic encephalopathy with renal failure - 2 5.Dengue fever with thrombocytopenia – 1 6.Post-partum sepsis with ARF – 1 7.Type 2 DM with cellulitis of left lower limb - 1 8.Acute Renal Failure with thrombocytopenia - 1 9.Acute inferior wall MI – 1 10.Infective endocarditis - 1	1.Severe MR -1 2.Severe calcific MS - 2 3.CAD -3 4.Ascending aortic aneurysm -1 5.Post-op case of left atrial myxoma -1 6. Pulmonary embolism-1	1.Hollow viscus perforation (Duodenal/Jejunal) – 3 2.Enteric fistula with pelvic abscess – 1 3.Ca stomach with cholilithiasis – 1 4.Renal failure with hepatic dysfunction – 1 5.Blunt injury abdomen and chest – 1 6.Periampullary carcinoma – 1 7.Carcinoma pancreas - 1	1.RTA with polytrauma with head injury – 3	1.G B S– 3	1.Acute pancreatitis – 1 2.Cirrhosis of liver with esophageal varices – 1

OPC: Organo Phosphorus Compound, ARF: Acute Renal Failure, MI: Myocardial Infarction, MR: Mitral Regurgitation,MS: Mitral Stenosis, CAD: Coronary Artery Disease, Ca: Carcinoma, RTA: Renal Tubular Acidosis.

Discussion:

Fresh frozen plasma is a frequently prescribed blood component. Inappropriate use of FFP exposes patients to risk of transfusion transmissible diseases or allergic and hemolytic reactions caused by A and B antibodies. In rare cases, antibodies against the patient's granulocytes may cause leukocyte aggregation in pulmonary vessels leading to transfusion-related acute lung injury (TRALI) (5). In our study, which aims to analyze the use of FFP and evaluate the audit of the transfusion, we determined that improper use of FFP had a rate of 55.2% and 44.8% were appropriate. This is in concordance with other studies (6, 7, 8). In a study conducted by Moylan et al in Australia, reported that 11% of the FFP transfusions had improper indication and 18% had uncertain indication (9). Luk et al. determined the improper use of FFP to be 45% in Canada (10). In study done by Pahuja et al. a total of 1763 units of FFP were transfused to 560 patients in 877 episodes of requisition. Out of 877 episodes, about 686 (78.2%) requests were found to be inappropriate (6). Sharma J et al from a tertiary care hospital in Mumbai reported 39% inappropriate request for FFP in 2010 (11).

Table 5: comparable data reported over national and international level

Study	Country	Appropriate usage (%)	Inappropriate usage (%)
Pahuja et al (6)	Delhi, India	21.8	78.2
Chng et al (7)	Singapore	27	73
Kaushal ML et al (8)	Shimla, India	22.38	77.62
Moylan et al (9)	Australia	68	32
Luk C et al (10)	-	55	45
Sharma J et al (11)	Mumbai, India	61	39
Lingegowda JB et al(12)	Salem, India	59.3	40.64
In our study	Tirupati, India	44.8	55.2

In a study the most common reported reasons for FFP usage was sepsis with disseminated intravascular coagulopathy, bleeding and patients undergoing invasive procedures (11). In our study also, the most common reasons for FFP usage are Surgery/invasive procedure, Plasma exchange, DIC/snake envenomation. In acute DIC, addressing the underlying cause is the foundation of treatment. In addition, patient should be supported with transfusion of FFP in combination with platelets and cryoprecipitate. If there is no bleeding, blood components are not indicated prophylactically regardless of lab results. Only in known congenital factor deficiencies, when specific factor is not available, prophylactic use is recommended.

In our study, 20.5% of FFPs were utilized for plasmapheresis for Guillain Barre Syndrome (GBS). Koushal M (12) from a tertiary care hospital reported that the use of FFP for GBS was about 6.12%. FFP substitute is currently the standard practice in cardiac surgery. Patients may bleed post-operatively because of surgical causes, platelet dysfunction or residual effects of heparin. Hence after excluding the above causes, FFP should be given when coagulopathy is suspected/ proven. But each patient is different; the clinical situations may vary; the clinician/surgeon should take the decision to use FFP, if either prophylactically or therapeutically before invasive procedure or surgery in bleeding patients. In the absence of facilities or the non availability of lab parameters, the clinical condition of the patient needs to be documented, to assess whether the usage of particular blood component was appropriate.

In our study, we did not observe any fatality due to transfusion of FFP. In case of 44 deaths, it could not be attributed to the FFP transfusion, because there was no documentation of sequence of events during/following transfusion. The exact cause of the death was not assessed.

Conclusion:

FFP should be reserved for situations in which coagulation factor deficiency is thought to be a major problem. In spite of the risks associated with FFP transfusion, its usage in conditions like snake bite with DIC has been noted to show a favorable outcome and so also in the patients undergoing plasma exchange, when Intravenous

Immunoglobulin was unaffordable by the patient due to high cost. There is a need for clinical studies evaluating the efficacy of plasma both in bleeding and non bleeding patients, to understand whether the presumed benefits outweigh the real risks. To the extent possible, the pre and post transfusion lab parameters should be available to assess the efficacy of any blood component. This is possible only with the co-operation of the consultants and with necessary documentation. We suggest that continual education, training and supervising the medical staff at regular intervals may help to prevent the inappropriate usage of FFP practices.

REFERENCES:

1. Department of Health. Fresh frozen plasma. In: Guidelines for the Blood Transfusion Services in the United Kingdom;1:50
2. Arya RC, Wander G, Gupta P. Blood component therapy: Which, when and how much. J Anaesthesiol Clin Pharmacol 2011;27:278-84.
3. Fresh frozen plasma:Indications and risks. National Institutes of Health Consensus Development Conference Statement. Natl Inst Health Consens Dev Conf Consens Statement. 1984;5:4.
4. Fresh-Frozen Plasma, Cryoprecipitate, and Platelets Administration Practice Development Task Force of the College of American Pathologists. Practice parameter for the use of fresh-frozen plasma, cryoprecipitate and platelets. Journal of the American Medical Association 1994; 271:777-81.
5. Nordhagen R, Conradi M, Dromtorp SM. Pulmonay reaction associated with transfusion of plasma containing anti-5b. Vox Sang 1986;51:102-8.
6. Pahuja S, Sethi N, Singh S, Sharma S, Jain M, Kushwaha S. Concurrent audit of fresh frozen plasma: experience of a tertiary care hospital. Hematology 2012;17:306-10.
7. 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.
8. Kaushal ML. Usage of FFP in a Tertiary Care Hospital in Himachal Pradesh. Asian J Transfus Sci 2011;5:63-109.
9. Moylan S, Szabo F, Scott H, Kwok G. Use of fresh-frozen plasma at Royal Darwin Hospital: a retrospective audit. Intern Med J. 2008;38:686-91.
10. Luk C, Eckert KM, Barr RM, Chin-yee IH. Prospective audit of the use of fresh-frozen plasma, based on Canadian Medical Association transfusion guidelines. CMAJ. 2012;166:1539-40.
11. Sharma J, Swarupa B, Prakash D, Charusmita M. Clinical Transfusion Practices: Uses and Misuses of FFP Audit of Fresh Frozen Plasma Usage in Tertiary Care Centre. Asian J Transfus Sci 2011;5:63-109.
12. Lingegowda JB, Jeyakumar JD, Muddegowda PH, Pitchai R, Gopal N, Sinha P. An audit of requests for fresh frozen plasma in a tertiary care center in South India. J Lab Physicians.2016;8:41-4.