Original Article

Appropriate and inappropriate use of Fresh Frozen Plasma

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Abstract

Objective: To analyze the current situation of use and misuse of fresh frozen plasma (FFP) in various clinical situations.

Methods: This was a cross sectional study done at Liaquat National Hospital (LNH) during a period of 4 months from December 2002 to March 2003. About 300 file records of those patients who received fresh frozen plasma were studied. Each file record was checked for the diagnosis of the patient, coagulation profile and doctor's trigger for blood transfusion. The indications of FFP were checked according to guidelines set by British Committee of Standards and Haematology.

Results: Of 1486 units of FFP that were transfused to 300 patients, it was observed that 78.6% (1169 / 1486) of FFP was appropriately transfused while the remaining 21.3% (317/1486 units) was used without any supportive evidence.

Conclusion: Although majority of the plasma was used appropriately, a considerable volume of plasma was also wasted (JPMA 56:356;2006).

Introduction

Fresh frozen plasma (FFP) has been used for treating a variety of clinical disorders since the early days of blood banking and transfusion.[1] However, the use of FFP in hospital practice has been rising over the past several years.[2] There exist only a few firm indications for fresh frozen plasma transfusions and there is a growing consensus that most of the time this blood product is used inappropriately and without any scientific rationale.[3,4] Other alternative and safer forms of treatment are available that can be used instead of plasma.[5] Yet, it has been observed that the use of plasma in hospital practices is rising.

To evaluate the misuse of plasma, the author

critically reviewed various clinical cases that received plasma therapy. The objective of this study was to evaluate the utilization of FFP in various clinical situations and to estimate the appropriateness of plasma transfusion in our setting. This may initiate the process of auditing of blood and of blood products on a regional basis that could help in developing strategies for avoiding wastage of blood and blood products.

Patients and Methods

This was a cross sectional study done in Liaquat National Hospital from December 2002 to March 2003 over a period of 4 months. This is a large, 750 bedded hospital in Karachi with a broad range of medical and surgical specialties. Our transfusion services noted that FFP usage in hospital was very high, so we decided to conduct an audit on this issue with specific aims of assessing our pattern of usage and rate of misuse.

Our blood bank records showed that a total of 1880 FFP units were arranged for the patients admitted in the hospital with various diseases during the study period. Out of these, only 1608 plasma bags were transfused while the requests for the rest of the units were cancelled by the clinicians. The total number of patients who received these transfusions was 332. However, 32 patients were excluded from the study because of non-availability of their records. Thus, the total number of patients during our study period was 300 receiving 1486 units of plasma. The file record of each patient was scrutinized by the author to observe the evidence of coagulopathy, presence of bleeding in the patients and finally the clinical diagnosis and trigger for FFP transfusion. The use of plasma was considered to be appropriate if it met the set criteria laid by the British Committee for Standards in Haemtology (BCSH)[6] (Table 1). According to these guidelines, FFP is indicated in the presence of active or anticipated bleeding and disturbed coagulation in some conditions like massive transfusion, liver disease and cardiopulmonary by pass surgery. Therefore, plasma treatment was regarded as inappropriate in conditions where there was no evidence of active bleeding or its risk due to coagulopathy. In other disorders, there was no ambiguity as either FFP was clearly indicated or contraindicated as per guidelines set by BCSH.

Table 1. Guidelines for FFP transfusion as laid by British Committee of Standards in Hematology and Blood transfusion Task

Definite indications for the use of FFP:
1. Replacement of single factor deficiencies
2. Immediate reversal of warfarin effect
3. Haemorrhagic disease of newborn
4. DIC with evidence of bleeding
5. Thrombotic thrombocytopenic purpura (TTP)

Conditional uses for the use of FFP:
1. Massive transfusion
2. Liver disease
3. Cardiopulmonary by pass surgery
4. Newborns with Septicaemia

No justification for the use of FFP:
1. Hypovolaemia
2. Plasma exchange procedures except TTP
3. Reversal of prolonged INR in the absence of bleeding

Results

The study of 300 patients' file records showed that they received 1486 units of plasma therapy. The majority of the patients (214/300) had appropriate plasma therapy but a substantial number (86/300) had unnecessary transfusions simultaneously.

Those patients in whom plasma infusion was justified were considered in detail in Table 2. Large proportion of these patients had deranged coagulation profile because of liver disease (116/214). These patients were classified under "appropriate" transfusions as they were actually bleeding or underwent surgery and some invasive procedure. The patients who underwent some surgical maneuver or were actively bleeding at the time of FFP transfusions for reversing the effect of warfarin (9/214) were also considered under the same heading. Similarly patients with acute DIC and neonatal septicaemia were also

Table 2. Appropriate use of FFP in various conditions (n=1486).

Clinical situations	Patients (n)	Plasma units (n and %)
Coagulopathy and surgery	35	196 (13.2)
Coagulopathy and invasive procedure	64	334 (22.4)
Coagulopathy and bleeding	67	414 (27.9)
Liver failure and bleeding	14	80 (5.4)
Reversal of Warfarin therapy	09	57 (3.8)
Acute DIC and bleeding	13	62 (4.2)
Haematological malignancy	03	10 (0.6)
Neonatal septicaemia	09	16 (1.1)
Total	214	1169

Table 3. Inappropriate use of FFP in various conditions (n=1486).

Clinical situations	Patients (n)	Plasma units (n and %)
Liver disease without bleeding	21	59 (3.9)
Cardiac by pass surgery	18	72 (4.8)
Infections	05	16 (1.1)
No evidence of coagulopathy	33	148 (9.9)
Coagulation tests not done	04	15 (1.01)
Others	05	07 (0.5)
Total	86	317

appropriately transfused because of coagulopathy and bleeding.

However, a significant proportion of plasma was used without any clear indication (Table 3). The patients who underwent coronary bypass surgery (n=18) had no coagulation abnormality and did not bleed peri-operatively. Similarly patients with liver disease (n=21) had prolonged prothrombin time, yet they were neither bleeding nor undergoing any surgical procedures. Hence, both these groups of patients were classified as inappropriate as the conditional use allowed by BCSH in these situations was not observed. Some patients received FFP for providing immunoglobulins during infections, and yet others were transfused without any evidence of coagulopathy. These patients (n=42) were also placed in the group of inappropriate as there was no justification for transfusions.

Discussion

It is very essential that blood and its components should be used appropriately. The clinicians prescribing such transfusion should have a sound and valid reason for doing so.

There are several reasons that blood transfusion should be done on a scientific basis. Plasma transfusion may lead to transmission of Hepatitis B and C and HIV viruses, allergic reactions, transfusion related acute lung injury and volume overload. Moreover, the blood is a scarce product obtained only from human beings so it should not be wasted. It is also necessary to rationalize plasma therapy, as many important products like albumin, globulin, factor VIII and IX etc. are prepared from plasma.[5]

There are very few firm indications for FFP infusion.[7] Using the guidelines set by the British Committee for Standards in Hematology, 21% of FFP units were inappropriately used in our study. Comparable data has been reported at national and international levels.[8-11] Using BCSH guidelines, 60.3% FFP prescriptions were found inappropriate by Kakkar et al in 2004 which however reduced to 26.6% after educational campaigns of clinicains.[12] Similarly 34% of patients appeared to have received FFP for reasons not clearly within these guidelines in an audit by National blood service hospitals in United Kingdom.[13] A significant proportion of FFP ranging from 37% to 73% was used outside of established international criteria in some audits.[14-16]

In our study, we found that plasma was used inappropriately in conditions like liver diseases, coronary bypass surgeries, infections and some clinical situations where indication of plasma transfusion was either vague or could not be defined.

Severe liver disease is one of the most common clinical indications for transfusion of FFP. The patients with liver disease have several abnormalities that can lead to bleeding like coagulopathy, disseminated intravascular coagulation (DIC), thrombocytopenia and surgical causes as esophageal varices. It is recommended that FFP should be given only when bleeding has taken place due to impaired coagulation or when surgery is anticipated in the patients with liver disease.[17,18]

FFP substitution is currently the standard practice in Cardiac Surgery. It has been claimed that routine use of FFP in coronary artery by pass grafting (CABG) cannot be recommended.[19] Such patients may bleed post operatively due to surgical causes, platelet dysfunction and residual effects of heparin.[20] FFP should be used only with proven coagulation abnormality. Routine prophylactic administration of FFP in uncomplicated elective CABG does not reduce the blood loss or transfusion requirement during or after surgery[21] and this practice is challenged by some.[22] Our audit showed that the patients who underwent elective CABG did not demonstrate any coagulation impairment before surgery or any significant post operative bleed; so, they were grouped as "inappropriate".

FFP should not be given to provide immunoglobulins during infections as commercially prepared immunoglobulins are available.[6] The use of such products minimise the risk of viral transmissions also. Our analysis showed that 16 units of plasma were used in 5 patients suffering from different infections, which was inappropriate.

In our country, no guidelines exist for the indications of blood components including plasma. There is a need to establish definite indications for transfusion of various blood components.

It is desirable that educational programs be arranged for doctors regarding appropriate use of blood to minimize existing ill practices. Also the blood bank associations and haematologists should more firmly adhere to the guidelines. Through continuous teaching programs and perseverance, one can achieve the desired goal.[10] It is also recommended that quality assurance and auditing programs should be started in the blood banks through out the country.

The study though small identified that although a good proportion of plasma transfusions were justified yet considerable proportion of it is also being used with out any appropriate indication.

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References

1. McCullough J. Introduction to Apheresis Donations including history and general principles. In: Mcleod BC, price TH, Drew MJ, eds. Apheresis: principles and practice Bethesda, MD: AABB Press, 1997, pp. 27-44.
2. Kahn RA, Staggs SD, Miller WR, Ellis FR. Use of Plasma products with whole blood and packed red blood cells. JAMA 1979; 242: 2087-90.
3. NIH consensus conference: Fresh frozen plasma: indications and risks. JAMA 1985; 253:551-3.
4. Snyder AJ, Gotschall JL and Menitove JE. Why is fresh frozen plasma transfused? Transfusion 1986; 26:107-12.
5. Britten AFH. A scheme for plasma management in a country blood center. In: Kolins J Britten AFH, Silvergleid AJ eds. American Association of Blood Banks 1982; 109-26.
6. British Committee for standards in Hematology, blood transfusion Task force. Guidelines for the use of Fresh frozen plasma, cryoprecipitate and cryo supernatant. Transfusion Med 1992; 2: 57-63.
7. Cohen H. Avoiding the misuse of fresh frozen plasma. BMJ 1993;307:395-6
8. Schofield WN, Rubin GL,Dean MG. Appropriateness of platelet, fresh frozen plasma and cryoprecipitate transfusion in New South Wales public hospitals. Med J Aust 2003; 178:117-21.
9. Beloeil H, Brosseau M,Benhamou D. Transfusion of fresh frozen plasma(FFP): audit of prescriptions. Ann Fr Anesth Reanim 2001; 20: 686-92.
10. Hameedullah, Khan FA and Kamal RS. Improvement in intra operative fresh frozen plasma transfusion practice-impact of medical audits and providing education. J Pak Med Assoc 2000; 50:253-6.
11. Shariff MM. Are we justifying the clinical uses of fresh frozen plasma? A data from department of Transfusion Medicine Shalamar Hospital Lahore. Proceedings of 7th National Hematology conference of PSH 2005 Feb 11-13, Karachi, Pakistan.
12. Kakkar N, Kaur R and Dhanoa J. Improvement in fresh frozen plasma transfusion practice: results of an out come audit. Transfus Med 2004; 14:231-5
13. http://www.blood.co.uk/hospitals/library/bm/issue/4/BM47.htm
14. Schofield WN,Rubin GL and Dean MG. Appropriateness of platelet, fresh frozen plasma and cryoprecipitate transfusion in New South Wales public hospital. Med J Aust 2003;178:117-21
15. 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. Can Med Assoc J 2002;166: 1539-40
16. Chng WJ,Tan MK and Kuperan P. An audit of fresh frozen plasma usage in an Acute General Hospital in Singapore. Singapore Med J 2003; 44: 574-8.
17. Spector I, Corn M and Ticktin HE. Effect of plasma transfusion on the prothrombin time and clotting factors in liver disease. Eng J Med 1966; 275: 1032-7
18. Mannucci PM, Franchi F, Dioguardi N. Correction of abnormal coagulation in chronic liver disease by combined use of fresh frozen plasma and prothrombin complex concentrates. Lancet 1976; 2: 542-5.
19. Consten E, Henny CP, Eijsman L, Donglemant DA, Van Oers MH. The routine use of fresh frozen plasma in operations with coronary by pass surgery is not justified. J thorac Cardiovasc Surg 1996; 112:162-7.
20. LA Harker, TW Malpass, HE Branson,EA 2d Hessel and SJ Slichter. Mechanism of abnormal bleeding in patients undergoing coronary by pass surgeries. Acquired transient platelet dysfunction associated with selective alpha granule release. Blood 1980; 56: 824-34.
21. Mario KS, Thorsten G, Peter L, Rainer S, Uwe M and Christoph MD. Failure of Autologous fresh frozen plasma to reduce blood loss and transfusion requirements in coronary artery bypass surgery. Anesth 2001; 95: 81-6.
22. Wilhelmi M, Franke U, Cohmert T, Weber P, Kaukemuller J, Fisher S, et al. Coronary artery by pass grafting surgery with out the routine application of blood products: Is it feasible? Eur J Cardiothorac Surg 2001; 19: 657-61