

An Audit of Fresh Frozen Plasma Usage in An Acute General Hospital in Singapore

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ABSTRACT

Background: FFP is often inappropriately used despite existence of guidelines. An audit was conducted with the aim of making recommendations to reduce inappropriate use.

Materials and Methods: A retrospective review of blood bank and electronic medical records of patients given FFP from October to December 2001 in an acute general hospital was undertaken. The criteria set by the College of American Pathologists in 1994 were used as the standards.

Results: Nine hundred and thirty-two units of FFP were used during the study period for 359 transfusion episodes. Only 98 (27%) episodes were deemed appropriate. Percentage of inappropriate requests was similar across specialties. FFP used in the setting of inadequately prolonged coagulation profiles or absence of bleeding or surgical intervention was the commonest reasons for inappropriate use.

Conclusions: Our results showed significant proportion of FFP used outside of established international criteria. There may be many reasons for this and we suggest that a continual system of staff education and administrative intervention may help to reduce the inappropriate usage.

Keywords: fresh frozen plasma, audit, guidelines

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INTRODUCTION

Fresh frozen plasma (FFP) is a blood product produced from plasma which is separated from packed red cells and platelets after centrifugation of donated whole blood and frozen to -30°C or below within six hours after collection⁽¹⁾. It is a good source of coagulation factors, including labile factors V and VIII. Important limitations need to be borne in mind when prescribing FFP. Half-lives of some coagulation factors are short, therefore FFP should be given close to the time of invasive procedure if correction of markedly prolonged prothrombin time (PT) or activated

partial thromboplastin time (aPTT) is required before surgery. For specific factor or fibrinogen deficiency, the volume of FFP required for adequate replacement far exceeds that of specific factor concentrates or cryoprecipitate respectively, and should not be the preferred choice in these situations. Furthermore, viral inactivated or recombinant factors would negate the risk associated with FFP use as listed below.

FFP contains antibodies including those against ABO antigens and is capable of causing antibody-induced complications like haemolytic reactions and transfusion related acute lung injury⁽²⁾. It is also capable of transmitting viruses like human immunodeficiency virus, hepatitis B virus, hepatitis C virus and parvovirus although transmission of agents transmitted by cellular products like herpes virus, malaria and cytomegalovirus has not been reported^(3,4). Other complications like allergic reactions⁽⁵⁾ and fluid overload associated with blood transfusion can also occur with plasma infusion. Hence the use of FFP is not without potential danger.

The appropriate use of FFP requires an understanding of the properties of FFP and its inadequacies, as well as an appreciation of the complications of FFP usage. The College of American Pathologists⁽⁶⁾ and the British Committee for Standards in Haematology⁽⁷⁾ have published guidelines to highlight these issues and minimise misuse. But many studies from around the world still report a high frequency of inappropriate usage⁽⁸⁻¹⁶⁾.

Our institution is a large 1300-bed acute general hospital in Singapore with a broad range of medical and surgical specialties. Our transfusion service noted that FFP usage in the hospital is very high (about half the number of units of red cells transfused each month), so we decided to conduct a retrospective audit on the hospitals FFP usage with the specific aims of assessing our pattern of usage and rate of misuse. This will subsequently allow us to set policies in place to improve the situation.

MATERIALS AND METHODS

Blood bank records from October 2001 to December 2001 were reviewed and all FFP requests and transfusion

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Table I. FFP transfusion guidelines, College of American Pahtologists, 1994.

- 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 procedures. This must be documented by at least one of the following:
 - a) PT greater than 1.5 times the mid point of 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 1 blood volume within several hours with evidence of a 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 (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

episodes identified. Electronic medical records and coagulation profiles of these patients were reviewed. Data recorded include, department requesting for FFP, patient's presenting problems, reason for FFP request, date of transfusion, number of units transfused, coagulation profile of patient, causes of coagulopathy if investigated and final outcome of patient. The guidelines published by CAP were used as standards (Table I). Usage outside of these indications was deemed inappropriate. Results were tabulated and where appropriate presented as bar charts.

RESULTS

During the study period, 932 units of FFP were used for 359 transfusion episodes. Only 98 (27%) of these transfusion episodes were deemed appropriate based on the CAP criteria. This also means that 653 units of FFP may have been wasted. FFP is used by both medical and surgical specialties with general surgery, general medicine and neurosurgery being the main users (Table II). The proportion of inappropriate request is similar between surgical and non-surgical specialties and also between intensive and non-intensive care units (Table III). When broken down into individual departments, the number of inappropriate requests consistently outnumbers appropriate requests across all departments (Fig. 1), suggesting that the problem needs to be tackled on a hospital-wide basis.

Table II. Distribution of FFP requests according to different departments.

Departments	Percentage of Total Request over Study Period
General Surgery	23%
General Medicine	18%
Neurology Intensive Care Unit	15%
Neurology	10%
Orthopaedics	10%
Surgical Intensive Care Unit	9%
Medical Intensive Care Unit	6%
Neurology	4%
Cardiology	3%
Ear, Nose and Throat	1%
Accident and Emergency	1%

The most common reasons for FFP usage is sepsis with disseminated intravascular coagulopathy (DIC), bleeding and patients undergoing invasive procedures (Fig. 2). FFP use is clearly appropriate in DIC where there is activation of the coagulation system with consumption of coagulation factors leading to a generalised coagulopathy but according to the CAP guidelines, FFP should be given only in the setting of bleeding in these patients. Seventy-three percent of request for patients with DIC were made in the absence

Table III. Inappropriate FFP request analysed by surgical vs non-surgical specialties and in intensive care vs non-intensive care setting.

Specialties	Appropriate Requests		Inappropriate Requests		Total		Units per Request
	Episodes	Units of FFP	Episodes	Units of FFP (%)	Episodes	Units of FFP	
Surgical	67	207	178	447 (68%)	245	654	2.67
Non-Surgical	31	72	83	206 (74%)	114	278	2.43
ICU	30	107	77	245 (70%)	107	352	3.3
Non-ICU	68	172	184	408 (70%)	252	580	2.3

of bleeding. For patients who were given FFP pre-operatively for prolonged PT and/or aPTT, or patients with bleeding who have had prolonged PT and/or aPTT, in 66% and 72% of these patients the PT and/or aPTT were not more than 1.5 times that of normal as stipulated in the guidelines. Admittedly, some of the patients with acute bleeding were given FFP prior to results of coagulation screen were available due to the urgency of the situation but these were the minority cases and excluding these cases would not have much overall impact on the results of our study. Furthermore, the practice of FFP use before the availability of coagulation results should be discouraged. For surgical specialties, FFP was often requested for correction of only mild prolongation of clotting times. Of the 86.9% of requests with abnormal coagulation studies, only 36.8% had PT and 26.3% had aPTT greater than 1.5 times normal. Amongst these patients with markedly prolonged clotting times, only about a quarter were bleeding or undergoing invasive procedures. For other common indications like liver disease and warfarin reversal, 71% and 44% of requests were made in the absence of bleeding or planned surgery respectively.

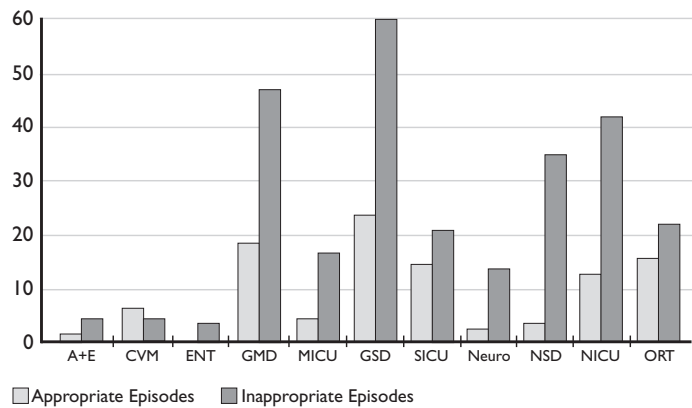
DISCUSSION

FFP is a frequently prescribed blood product. A high rate of inappropriate use has been reported around the world⁽⁸⁻¹⁶⁾. Inappropriate use not only leads to a wastage of limited resources and depriving more needy patients of their use, it also leads to increased healthcare cost and risk of transfusion related complications like viral transmission which could lead to significant morbidity and mortality.

Guidelines exist for FFP usage. However several caveats exist for these guidelines. First, they were published 10 years or more ago. Second, they were mainly expert consensus rather than recommendations derived from well-conducted prospective randomised controlled studies. Unlike red cell transfusion, where the traditional threshold of 10 g/dl has been found to be unnecessarily high in some settings like surgery and intensive care by prospective randomised studies⁽¹⁷⁻¹⁹⁾, such studies do not exist for FFP usage. Even, the threshold of PT and aPTT prolongation of 1.5 times normal was based on dated retrospective studies^(20,21). Furthermore, some studies have shown that PT and aPTT were only crude predictors of surgical bleeding and their utility had been questioned^(22,23).

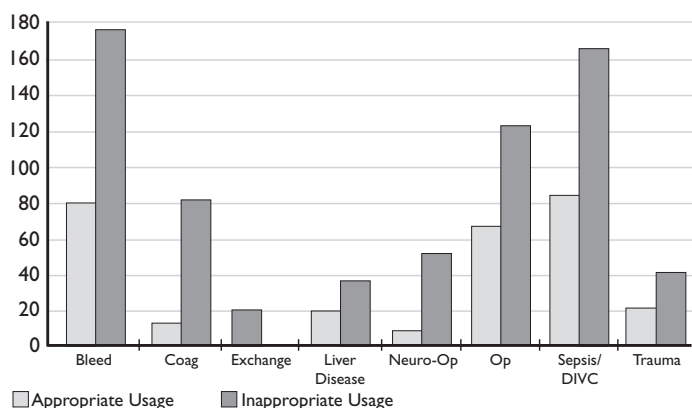
There are some situations where FFP is clearly indicated: bleeding patients or patients undergoing invasive procedures with coagulopathy resulting from DIC, massive blood transfusion or liver failure, and plasma exchange for thrombotic thrombocytopenic

Fig. 1 Appropriate vs inappropriate FFP usage by individual department.



Abbreviations: A+E = Accident and Emergency Department; CVM = Cardiology Department; ENT = Ear, Nose and Throat; GMD = General Medicine Department; MICU = Medical Intensive Care Unit; GSD = General Surgery Department; SICU = Surgical Intensive Care Unit; Neuro = Neurology; NSD = Neurosurgery Department; NICU = Neurology Intensive Care Unit; ORT = Orthopaedics Department.

Fig. 2 Appropriate vs inappropriate FFP usage by indications.



Abbreviation: Op = Operation.

purpura. In massive transfusion, there is no evidence that prophylactic replacement of FFP prevents the onset of abnormal bleeding or reduces transfusion requirements⁽²⁴⁾. In liver disease, complete correction of coagulation defect is often impossible and there is no agreement on the levels of coagulation factors which are safe for these patients prior to surgical intervention.

There are other situations where products more effective and safer than FFP are available for correction of coagulopathy: recombinant or virally inactivated specific clotting factor concentrates for treatment of haemophilia, von Willebrand's disease and hypofibrinogenemic states; and prothrombin complex concentrates and vitamin K for warfarin reversal⁽²⁵⁾. Lastly, there are situations in which FFP is clearly not indicated like volume resuscitation, nutritional support in protein losing states like burns and plasma exchange procedures for conditions other than TTP.

Grey areas exist. For example, is prophylactic FFP required for patients with coagulopathy due to DIC and liver disease in the absence of bleeding and invasive procedures? If so, what should be the threshold for transfusion? Is FFP indicated for patients who are bleeding or going for invasive procedure with only mildly prolonged clotting times (less than 1.5 times normal)? Again if so, is there a threshold below which FFP transfusion will not make a clinical difference? These are questions that require randomised studies to answer.

Our audit showed widespread uncertainty about the appropriate use of FFP amongst our doctors resulting in a high number of inappropriate requests for FFP if the CAP guidelines were to be followed. The percentage of inappropriate usage in our study was similar to those published from other series. Most requests do not fulfil all the conditions that constitute appropriate FFP usage, i.e. presence of bleeding or invasive procedure plus coagulopathy due to conditions like DIC, liver failure, massive transfusion and over-anticoagulation with warfarin plus prolongation of PT or aPTT to 1.5 times that of normal control. Many of the requests in this audit failed to meet all three criteria and were hence deemed inappropriate. This suggests that although most doctors have some idea of when FFP should be used, they do not fully appreciate the exact situations in which FFP usage is warranted based on existing guidelines. There may be several reasons for this. First, guidelines are old and many doctors may not be aware of their existence. Second, physicians may not be aware of changes in transfusion practice and are relying on outdated knowledge. Junior doctors are taught these outdated practice and the problem is thus perpetuated. Third, in a litigious society, precautionary attitude prevails resulting in over-treatment especially in acute bleeding situations or patients going for invasive procedures when there is the slightest coagulation defect. Lastly, in the age of evidence-based medicine, guidelines for FFP usage are not based on Grade A evidence.

Various strategies have been used to reduce inappropriate use of blood products. These may include administrative intervention like screening of requests by haematologists and request form incorporating appropriate indications to remind doctors, education for junior and senior staff, and audit cycles⁽²⁵⁾. Some of these measures have been shown to be very effective in reducing inappropriate FFP usage^(14,26,27). We have decided to implement some changes to improve the situation. Hospital transfusion guidelines should be established based on existing international guidelines and agreed upon by all the

departmental chiefs. These guidelines should be strictly enforced and should be disseminated throughout the clinical services from senior down to junior doctors. Transfusion guidelines should be included in all junior doctor handbooks and included in all new doctor's hospital orientation programme. Transfusion topics and guideline should be re-enforced regularly during various departments continuing medical education (CME) programs. Educational approach may take time to work but will have a more lasting impact. Request forms will be re-designed to include appropriate indications for FFP transfusion to serve as a reminder of the appropriate indications for doctors requesting for FFP. This measure will hopefully produce a more immediate effect.

FFP misuse results in wastage and subjecting recipients to unnecessary risk. Despite availability of guidelines, inappropriate FFP use is a significant problem worldwide, both in developed and developing countries. Our audit provides further evidence that this is an on-going problem. Since this audit we have decided to implement some measures that we think will have immediate as well as lasting effects. The audit will be repeated two to three years after the implementation of these measures. More importantly, we feel that the conduct of prospective randomised controlled studies to better define guidelines for FFP usage is urgently needed.

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