



FRESH FROZEN PLASMA; INAPPROPRIATE USE OF FRESH FROZEN PLASMA AN AUDIT OF A TERTIARY CARE HOSPITAL.

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INTRODUCTION

Since the advent of blood transfusion and blood banks in world war two, human blood has been marketed in various forms for various indications. Whole blood, packed cells, albumin, plasma, fresh frozen plasma, cryoprecipitate, clotting factor concentrates, platelets transfusions etc. have all been used worldwide.

Each donation of whole blood (450ml) can be used to create four different products (packed red cell concentrate, platelet concentrate, fresh frozen plasma and cryoprecipitate). If plasma unit is isolated from whole blood and frozen within eight hours from donation, the unit is termed fresh

ABSTRACT... Introduction: As the use of Fresh Frozen Plasma (FFP) is having established complications including Allergic reactions, infectious complications, hemolysis, fluid over load, transfusion related acute lung injury (TRALI) and immune suppression, therefore it must be used cautiously. **Objectives:** To evaluate the inappropriate use of FFPs, to carry out an audit of appropriateness of FFP transfusion with reference to international guidelines and set foundations for blood bank and transfusion protocols. **Study Design:** Cross sectional study. **Setting:** Khyber Teaching Hospital Peshawar. **Period:** 6 months, 1st January 2016 to 30th June 2016. **Methods:** During which FFP transfusion requests made to the blood bank by various units of the hospital were studied including general surgery, surgical ICU, general medicine, medical ICU, gynecology and obstetrics. Seventy Six requests were received that were judged using 6 variables: indication for FFP use, sampling errors, laboratory analysis errors, interpretation errors, dosage of FFP (number of units being transfused) and timing of FFP transfusion. Score of "1" was given for each correct variable. After matching data to the international protocols, a score of 4-5 was taken as appropriate and <3 was classified as inappropriate. **Results:** Twenty Seven (35.5%) FFP transfusions were done with a score of 4-5 and were considered appropriate while 49(64.5%) FFP transfusions were given a score of 3 or less and were considered inappropriate. **Conclusions:** Almost two third of FFP were used inappropriately in our hospital, the commonest indication being acute Disseminated Intravascular Coagulation (DIC) and mostly requested from surgical units. Maximum cases of inappropriate transfusions were due to wrong sampling techniques and wrong dosage calculations. Most inappropriate transfusions were done in MICU. It is recommended that annual clinical audit of all blood products usage should be conducted. Local guidelines for physicians and training programs for nurses and paramedics regarding proper use of blood products should be established.

Key words:

Fresh Frozen Plasma, Platelet-Rich Plasma, Blood Component Transfusion, Clinical Audit.

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frozen plasma (FFP).¹ Each pint of FFP measures 175–250 ml and it contains 70–80 units of factor VIII, IX, VWF and other clotting factors. FFP is the most commonly requested hemostatic agent from blood banks, over 300 000 units are transfused in England annually and 4.4 million units in USA.^{2,3} Its use has increased a lot during the past decade mostly because no clear cut indications have been marked out for its use at hospital level, no proper protocols are followed while measuring the coagulation profile and usually no accountability exists if used inappropriately.

The use of FFPs is not free of danger, there are established complications including Allergic

reactions¹, infectious complications, hemolysis, fluid overload, transfusion related acute lung injury (TRALI) and immune suppression therefore it must be used cautiously.⁴

Current guidelines of British Committee for Standards in Hematology the definitive indications for the use of FFPs include: correction of single factor deficiency for which a specific concentrate is not available, immediate reversal of warfarin overdose, acute DIC, TTP.

FFP use is only conditionally allowed in the following situations when there is evidence of bleeding: massive transfusion, liver disease and cardio pulmonary bypass surgery. There is no indication of using FFP in the following conditions like hypovolemia, nutritional use, plasma exchange.⁵

The College of American Pathologists (CAP) has determined following practical parameters for FFPs transfusion (1994). If there is a 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: 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) c) Coagulation factor assay of less than 25% activity.⁶

In our setup FFPs are usually used in surgical wards while preparing patients for surgery with coagulopathy resulting from DIC, massive blood transfusion or liver failure or sepsis. Intraoperative and post-operative use is also common. In medical wards, FFPs are used in liver disease, warfarin overload. While in gynecology, FFPs find their use in DIC due to placental abruption etc.

FFP is a precious human resource produced from humans for humans, any decrease in supply or increase in demand can have adverse outcome on patient care therefore we aimed to conduct a study in our hospital to evaluate the

inappropriate use of FFPs, to carry out an audit of appropriateness of FFP transfusion with reference to international guidelines and set foundations for blood bank and transfusion protocols.

MATERIALS AND METHODS

This was a cross sectional study conducted in Khyber Teaching Hospital Peshawar over a period of 6 months, 1st January 2015 to 1st July 2015. After taking approval from the hospital ethical committee both male and females between ages of 18-70 years were included in the study while Pediatric wards were not included in the study. During this period, the FFP transfusion requests made to the blood bank by various units of the hospital were studied including general surgery, surgical ICU, general medicine, medical ICU, gynecology and obstetrics. A total of 76 requests were made during this period. These patients were evaluated for age, gender and ward.

All patients were then judged using 6 variables: indication for FFP use, sampling errors, laboratory analysis errors, interpretation errors, dosage of FFPs (number of units) and timing of FFPs transfusion. A score of 1 was given for each correct variable. After matching data to international protocols, a score of 4-5 was taken as appropriate and <3 was classified as inappropriate.

All data was collected on specially designed proformas, mean and standard deviation were calculated for all continuous variables while percentage was calculated for categorical variables. All data was analyzed in SPSS version 20.0.

RESULTS

A total of 76 patients received FFP's during the study period, the mean age was 41.68 ± 15.6 SD (range = 70-19years). The gender ratio was almost similar with 36 males and 40 female patients.

Total units of FFPs ordered during 6 months was 280 units. The transfusions according to departments are given in the table below:

Unit	Requests Made	Units Transfused	Appropriate	Inappropriate
Surgery	24 (31.6%)	96 (34.3%)	08	16
Surgical ICU	08 (10.52%)	24 (8.56%)	03	05
Medical	16 (21.05%)	64 (22.86%)	11	05
Medical ICU	12 (15.8%)	32 (11.42%)	00	12
Gynae/Obs	16 (21.05%)	62 (22.1%)	05	11
Total	76 (100%)	280 (100%)	27 (35.5%)	49 (64.5%)

Table-I. FFPs transfused unit wise

Indications	Frequency/Percentage
Disseminated Intravascular Coagulopathy	16 (21.05 %)
Pre-operative Coagulopathy	14 (18.42 %)
Warfarin Overdose	02 (02.63%)
Sepsis	21 (27.63%)
Bleeding due to cirrhosis	14 (18.42%)
Post-operative Bleeding	10 (13.16%)
Total	76 (100%)

Table-II. FFPs transfused according to indications

Variable	Correct (%)	Incorrect (%)
Indication	40	36
Sampling	28	48
Laboratory Error	40	36
Interpretation Error	40	36
Dosage Error	24	52
Timing Error	52	24

Table-III. Variables to determine inappropriate use.

27 (35.5%) FFP transfusion were done with a score of 4-5 and were considered appropriate while 49(64.5%) FFP transfusion were given a score of 3 or less and were considered inappropriate.

DISCUSSION

In our study the most common indication of using FFPs was DIC and the commonest cause of inappropriate FFP transfusion was dosage calculation (68.42%) and sampling errors (63%). While taking samples for PT/APTT/INR measurements, certain precautions need to be followed; the sample must be collected in fasting state as lipemia of blood can interfere with the spectrophotometric analysis and cause falsely prolonged PT/APTT. In our study, 48 (63.15%) of the samples were taken in the non-fasting state. Once samples are taken, care must be taken to analyze them within 4 hours, delays in transport may affect in particular the labile factors (FV, FVIII), leading to prolonged clotting times and in vitro loss of factor activity and extremes of temperature should be avoided during transport of samples.^{7,8} In our study 36 samples were

analyzed within time while 40(52.63%) samples were analyzed late leading to false prolongation especially of APTT.

According to the New York State Council on Human Blood and Transfusion 2004 guidelines, the PT/PTT is considered prolonged only if it is >1.5 times normal reference range.^{9,10} In our study this criteria was met in 40 (52.63%) cases. The average dosage of FFPs is between 8-12 ml/kg according to various guidelines; thus each patient needs different dose according to weight. In case of emergency reversal of warfarin a higher dose is needed up to 15 ml/kg is needed. In our study only 24 patients (31.6%) received FFPs after proper weight and dosage calculations, while 52 (68.42%) patients were transfused without any proper calculations of weight and dose. The half-life of certain clotting factors is less such as factor v and viii, Factor VII has a short half-life (4-6 hours) thus if plasma is administered more than 8-10 hours before the planned procedure, it will have gone through at least 2 half-lives thus reducing its hemostatic efficacy at the time of

surgery.¹¹ In our survey, 62.7 % (52) transfusions were made within 8 hours of expected surgery while 28.9% were made more than 8 hours before interventions thus deemed inappropriate.

In our study 64.5% FFPs were transfused inappropriately, comparison with local and international studies is shown in the following table.

Country	Study	Sample size Patients and FFP units	% inappropriate
Turkey	Akkas and Atman	204/456	67%
India	Kullarni N	945/1884	52%
Pakistan/ Rawalpindi	Iqbal H	84/498	56%
Pakistan/ Karachi	Moiz B	300/1486	21.3%
Malaysia	Pratibha R	931/2665	60%

Table-IV. Inappropriate use of FFPs in various studies.^{1,4,12,13,14}

FFP is a precious human resource, in recent times the demand has greatly superseded the supply resulting its scarcity in emergency situations. Our study highlights the common pitfalls in the laboratory evaluation of coagulopathy, determining the correct indications and administration of FFPs in correct timing and dosage. The high rates of inappropriate transfusion reflect the lack of knowledge as well as non-adherence to the international guidelines among clinicians and lack of training of nurses and laboratory personnel in terms of sampling.

CONCLUSIONS

Almost 64.5% of FFPs are used inappropriately in our hospital, the most common indication being acute DIC and the most number of requests are made from surgical units, while most cases of inappropriate transfusions include wrong sampling techniques and wrong dosage calculations. Most transfusions done in MICU were inappropriate.

RECOMMENDATIONS

It is recommended that annual clinical audit of all blood products usage is done, establishment of local guidelines for physicians and training programs for nurses and paramedics are carried out.

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*We can complain because roses have thorns,
or rejoice because thorns have roses.*

– Unknown –

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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Muhammad Asim Khan	Concept, design, drafting	
2	Maryam Alam Khan	Concept, design, Literature review.	
3	Aneela Dar	Data collection and interpretation/analysis, Final drafting.	
4	Syed Asad Maroof	Data analysis, Proof reading and final drafting.	
5	Mohammad Zarin	Literature review, proof reading.	
6	Rooh ul Muqim	Proof reading, Final drafting	
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