



Pseudo alteration of Coagulation Profile- In vivo Biochemical reactionary effect of Fresh Frozen Plasma after Infusion

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Abstract

Aims & Objective: *The use of fresh frozen plasma (FFP) continues to rise, despite the fact that the supply of plasma derived from allogenic blood donation is finite. The safety and effectiveness of transfusion depend on the appropriate clinical use of blood and blood products. This study was evaluated of coagulation profile in various common disease conditions and conducted to review the effect of FFP transfusion on coagulation profile (INR).*

Methodology: *A retrospective study of blood bank records and coagulation profile results of the patients given FFP from September 2006 to August 2007, in Gandhi Medical College and Hospital, Bhopal was undertaken. The criteria set by the department of pathology were used as the guidelines.*

Results: *Total 1064 coagulation studies were performed and 481 were deranged results (exclusive of CT-ICU and ICCU patients). Out of that 112 was in pediatric patients 16 patients was non pediatric illness, 105 in emergency medicine, 70 in surgical, 177 in medical 11 in gynecologic and 19 was unclassified patients (Burn, orthopedics). Total 874 numbers of patients to which FFP were supplied. 1.70 FFP units supplied per patient. Pediatric patients were 345 and 529 adult and elderly. An in depth analysis of the rationale behind prescribing FFP to each patient was made. Every possible justification was sought from the clinician for prescribing FFP.*

Conclusion: *FFP is a vital component of blood, not just a substitute. Although very useful clinico-pharmacologically, FFP also carries potential adverse effects. Clinicians must abide by the rules and guidelines that exist pertaining to its rational usage. A clinician may have a thousand things in mind but the transfusion personnel are more competent in dealing with the use of components. Let the clinicians know about the indications and usage of blood component, particularly FFP. Even if the indication for FFP is clinically valid, suggest the clinician to be wise still in using the component. Stop the practices that may encourage the irrational use of blood products.*

Keywords: *Fresh Frozen Plasma (FFP), INR categories, Transfusion.*

Introduction

The process of coagulation is a highly complex yet a perfectly balanced physiological phenomenon. The components involved in it are

blood vessels, platelets, plasma coagulation factors & inhibitors and fibrinolytic system.^[1-4] Many of the bodily functions and organs are directly or indirectly involved in it. If properly

carried out, coagulation profile testing can spot to accuracy, the exact point of defect in the entire haemostatic process. Various tests in coagulation profile fall in primary and secondary categories. The primary ones are Platelet count (PLC) and bleeding time (BT) besides CBP and hemoglobin (Hb) and secondary tests include Prothrombin time (PT), Activated partial thromboplastin time (APTT) and thrombin time (TT).^[5-9]

The clinical signs and symptoms of abnormal hemostasis are bleeding, which is out of proportion to the expected level, which could be following trauma, surgery and tooth extraction etc. Petechiae and ecchymosis, hematoma and hemarthroses, purpura, uncontrolled umbilical cord bleeding at birth and uncontrolled epistaxis are the other presentations. The diseases and conditions where abnormal hemostasis as cause of bleeding should be kept in mind include liver diseases, burn patients, Eclampsia, snake bite, cardiac patients, patients with aplastic anemia and bone marrow infiltration and patients with leukemia.^[10,11] The possible causes of abnormal hemostasis could be quantitative or qualitative defect in any of the components of normal coagulation process e.g. hemophilia and von Willebrand's disease. Prothrombin time (PT) and Activated plasma thromboplastin time (APTT) form the most important investigation to assess coagulation process status and efficiency. Prothrombin time (PT) represents the extrinsic pathway. Activated plasma thromboplastin time (APTT) represents the intrinsic pathway. The INR is a statistically standardized value, which is an internationally recognized parameter to evaluate the coagulation time.^[12-15]

Fresh Frozen Plasma (FFP) is available since 1941 and was initially often used for volume replacement. FFP is contraindicated for volume expansion, for which products like albumin and hydroxyethyl starch are available^[16]. FFP is used in cases with excessive bleeding or to prevent bleeding in patients with abnormal coagulation profile undergoing invasive procedure. FFP is a good source of coagulation factors, including

labile factors V and VIII as well as albumin and immunoglobulin.^[17,18] FFP differs from plasma in that the latter has almost negligible amount of factors V and VIII. FFP can be used to treat conditions such as parvovirus infection and coumarin toxicosis and plasma can be used for albumin replacement as well as for passive immunity to orphaned neonates. FFP is less expansive than factor concentrates. However, it requires very large volumes of plasma to provide enough clotting factor to prevent bleeding, and it requires stringent storage conditions. There are various types of FFP available; these are standard FFP, methylene blue treated FFP and solvent detergent FFP.^[19,20] They differ in their source, virus risk, volume, coagulation factor content, etc. FFP is also associated with certain potential risks. These include virus risks such as HIV 1 & 2, hepatitis B, C and A, Parvovirus B19, allergic reactions and adverse reactions due to antibody.^[18,20]

Material and Methods

This retrospective study was conducted from September 2006 to August 2007. Blood bank records and coagulation profile results of the patients given FFP in Gandhi Medical College and Hospital Bhopal were taken. Data such as department requesting for FFP, patient's presenting problem, reason for FFP request, date of transfusion, number of units transfused, coagulation profile of patient, and causes of coagulopathy if investigated, were recorded. The criteria set by the department of pathology, were used as guidelines. An FFP transfusion was considered inappropriate if a coagulation profile was not done at the time of request and the prolongation of PT/PTT was less than 1.5 times that of normal control plasma.

Results

Total 1064 coagulation studies were performed and 481 were deranged results (exclusive of CT-ICU and ICCU patients). Out of that 112 was in pediatric patients 16 patients was non pediatric

illness, 105 in emergency medicine, 70 in surgical, 177 in medical 11 in gynecologic and 19 was unclassified patients (Burn, orthopedics).

FFP Transfusions

Total 874 numbers of patients to which FFP were supplied. 1.70 FFP units supplied per patient. Pediatric patients were 345 and 529 adult and elderly. Conditions and diseases for which FFP was indicated with deranged coagulation profile in emergency medicine 95% was liver disease (hepatic encephalopathy/acute phase of hepatitis or cirrhosis/jaundice), 2% was portal hypertension with/without bleeding and 1% was snake bite, bleeding disorder and complicated malaria/chronic infections. In Surgery department 55% was post-operative case with and without bleeding, 15% was cholelithiasis and carcinoma with and without bleeding, 10% was intestinal obstruction or perforation peritonitis and 5% was other causes (hepatic and peri hepatic pathology). In obstetrics and gynecology department 60% was eclampsia and pre-eclampsia, 10% was post-operative case with and without bleeding, 10% was IUFD, DIC uncontrolled bleeding and other causes (associated renal disorder, hypoproteinemia). In pediatric department 40% was viral hepatitis or hepatic encephalopathy, 20% was nephrotic syndrome, hypoalbuminemia, DIC with and without bleeding, 10% was sepsis, necrotizing enterocolitis, hemorrhagic disease and bleeding disorder. Total 251 was found problems encountered while testing. Out of that 186 was insufficient quantity of sample (poor ratio), 34 coagulated sample, 21 was hemolysed sample and 10 was too long and too short coagulation time.

Result & Observation

Total 102 patients were included average duration between FFP infusion and repeat coagulation profile testing was 12 hours, INR before infusion was 2.28 and INR after infusion was 1.41. 54 patients were received only FFP transfusion average INR before infusion was 2.20 and INR after infusion was 1.50. Patients that received additional transfusion were 48, average INR before infusion was 2.33 and INR after infusion was 1.47.

Average INR before & after transfusion (Overall)

Average INR Before & After Transfusion		
	PRE	POST
Only FFP	2.28	1.50
Additional	2.33	
Change IN INR (Category Wish)		
Category 1 (INR > 3)		
Only FFP	4.44	1.77
Additional	3.91	1.49
Category 2 (INR > 2-3)		
Only FFP	2.24	1.65
Additional	2.61	1.45
Category 3 (INR 1-2)		
Only FFP	1.61	1.34
Additional	1.57	1.18
Change in INR (Addition Transfusion)		
1 (INR > 3)		
FFP	4.44	1.77
WB (0)	--	--
PC/PRC (9)	3.91	1.49
2 (INR 2-3)		
FFP	2.24	1.65
WB (12)	2.51	1.25
PC/PRC (3)	2.71	1.65
3 (INR 1-2)		
FFP	1.61	1.34
WB (18)	1.58	1.19
PC/PRC (6)	1.55	1.17

Difference (Range of Change) of INR

RANGE	PC	PRC	WB	NONE	TOTAL
<1	3	3	18	42	66
1-2	3	6	12	6	27
3+	0	3	0	6	09
	6	12	30	54	102
*Chi Square Value: 22.36					
*Degrees of freedom: 6					
*P Value: 0.00104157					

Grouping of Cases Based on INR	
Category	
A (>3)	18
B (2-3)	30
C (1-2)	54
Additional Transfusion Prescribed (45)	
A (3-PC, 3-PRC, WB-NONE)	18
B(12-WB, 3-PC, PRC-NONE)	30
C (18-WB, 3-PC,3 PRC)	24

Additional transfusion prescribed whole blood was 30, platelet concentrate was 9 and packed red cell was 6. Grouping of cases based on INR category A (>3) was 18, category B (2-3) was 30 and category C (1-2) was 54.45 additional transfusion were prescribed in that category A was 6 (3-PC; 3-PRC; WB-None), category B was 15 (12-WB; 3-PC, PRC-None) and category C was 24 (18-WB, 3-PC, 3-PRC) (table 1). In only FFP average INR before and after transfusion was (2.28 and 1.50) and in FFP & additional was (2.33 and 1.47). Pre and post change in INR in only FFP and additional according to category and range showed in table 2&3.

Discussion

The purpose of this entire work is not just to compare it with some significant works done earlier in this field or related to this field. The comparison, however, is a must in order to know the significance of this study keeping in mind the observations and results of other studies done so far. Fresh frozen plasma (FFP) is a frequently prescribed blood product. 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 lung injury (TRALI syndrome).^[21] Any inappropriate use of blood and its components will lead to a wastage of limited resources, depriving more needy patients of their use, increased healthcare cost, and risk of transfusion-related complications, such as viral transmission, which could lead to significant morbidity and mortality. Therefore, it should only

be used when there is a documented coagulation defect, which could be corrected by a reasonable amount of FFP. Despite the availability of guidelines and protocols, a high rate of inappropriate use has been reported around the world, both in the developed and developing countries.^[22] In our study too, 24% requests were from this unit but the maximum usage was in the pediatric medicine unit (39%) and the maximum irrational use was in the surgery units amounting to 72%.

Fortunately, in the institution of the present study, which is a government hospital and a tertiary care centre, the indications for performing coagulation studies are remarkably lower than the only other study institution pertaining to it. Fraction of patients having irrational prescription of coagulation profile Thomas E. Auble et al 2002 was found 34.4 %. In our study was found 18.0 %.^[23]

Disseminated intravascular coagulation, chronic liver disease, blunt trauma and septicemia were the common indications for carrying out coagulation profile analysis in most study institutions or hospitals. In the present study liver diseases, viral encephalopathy and Eclampsia formed the predominant indications for coagulation studies. The present study worked extensively on this part of the entire work here. Whereas the study conducted in Oklahoma (Holland & Brooks) and UAE (Abdel-Wahab et al 2005)^[24] dealt only with the fraction of patients showing normalization of INR, the present study not only qualitatively and quantitatively assessed the change in INR but also worked on the effect of FFP on various ranges of INR. This study included 54 male patients and 48 female patients. The number of patients aged less than 14 years was 60. The maximum number of patients had an INR between 1 and 2. The average INR before transfusion was 2.2 in study conducted in Oklahoma (Holland & Brooks) and post transfusion value was 1.5. The corresponding values in the present study were 2.30 and 1.48 respectively. The Holland and Book's study also

observed a linear relationship between pre transfusion INR and the decrease in INR per unit FFP; so was the observation in the present study (with precise quantization). The median change in INR was 0.07 for UAE (Abdel-Wahab et al) [24] study and 0.10 for Oklahoma (Holland & Brooks) study. The corresponding value for the present study was 0.08. The present study came at par with the other studies conducted on this or related issues and worked maximum (more than any other study) in assessing the effect of FFP infusion on coagulation profile.

Conclusion

An exhaustive knowledge of disease conditions as well as technical/clerical errors that may result in deranged coagulation profile must be kept in mind while performing coagulation studies. This is particularly important for institutions or set ups where this is performed manually and the resources are limited. Even in a country like India, with limited resources, the use of FFP is generally very inappropriate and often irrational as well. Every clinician as well as transfusion personal must keep in mind the potential adverse effects and effects of overuse of FFP before prescribing this vital component of whole blood having the longest shelf life. FFP does not significantly improve minimally prolonged INR values. Minimally deranged coagulation profile can be corrected by the treatment of underlying disease itself. Higher the INR more is the correction in coagulation profile observed with FFP infusion. An associated fresh Whole Blood transfusion adds to the change in INR observed with FFP infusion. The change in INR also depends on the underlying disease condition of the patient. Even PC/PRC may affect the value of INR (but that depends on the underlying condition, again). FFP is a vital component of blood, not just a substitute. Although very useful clinico-pharmacologically, FFP also carries potential adverse effects. Clinicians must abide by the rules and guidelines that exist pertaining to its rational usage. A clinician may have a thousand things in mind but

the transfusion personnel are more competent in dealing with the use of components. Let the clinicians know about the indications and usage of blood component, particularly FFP. Even if the indication for FFP is clinically valid, suggest the clinician to be wise still in using the component. Stop the practices that may encourage the irrational use of blood products.

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