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EFFECT OF FFP TRANSFUSION ON INR IN PATIENTS OF LIVER DISEASES

Transfusion Medicine

Dr. Sushil Songara* Post graduate resident, Department of Pathology, Gandhi Medical College Bhopal *Corresponding Author

Dr. Rajni Choudhary Associate Professor, Department of Pathology, Gandhi Medical College Bhopal

Dr. Varsha Rampuri Assistant Professor, Department of Pathology, Gandhi Medical College Bhopal

Dr. R. K. Nigam Professor, Department of Pathology, Gandhi Medical College, Bhopal

Dr. Reeni Malik Professor & Head, Department of Pathology, Gandhi Medical College Bhopal

ABSTRACT

Context: Fresh frozen plasma (FFP) is being transfused in large number by clinicians in liver diseases, both therapeutically and prophylactically to correct deranged coagulation. It has not been reported with significant improvement in INR in chronic liver disease. Association with various complications like haemolytic reactions and transfusion-related acute lung injury are commonly seen. Effect of FFP transfusion on coagulation profile have been reported by various authors but not much have been done to study this effect in patients with liver diseases. **Aim:** The main aim of this study was to analyse the pattern of FFP usage in liver diseases and its effect on International normalized ratio (INR) and also to study the change in INR per unit of FFP transfused in patients with liver diseases. **Settings and Designs:** An Observational hospital-based study **Materials and Methods:** The prospective study was done after getting ethical clearance from the institution at tertiary care centre during 1st January 2021 to 30th June 2022 in which 32 cases of liver disease were studied. **Results:** The commonest category of liver disorder was chronic liver disease (CLD) (37.5%) followed by acute liver disease (21.8%), alcoholic hepatitis (18.75%). The commonest indication for transfusion was coagulopathy with deranged INR. 75% transfusions were given before invasive procedures and 25% were given to patients with active bleeding. Also, Patients receiving 5 units or more FFP have shown significant INR improvement. Mean change in INR in acute liver diseases was found to be 1.38±0.64, in alcoholic hepatitis 3.6±1.55, in chronic liver disease 1.2±0.64, in liver abscess 0.35±0.43, in chronic hepatitis related chronic liver disease 1.15±0.50. Based on the 't' test, improvement was not significant in patients with liver abscess and chronic hepatitis. **Conclusion:** FFP in small volume is less effective in correcting mild to moderate coagulation defects in liver diseases. Large volumes are required to cause significant INR improvement. Considering the risks associated with FFP transfusion, decision of transfusion should be carefully weighed.

KEYWORDS

Fresh Frozen Plasma, International Normalized Ratio, Liver diseases

INTRODUCTION-

In the vast majority of the developing world, there is a shortage of blood and blood components. In order to meet the rising demand for blood components, the available resources are insufficient. To ensure that blood components are available for patients in need and to reduce the needless risk of transfusion transmitted diseases, proper use of blood components is necessary. Each donation of whole blood can be used to create as many as four different products (packed red cell concentrate, platelet concentrate, fresh frozen plasma and cryopreciptate) that can be transfused to patients. [1]

Fresh frozen plasma (FFP) is being transfused in large number by clinicians in liver diseases, both therapeutically and prophylactically to correct deranged coagulation [2]. It has not been reported with significant improvement in INR in chronic liver disease [3][4]. Association with various complications like haemolytic reactions and transfusion-related acute lung injury are commonly seen.[5] Prothrombin time (PT) and international normalized ratio (INR) are commonly abnormal in patients with liver disease, this directly should correlate with increased risk for significant bleeding in the cirrhotic patients, but this has not been proven despite significant research.[5][6] Effect of FFP transfusion on coagulation profile have been reported by various authors [9][10] but not much have been done to study this effect in patients with liver diseases [7][8].

Understanding the properties of FFP as well as appreciation of its complications is very important in ensuring appropriate use of FFP [6]. Considering the increasing demand and utilization of FFP, the primary aim of the study is to observe the effect of FFP transfusion on pre-transfused INR. This study done exclusively on liver disease patients to analyse the effect of FFP on international normalized ratio (INR).

MATERIALS AND METHODS-

The prospective study was done after getting ethical clearance from the institution at tertiary care centre during 1st January 2021 to 30th June 2022 in which 32 cases of liver disease were analysed with duly filled consent form along with detailed history and clinical details. Patient's age, sex, diagnosis, indication for FFP transfusion were recorded from the blood requisition forms. Blood sample was collected prior to FFP transfusion and within 8 hours post FFP transfusion, in 3.2% trisodium citrate vial in the ratio of 1:9 (anticoagulant: blood) which was then centrifuged within 1 hour at 3000 rpm for 20 minutes to separate the platelet poor plasma.PT-INR test was done by manual method. The result was noted and compared with pre- transfusion PT-INR value.

Patients with liver diseases with pre transfusion INR more than 1.5 were included in the present study while patients receiving any other blood product along with FFP and those patients who were on anticoagulation therapy were excluded from this study.

The main aim of this study was to analyse the pattern of FFP usage in liver diseases and its effect on International normalized ratio (INR) and also to study the change in INR per unit of FFP transfused in patients with liver diseases.

RESULTS-

A total of 111 units of FFP were transfused to 32 patients who did not receive any other blood product. Among them, 75% (24/32) were males and 25% (8/32) were females. The mean age was 48.2 years. 25 patients (78.12%) received 3-6 units of FFP per episode.

The commonest category of liver disorder was chronic liver disease (CLD) (37.5%) followed by acute liver disease (21.8%), alcoholic hepatitis (18.75%). The commonest indication for transfusion was coagulopathy with deranged INR. 75% transfusions were given before invasive procedures and 25% were given to patients with active bleeding. Table 1 shows common liver diseases in which transfusion of FFP was done in present study.

Table 1: Transfusion Of FFP In Various Liver Disease-

S. No.	Liver disease	No. of patients	Percentage
1.	Acute liver disease	7	21.8%

2.	Alcoholic hepatitis	6	18.75%
3.	Chronic liver disease	12	37.5%
4.	Hepatic encephalopathy	1	3.12%
5.	Chronic hepatitis related chronic liver disease	3	9.375%
6.	Liver abscess	2	6.25%
7.	Liver cirrhosis	1	3.12%

We found in our study, a high linear correlation between pre transfusion INR and change in INR per unit of FFP. Also, Patients receiving 5 units or more FFP have shown significant INR improvement.

Mean change in INR in acute liver diseases was found to be 1.38±0.64, in alcoholic hepatitis 3.6±1.55, in chronic liver disease 1.2±0.64, in liver abscess 0.35±0.43, in chronic hepatitis related chronic liver disease 1.15±0.50. Based on the 't' test, improvement was **not significant in patients with liver abscess and chronic hepatitis.** Table 2 shows mean pre-transfusion INR, post transfusion INR and mean change in INR after FFP transfusion.

Table 2: Change in INR in various liver disease-

S.No	Liver disease	No. of patients	Average no. of FFP transfused (range)	Mean Pre transfusion INR	Mean Post transfusion INR	Mean Change in INR ±SD	Mean change in INR per unit of FFP
1.	Acute liver disease	7	3.57 (3-6 units)	2.84	1.50	1.34±0.64	0.37
2.	Alcoholic hepatitis	6	4.4 (3-6 units)	3.2	1.65	1.55±1.76	0.35
3.	Chronic liver disease	12	4.3 (3-6 units)	2.9	1.7	1.2±0.64	0.27
4.	Hepatic encephalopathy	1	3	2	1.35	0.65	0.2
5.	Chronic hepatitis related chronic liver disease	3	3.3 (3-4 units)	2.9	1.9	1.0±0.60	0.30
6.	Liver abscess	2	2.5 (2-3 units)	2.1	1.75	0.35±0.43	0.14
7.	Liver cirrhosis	1	2	1.6	1.2	0.4	0.2

DISCUSSION-

In this study, we examined how FFP transfusion affected INR in patients with different liver diseases and observed that FFP was ineffective in lowering mildly elevated INR. Holland and Brooke retrospectively demonstrated that supportive care was effective in lowering mildly elevated INRs (1.3–1.6). FFP transfusion had very little impact in raising INR above 1.7. [12] Additionally, we found in our study that post-transfusion values only significantly improved when 6 units or more of FFP were administered. Youssef et al's retrospective study [3] of patients with chronic liver disease and prolonged PT found that the infusion of 2–6 units of FFP only marginally improved PT.

In our study, acute liver disease and alcohol hepatitis cases had improved post-transfusion INR more than chronic liver disease cases did. This might be because acute liver disease still has compensatory mechanisms in place while chronic liver disease causes irreversible damage.

Response to FFP is often unpredictable in liver disease patients and does not completely normalise PT or INR values [13]. Conventional coagulation tests used as a guide to FFP transfusion have a poor predictive value for risk of bleeding in liver diseases [14]. Hshieh et al. [15] conducted a study on chronic liver disease patients with oesophageal varices who were given FFP transfusions based on raised INR and concluded that INR is a poor predictor of bleeding and it more likely reflects liver dysfunction than bleeding risk. Recent guidelines of the American Association for the study of liver disease advises against FFP transfusion to correct INR before liver biopsy [16]. Our study is one of the few in the body of literature that discusses the impact of FFP transfusion on disorders of the liver. The inability to evaluate the clinical response of patients to FFP transfusion and to evaluate the change in INR based on disease severity is a limitation of our study. Being a tertiary care facility and located in the state capital, it serves the typicalpopulation surrounding it, which is typically urban, suburban, and near the periphery. However, a significant portion of the periphery is still unscreened for this study. The results may differ if the study had a larger sample size because this one had a relatively small sample size. Our study's additional hypotheses regarding changes in INR by FFP transfusion should not be regarded as conclusive and should instead be properly validated with a sizable study group and patient follow-ups. Finally, the COVID-19 pandemic's occurrence proved to be a challenge because it limited patient inflow during the study period.

Our's is a small study group, resulting a lack of statistical power, therefore further studies with large cohort preferably multicentric, are needed along with proper follow-up to explore the role of FFP transfusion in correction of INR in patients with liver disease.

CONCLUSION-

When administered in small doses, FFP is less effective at treating liver diseases' mild to moderate coagulation defects. In order to improve the INR significantly, large volumes are needed. The risks involved in transfusing FFP should be carefully considered when making this decision.

Patients with liver diseases have a complex haemostatic system, and it is still debatable whether FFP can correct mild to moderate coagulation abnormalities. Even after receiving an adequate dose of FFP, patients with a high pre-transfusion INR may not experience a significant improvement in INR.

The need of the hour is to adopt strict guidelines for appropriate FFP transfusion in liver diseases and concentrate on global tests of coagulation like thrombo-elastography to guide transfusion in light of the known risks associated with FFP transfusion and the lack of evidence of beneficial effects. For the purpose of developing plasma transfusion guidelines for liver diseases and obtaining more conclusive evidence, additional research with prospective randomized control trials is necessary.

REFERENCES-

1. Shariff MM, Maqbool S, Butt TK, Iqbal S, Mumtaz A. Justifying the clinical use of fresh frozen plasma an audit.J Coll Physicians Surg Pak 2007;17(4):207–10.
2. Stanworth SJ (2007) The evidence based use of FFP and cryoprecipitate for abnormalities of coagulation tests and clinical coagulopathy. In: Hematology. American Society of Hematology Educational Program, pp 179–186
3. Youssef WI, Salazar F, Dasarathy S, Beddow T, Mullen KD (2003) Role of FFP infusion in correction of coagulopathy of chronic liver disease: a dual phase study. Am J Gastroenterol 98(6):1391–1394
4. Stanworth SJ, Brunskill SJ, Hyde CJ, Murphy MF, McClelland DB (2004) Is fresh frozen plasma clinically effective? A systematic review of randomized controlled trials. Br J Haematol 126(1):139–152
5. Haas T, Fries D, Tanaka KA, Asmis L, Curry NS, Schöchl H. Usefulness of standard plasma coagulation tests in the management of perioperative coagulopathic bleeding: is there any evidence Br J Anaesth. 2015;114:217–224
6. Katherine T. Forkin, Douglas A. Colquhoun, Edward C. Nemergut, and Julie L. Huffmyer. The Coagulation Profile of End-Stage Liver Disease and Considerations for Intraoperative Management. International Anesthesia Research Society 126. 2017; 49,
7. Shinagare SA, Angarkar NN, Desai SR, Naniwadekar MR (2010) An audit of fresh frozen plasma usage and effect of fresh frozen plasma on the pre-transfusion international normalized ratio. Asian J Transfus Sci 4:128–132
8. Sukanya Baruah, Meenu Bajpai: Effect of FFP Transfusion on International Normalized Ratio in Liver Disease Patients. Indian J Hematol Blood Transfus (Oct- Dec 2018) 34(4):719–722
9. Raturi M, Shastry S, Murugesan M, Baliga PB, Chakravarthy K. Effect of plasma component transfusion on conventional coagulation screening tests. Asian J Transfus Sci 2018;12:57-61
10. Kulkarni N. Evaluation of fresh frozen plasma usage at a medical college hospital - A two year study. International Journal of Blood Transfusion and Immunohematology 2012;2:16–20.
11. Garcia K. A Brief History of Blood Transfusion Through the Years [Internet]. Stanford Blood Centre.2017. Available from: http://stanfordblood centre.org/a-brief-history-of-blood-transfusion-through-years.
12. Holland LL, Brooke JP. Toward rational fresh frozen plasma transfusion: the effect of plasma transfusion on coagulation test results. *Am J Clin Pathol.* 2006;126(1):133–139. doi: 10.1309/NQXHUG7HND78LFFK.
13. Lisman T, Caldwell SH, Burroughs AK, et al. Hemostasis and thrombosis in patients with liver disease: the ups and downs. *J Hepatol.* 2010;53:362–371.
14. Wong MP, Droubatchevskaia N, Chipperfield KM, Wadsworth LD, Ferguson DJ. Guidelines for frozen plasma transfusion. *BCMJ.*

15. Hshieh TT, Kaung A, Hussain S, Curry MP, Sundaram V. The international normalized ratio does not reflect bleeding risk in esophageal variceal hemorrhage. *Saudi J Gastroenterol.* 2015;21:254–258.
16. Pandit TN, Sarode R. Blood component support in acquired coagulopathic conditions: Is there a method to the madness? *Am J Hematol.* 2012;87:S56–S62.