Original Research Article

Indian Journal of Emergency Medicine
Volume 5 Number 1, January - March 2019
DOI: http://dx.doi.org/10.21088/ijem.2395.311X.5119.6

The Effectiveness of FFP Transfusion on INR Values in Chronic Liver Patients with Deranged INR

Sona Kurian[1], Gireesh Kumar[2], Dhanasekharan BS[3], Naveen Mohan[4], Sreekrishnan TP[5], Arun Kumar[6], Bharath Prasad[7]

Author's Affiliation:
[1]PG Student [2]Professor and Head [3]Professor [4,6,7]Assistant Professor [5]Associate Professor, Department of Emergency Medicine and Critical Care, Amrita Institute of Medical Sciences, Kochi, Kerala 682041, India.

Corresponding Author:
Gireesh Kumar, Professor and Head, Department of Emergency Medicine and Critical Care, Amrita Institute of Medical Sciences, Kochi, Kerala 682041, India.

E-mail: Gireesh Kumarkp@aims.amrita.edu

Received on 29.10.2018,
Accepted on 28.12.2018

Abstract

Objective: To find the effectiveness of FFP transfusion on INR values in Chronic Liver Disease patient with deranged INR. The aim of this study is to find the usefulness of FFP transfusion before emergency invasive procedure in chronic liver disease patients with deranged INR in emergency department. *Materials and Methods:* This is a prospective observational study conducted in a total of 62 chronic liver disease patients with CHILD C grade with deranged INR who require emergency invasive procedure like central line insertion. Pre and post transfusional INR measured and mean improvement in INR calculated. Relationship between pre transfusional INR and improvement in INR per FFP was studied using Pearson correlation coefficient. *Results:* The mean improvement in INR was 0.55 (standard deviation 0.88). The correlation coefficient between pre and post transfusional INR was 0.50 and significance is 0.000. The linear relationship was noted between pre transfusional INR and improvement in INR per unit of FFP. *Conclusion:* FFP transfusion before emergency invasive procedure in chronic liver patients with deranged INR is effective in reducing INR values to some extend but not effective in normalisation of INR value.

Keywords: Chronic Liver Disease; FFP; INR.

Introduction

Liver disease results in alteration of all three phases of haemostasis- primary hemostasis, coagulation and fibrinolysis. Liver parenchymal cells produces all the coagulation factors in generation of fibrin clot except Factor VIII, which is synthesised by hepatic endothelium and extrahepatic endothelial cells [1]. Chronic Liver Disease is characterised by reduced synthesis of procoagulant protein like Factor II, V, VII, IX, X, XI. Clotting factors usually fall in parallel with progression of liver disease although levels vary considerably [2]. Coagulopathy of liver disease has been replaced by the concept of rebalanced haemostasis. High von Willebrand factor level and low ADAMTS 13 level counteracts defect in primary hemostasis. Reduced level of procoagulant factors are balanced by parallel decline in anti coagulant factors. Fibrinolysis is rebalanced by parallel changes in profibrinolytic and antifibrinolytic proteins [3].

Conventional coagulation tests such as PT/INR and APTT measure procoagulant factors but do not reflect the reduction in anticoagulant factors or the complex interaction between coagulation factors in whole blood. International Normalised Ratio was developed to standardize PT reporting for patient on stable anticoagulant with Vit K antagonist. INR is calculated from the PT ratio (Patient PT/Control PT) adjusted for the International Sensitivity Index. It has been argued that extrapolation of PT to INR is really only valid for those patients anticoagulated with Vitamin K antagonists and may not be valid for patients with liver disease [4]. Conventional coagulation tests do not accurately predict the risk of bleeding in patients with liver disease. There is no evidence that a prolonged PR/INR predicts bleeding at the time of invasive diagnostic procedures [5]. A systematic review found no

significant difference in bleeding rate between patient with and those without prolonged PT prior to liver biopsy [6]. There is evidence that the platelet count is better indicator of bleeding than INR.

Fresh plasma is human donor plasma either recovered from a single whole blood donation or obtained by plasmapheresis, frozen within 8 hours after collection and stored at a defined temperature (typically -30 degree), and can be utilized till one year from the date of collection. Standard FFP unit derived from single unit of whole blood have volume of approximately 200-250 ml. FFP contain near normal level of most plasma proteins, including procoagulant and inhibitory component of the coagulation system, acute phase proteins, immunoglobulin and albumin although all levels are diluted by the citrate anticoagulant solution. Goal of plasma transfusion is to increase plasma level of each coagulation factor above 30%. Haemostasis can be achieved when activity of coagulation factor is at least 25 to 30% of normal in the absence of inhibitor such as heparin and level of fibrinogen is at least 75-100 mg/dl [7]. A dose of 10-15 ml/kg of FFP will increase the coagulation factor by 8-10% while a dose of 30-35 ml/kg will increase them by 30-35%. The low dose corresponds to 3-6 bags of plasma in average 70 kg adult, while higher dose corresponds to 8-14 bags. Infusion rate in healthy individual is 2-3 ml/kg/hour approximately one unit in 1.5 hrs. In individual with volume overload or heart failure infusion rate is 1 ml/kg/hr. Peak action of FFP is about 2-4 hours.

Materials and Methods:

This is an observational prospective study conducted in Emergency Medicine Department in Amrita Institute of Medical Sciences, Kochi from June 2018 to Aug 2018. The study was conducted on 62 Chronic Liver Disease patients in CHILD C category, who presented to the Emergency department, with INR > 2 and for whom FFP transfusion was performed. Chronic Liver Disease patients who simultaneously received cryoprecipitate and packed red blood cell transfusion, those who are on anticoagulants and those with specific coagulation factor (inherited) deficiencies were excluded from our study. Blood sample is drawn at 6 hours after starting FFP and post transfusional INR measured within 1 hour of sample withdrawal using AMAX DESTINI machine. Pre and post transfusional INR, age and gender of the patient were recorded and tabulated. The mean improvement in INR after transfusion was calculated and correlation of pre transfusional INR and improvement in INR per unit of FFP calculated using Pearson correlation coefficient.

Results

A total of 62 chronic liver disease patients with CHILD C grade were included in this study which includes 9.6% females with mean age of 53 (range 43-66) and 90.4% male with mean age of 58 (range of 31-76 years). Mean pre transfusional INR was 3.32 (standard deviation 0.96; standard error mean: 0.12) and mean post transfusional INR was 2.76 (standard deviation 0.78; standard error mean 0.09). The mean improvement in INR was 0.55 (standard deviation 0.88; standard error mean 0.11). The Pearson correlation between pre and post transfusion INR was 0.50 and significance is 0.000.

Discussion

The mean improvement in INR in our study was 0.55 with standard deviation of 0.88. This study shows that FFP transfusion in chronic liver patients with deranged INR is effective in reducing INR values, but not effective in normalisation of INR value in chronic liver patients. But the heamorrhagic risk during invasive procedure in chronic liver disease is based on multiple factors like platelet count, PT-INR, APTT, fibrinogen and clotting factors. According to Michael et al. abnormal coagulation testing in the background of chronic liver disease may be best used to provide the practitioner with information about the synthetic function of the liver but not to assess hemorrhagic risk [8]. Retrospective studies suggest that no preprocedure reversal is warranted for platelet count more than 20,000 and INR <3 in case of central line insertion [9]. However, when the INR is substantially elevated (eg, >2)transfusion can be considered in preparation for urgently required invasive procedures. According to Youssef et al FFP transfusions using the number of units commonly employed in clinical practice infrequently correct the coagulopathy of patients with chronic liver disease, higher volumes (6 or more units) may be more effective but are rarely employed [10]. Abdel-Wahab Ol, et al. concluded in his study that transfusion of FFP for mild abnormalities of coagulation values results in partial normalisation of PT in minority of patients and fails to correct the PT in 99 percent of patients [11]. In this study normalisation of INR seen in less than one percent of patients and 99 percent of patients fails to correct

the INR to normal value. INR is a poor predictor of bleeding risk and the common practice of transfusing fresh frozen plasma before surgery or procedure in otherwise stable patients with liver disease and an elevated INR is questionable. Inappropriate use of FFP not only leads to a wastage of limited resources depriving more needy patients, but also leads to an increased healthcare cost and increased risk of transfusion related complications.

Conclusion

The typical practice of infusion of 10-15 ml/kg of FFP in chronic liver patients fails to correct INR to normal value, but it is effective in reducing INR value to some extend. Whether higher volumes of FFP would more frequently correct the INR remains to be determined. The usefulness of FFP transfusion before emergency invasive procedure in emergency department is questionable, since INR is poor predictor of bleeding tendency.

Limitations of this Study:

The study is conducted in a small group of people.

Abbreviation

CLD- chronic liver disease.

INR- international normalised ratio.

FFP- fresh frozen plasma

TTP- trombotic thrombocytopenic purpuera

References

1. Everett LA, Cleuren AC, Khoriaty RN, and Ginsburg D. Murine coagulation factor VIII is synthesized in endothelial cells. Blood. 2014;123(24):3697-3705.
2. Tripodi A, Primignani M, Chantaangkul V, et al. An imbalance of pro-vs anticoagulation factors in plasma from patients with cirrhosis. Gastroenterology. 2009;137(6):2105-11.
3. Tripodi A and Mannucci PM. The coagulopathy of chronic liver disease. Nengl J Med. 2011;365(2):147-56.
4. Keeling D. International normalised ratio in patients not on vitamine K antagonists. J Thromb Haemost. 2007;5:188-89.
5. Townsend JC, Heard R, Powers ER, and Reuben A. Usefulness of international normalised ratio to predict bleeding complications in patients with end-stage liver disease who undergo cardiac catheterization. Am J Cardiol. 2012;110(7):1062-65.
6. Segal JB, Dzik WH, and Transfusion Medicine/ Hemostasis Clinical Trials N. Paucity of studies to support that abnormal coagulation test result s predict bleeding in the setting of invasive procedures: An evidence-based review. Transfusion 2005;45(9):1413-25.
7. Friedman KD, Menitove JE. Preparation and clinical use of plasma and plasma fractions. In: Williams Hematology, 6th ed, Beutler E, Lichtman MA, Coller BS, et al. (Eds), McGraw-Hill, New York. 2001.p.1917
8. Michael F. Harrison, The misunderstood coagulopathy of liver disease: A Review for the acute setting. West J Emerg Med. 2018 Sep;19(5): 863–871.
9. Van de Weerdt EK, biemond BJ, Baake B et al. central venous catheter placement in coagulopathic patients risk factors and incidence of bleeding complications. Transfusion. 2017 Oct;57(10):2512-25.
10. Youssef Wl, et al. Am J Gastroenterol. Role of fresh frozen plasma infusion in correction of coagulopathy of chronic liver disease: a dual phase study. Am J Gastroenterol. 2003 Jun;98(6):1391-4.
11. Abdel-Wahab Ol, et al. Effect of fresh-frozen plasma on prothrombin time and bleeding in patients with mild coagulation abnormalities. Transfusion. 2006 Aug;46(8):1279-85.