



Early Transfusion vs. Delayed Transfusion of Blood and other Blood Components in Cirrhotic Patients with Active Bleeding



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Abbreviations: FFP: Fresh Frozen Plasma; UGIB: Upper Gastro Intestinal Bleeding; PT/INR: Pro-Thrombin Time and International Normalized Ratio

Introduction

Upper gastro intestinal bleeding (UGIB) due to varices in patients with cirrhosis is a major medical problem in the emergency department [1]. It is also a most important indication for resuscitation with blood components. It is important to follow safe and effective blood transfusion strategies in acute variceal bleed patients with cirrhosis, as the concept of early blood transfusion in these patients is questioned nowadays. Over a period of time, the understanding of the coagulopathy in cirrhosis has evolved, as has the management protocol.

Coagulopathy in Cirrhosis

Cirrhosis is considered as a global multifaceted acquired disorder in hemostasis since; all the blood coagulation products (coagulation factors, platelets and hemoglobin) are deficient in cirrhotic. Because of alteration in hemostasis, normal coagulation pathway is affected at various levels in cirrhosis. There is imbalance between increased yield and decreased production of fibrinogen. Cirrhosis is deliberated as an acquired coagulation disorder in haemostasis rather than a bleeding disorder since fibrinogen levels are also significantly reduced in patients with cirrhosis. Increased transfusion of RBC in patients with cirrhosis is associated with poorer outcome, since it further increases the portal pressures and promotes additional bleeding.

Transfusion of Individual Blood Components

Application of transfusion strategies in patients with cirrhosis remains puzzling since different guidelines are formulated differently in patients with compensated cirrhosis with mild/clinically significant portal hypertension, with or without varices. Thrombin production is compromised in cirrhotic patients only when the platelet amount declines to less than $50 \times 10^9/L$ [2]. Platelet transfusion is usually advocated when platelet count drops below $30 \times 10^9/L$ [3]. No specific recommendations for platelet transfusion exist for patients with cirrhosis. The consequence of fresh frozen plasma (FFP) transfusion has not been assessed during active variceal bleeding and no proposals exist now. It is essential to comment that pro-thrombin time and International Normalized Ratio (PT/INR) are reflected as indicators of liver function and not of coagulation ailments [4]. Baveno VI [5] guidelines state that PT/INR do not represent the bleeding tendency in cirrhotic patients and it cannot be used to monitor blood transfusion evaluations.

Fresh frozen plasma (FFP) is transfused in patients with cirrhosis both therapeutically and prophylactically to correct altered coagulation parameters (PT/INR) [1]. In many studies, it has been reported that FFP transfusion does not show any signifi-

cant improvement in INR in patients with cirrhosis [6]. Hence FFP transfusion in cirrhotic patient had a negligible influence in revising INR below 1.7 [6]. It may be due to a continuing depletion of pre and anti-coagulation factors, altered endothelial function, portal hypertension, sepsis and renal failure in bleeding cirrhotic patients. In view of potential side effects and unspecified efficacy, prophylactic transfusion of FFP based on altered PT/INR values is not suitable in cirrhotic patients. However, FFP transfusion is being transfused in many centers to cirrhotic patients with active bleeding or prior to invasive endoscopy procedures. However, other blood component transfusion necessities are not reduced in patients with cirrhosis [6].

Only few studies have assessed the influence of recombinant factor VII transfusion during active variceal bleeding [7]. No significant conclusions have been gained across various studies. Significant efficacy was achieved only in patients with severe cirrhosis (Child Pugh C) with active bleeding. Recommendation for therapeutic administration is not available for other group of cirrhotic patients. Amending coagulation factors is not considered as part of the variceal bleeding treatment. Transfusion of individual blood components should be customized precisely according to individual patient cirrhotic conditions.

RBC Transfusion Guidelines

Elliot et al. published a report on the response to transfusion in the management of massive UGIB. They inferred that there was no point in transfusing a patient beyond 48 hours [6]. This can probably be considered as an early pointer towards a restrictive transfusion strategy. In 2003, Barkun et al. [2] in the non-variceal UGIB consensus conference group came forward with the consensus guidelines. The indications for transfusion of blood as per those guidelines were severe bleeding and haemoglobin less than 10g/dL. A current blood transfusion concept in patients with cirrhosis depends on consensus expert opinion. The recent Baveno VI [5] and UK guidelines recommend blood transfusion to be started when the hemoglobin is between 7-8g/dL [8]. For bleeding due to portal hypertension, the guidelines also recommended maintaining a target hemoglobin level of about 8g/dL [9]. These guidelines also recommend considering further patient factors like cardiovascular status, hemodynamic status, age and active bleeding.

Conclusion

Patients with cirrhosis have an altered haemostatic imbalance. Before resuscitation of bleeding cirrhotic patients, treating surgeon should understand the coagulopathy and bleeding risk in cirrhosis. FFP and platelets transfusion in correcting mild to moderate liver coagulation parameters remains uncertain. RBC transfusion should not be immediately given to a cirrhotic patient with active UGIB. In view of increased transfusion complications and less mortality, delayed transfusion is better than the early one. Further randomized trails comparing early vs. delayed transfusion in bleeding cirrhotic patients are required to substantiate our opinion.

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