Editorial Commentary

Human albumin infusion strategy in liver cirrhosis: liberal or restrictive?

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Human albumin, which not only expands intravascular volume and improves microcirculation, but also binds numerous substances, such as bile acids, nitric oxide, and cytokines, has been widely employed for the management of several complications of cirrhosis in clinical practice (1,2). However, the proper time duration and dosage and effect of human albumin in liver cirrhosis and its complications remain controversial (3-5).

Recently, a randomized control trial (RCT) has explored the effect of human albumin on patients with decompensated cirrhosis (6). It found that human albumin infusion was not more beneficial than standard care, and led to more severe or life-threatening serious adverse events, especially pulmonary edema and fluid overload. One of the major reasons for this unexpected phenomenon might be the use of a liberal human albumin infusion strategy that human albumin infusion would be continued, if serum albumin concentration was less than 35 g/L in the albumin group (6). By comparison, a restrictive human albumin infusion strategy is often employed in previous studies and our clinical practice, because only a very low serum albumin concentration would significantly increase mortality. For example, serum albumin concentration ≤20 g/L was significantly associated with a higher risk of spontaneous bacterial peritonitis recurrence in liver cirrhosis (7), and human albumin infusion improved the survival of spontaneous bacterial peritonitis (8). Additionally, serum albumin concentration ≤22.8 g/L was an independent risk factor for death in liver cirrhosis with hepatic encephalopathy, and human albumin infusion decreased the in-hospital mortality of patients with hepatic encephalopathy (9,10).

Another reason for this unexpected phenomenon is that the daily dosage and frequency of human albumin infused might be higher in the recent RCT (6). In the human albumin infusion group, the median total dosage of human albumin infused was 200 g per patient during two weeks, and the dosage of human albumin infused was 60–80 g per day in patients with serum albumin concentration <25 g/L at baseline (6). Such a liberal human albumin infusion strategy will lead to a rapid correction of serum albumin concentration, thereby causing more adverse events, which is consistent with the harms caused by a rapid correction of serum sodium concentration in patients with hyponatremia (11). By comparison, previous studies supporting the benefit of human albumin infusion employed a lower dosage of human albumin. For example, in a previous multicenter RCT, which showed a benefit of human albumin for prolonging the overall survival of cirrhosis with uncomplicated ascites and a similar incidence of non-liver related adverse events, the dosage of human albumin was 40–80 g per week for 18 months (12). In a cohort study, which showed a benefit of human albumin for improving the survival of cirrhosis with refractory ascites, but without any serious adverse event related to human albumin, the dosage of human albumin was 40 g per week for 24 months (13). In another RCT, which didn't show a benefit of human albumin infusion for preventing the development of complications and improving the survival of patients awaiting liver transplantation, but a similar incidence of treatment related adverse events, the

dosage of human albumin was 40 g per 15 days (14). Our retrospective study, which showed the efficacy of human albumin infusion for preventing the development of hepatic encephalopathy and improving the outcomes of hepatic encephalopathy in cirrhosis, the median total dosage of human albumin was 30–40 g during hospitalizations (10). Regardless, central blood volume monitoring should be considered to prevent circulatory overload by optimizing the fluid balance, especially in cirrhotic patients receiving high dosage human albumin (1).

In addition, the study population who received human albumin infusion in the recent RCT was too heterogeneous (6). The current guideline recommended human albumin infusion for the prevention of post-paracentesis circulatory dysfunction after large volume paracentesis, spontaneous bacterial peritonitis, and hepatorenal syndrome in liver cirrhosis (1). However, 13.7% of the patients included in the human albumin group in the recent RCT had variceal bleeding (6). A high dosage of human albumin infused may increase the risk of volume overload in such patients, thereby probably elevating portal pressure (15).

Taken together, a restrictive human albumin infusion strategy might be more reasonable for cirrhotic patients, which should be in accordance with blood transfusion strategy in cirrhosis with acute gastrointestinal bleeding (16). Besides, considering that higher dosage and frequency of human albumin will lead to economic burden and waste of medical resources, the appropriate use of albumin in patients with cirrhosis should be crucial.

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