Does albumin supply is needed for the management of ascites?

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Albumin has been used in clinical practice in patients with cirrhosis in an attempt to reduce the formation of ascites, to improve circulatory and renal function. While some of these indications are supported by the results of randomized studies, others are based on only clinical experience and have not proved in prospective studies. The paucity of well-designed study, the cost of albumin, lack of clear-cut benefits for survival and fear of transmitting unknown viruses make the use of albumin controversial. Recently, the benefits of albumin infusions are well established in preventing the deterioration in renal function associated with large volume paracentesis, spontaneous bacterial peritonitis and established hepatorenal syndrome in conjunction with vasoconstrictor. In contrast, when circulatory dysfunction is already established, albumin alone is not effective in improving renal function. Efforts should be made to define the indications for albumin use, dose of albumin required and predictors of response, so that patients gain the maximum benefit from its administration.

Keywords: *

Introduction

Albumin is an effective plasma volume expander due to its high oncotic activity and prolonged half-life in the intravascular compartment. Considering these factors, it is not surprising that it has been used for many years in the management of patients with cirrhosis and ascites. There is evidence to support albumin use in the management of complications of cirrhosis, but there are also arguments against its use in cirrhosis, especially since albumin infusions are costly and survival has not been shown to be improved with this treatment. Recently, this debate has been fostered by the results of a meta-analysis showing that albumin administration may increase mortality in critically ill patients. This will review the use of albumin infusions in the management of patients with cirrhosis and ascites on the basis of the current knowledge of the pathogenesis of ascites and renal dysfunction in cirrhosis.

The physiologic functions of albumin

1. Colloidal osmotic pressure

The most important function of albumin is to maintain colloidal osmotic pressure. As albumin contributes to 60% of the
intravascular protein pool, it provides 60% of the colloidal osmotic pressure. Albumin is a negatively charged molecule and, therefore, it attracts sodium ions, which in turn leads to water retention. In patients with hypoalbuminemia (especially when it is associated with inflammation or sepsis) whose capillaries are known to be hyper-permeable, the leakage of albumin into the interstitial space draws water with it, producing edema. 4

2. Transport

Albumin has a strong negative charge, but binds weakly and reversibly to both cations and anions. Therefore, it functions as a transport molecule for a large number of metabolites including fatty acids, ions, thyroxine, bilirubin and amino acids. Albumin also binds covalently and irreversibly with d-glucose and d-galactose. The glycosylation of albumin, which is to a certain extent age-dependent, has effects upon its charge and therefore may influence capillary permeability characteristics. 5

3. Antioxidant effects

Albumin is the major extracellular source of thiols. These sulphhydryl groups are scavengers of reactive oxygen and nitrogen species. Albumin also can influence plasma redox status by binding heavy metals such as iron and copper. 6

4. Endothelial stabilization

Albumin’s ability to reduce injury to the endothelium caused by reactive oxygen and nitrogen species means that it could potentially have a stabilizing effect on the endothelium and help to maintain capillary permeability. Albumin also interferes with neutrophil adhesion to the capillary endothelium, thereby, reduces inflammation and adds to the maintenance of endothelial integrity.

5. Pharmacological interactions, drug binding

Drugs with which albumin interacts in a highly clinically significant fashion owing to their highly protein-bound state and low margins of safety include warfarin, phenytoin, non-steroidal anti-inflammatory drugs, digoxin. midazolam, thiopental and a number of antibiotics. The volume of distribution of drugs bound to albumin may increase in hypoalbuminemic states, thereby reducing their efficacy. 5

Pathogenesis of ascites and renal dysfunction in cirrhosis

There is a strong evidence indicates that renal dysfunction and ascites formation in cirrhosis are the final consequence of circulatory dysfunction characterized by marked splanchnic arterial vasodilatation causing a reduction in effective arterial blood volume and homeostatic activation of vasoconstrictor and anti-natriuretic mechanisms. The exact mechanism(s) leading to this vasodilatation is not completely understood but may involve increased synthesis/activity of vasodilator factors, including nitric oxide and vasodilator peptides. 8-9 These splanchnic arterial vasodilatations would be responsible not only for the reduction in total systemic vascular resistance but also for an abnormal distribution of blood volume with reduction of effective arterial blood volume. Reduction of effective arterial volume stimulates the rennin-angiotensin system and vasopressin release which leads to continuous renal sodium and water retention and ascites formation. 10 In contrast, there is no