Intravenous albumin for spontaneous bacterial peritonitis and renal dysfunction in patients with cirrhosis-short review

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Abstract

Current clinical guidelines for albumin use in decompensated cirrhosis recommend the use of intravenous albumin infusions for management of ascites-related symptoms and paracentesis (removal of ascitic fluid) and for the management of spontaneous bacterial peritonitis (SBP), renal dysfunction and variceal bleeding. Routine albumin use is not recommended for the management of non-SBP infections.

The aim of this review is to improve our understanding of the effects of albumin use in cirrhosis by reviewing the currently available and quantifying the effectiveness of intravenous albumin therapy to prevent specific cirrhosis complications, spontaneous bacterial peritonitis (SBP) and renal dysfunction.

Long-term albumin administration to patients with decompensated cirrhosis improves survival, prevents complications, eases the management of ascites and reduces hospitalizations, thus being cost-effective. However, variant results indicate that further investigations are needed, aiming at confirming the beneficial effects of albumin, clarifying its optimal dosage and administration schedule and identify patients who would benefit most from long-term albumin administration.

Key words: spontaneous bacterial peritonitis (SBP), cirrhosis, albumin, acute-on-chronic liver failure (ACLF)

Background

More than 45 million people globally have cirrhosis and other severe forms of chronic liver disease [1]. Over a 10-year period of observation, cirrhotic liver disease develops ascites placing patients with cirrhosis at risk for developing spontaneous bacterial peritonitis (SBP) [2]. It is estimated that 12-25% of patients with ascites in the end-stage liver disease will have spontaneous bacterial peritonitis (SBP) but the classic triad of fever, abdominal pain, and worsening ascites is often absent [3]. With a mortality rate approaching 40%, rapid diagnosis and evidence-based treatment is critical in the management of patients presenting with SBP [4]. Diagnosis of SBP is based on ascitic fluid analysis (PMN count ≥250 cells/mm³). Leukocyte reagent strips are not useful as screening test considering their variable sensitivity (45%-100%). Secondary peritonitis constitutes the main differential diagnosis of SBP and is often due to a perforated viscus or infection in adjacent organs. Runyon's criteria (glucose levels <50 mg/dL, protein concentration >10 g/L, lactate dehydrogenase concentration > normal serum levels) are clues to this diagnosis and prompt computed tomography examination of the abdomen and early surgery in the management of patients with secondary bacterial peritonitis [5, 6].

The aim of this review is to improve our understanding of the effects of albumin use in cirrhosis by reviewing the currently available evidences and quantifying the effectiveness of intravenous albumin therapy to prevent specific cirrhosis complications, spontaneous bacterial peritonitis (SBP) and renal dysfunction.

The cirrhosis stage preceding the occurrence of complications is known as compensated cirrhosis, as opposed to the decompensated stage during which patients develop complications. In addition to the array of complications related to portal hypertension, complexity of cirrhosis is amplified by the development of an acute-on-chronic liver failure (ACLF). ACLF is a clinical syndrome characterized by rapid onset of failure of the liver and/or extrahepatic organs, including kidneys, systemic circulation or brain, within the context of an acute decompensation (AD) of the disease as defined by the development of ascites, encephalopathy, gastrointestinal bleeding and/or bacterial infection [7]. ACLF often occurs in patients with prior history of decompensated cirrhosis but also develops without of previous decompensation. It is associated with high short-term (1 month) mortality rate, being the most frequent cause of death of cirrhosis [8]. The pathophysiological mechanisms underlying the clinical manifestations of decompensated cirrhosis and ACLF represent novel targets for pathogenic treatments. There are two working hypotheses for the mechanisms of organ failures in ACLF. Pathogen-associated molecular patterns (PAMPs; e.g., lipopolysaccharide (LPS)) are specifically recognized by pattern-recognition receptors (PRRs; egg. Toll-like receptor (TLR) 4 for LPS) expressed in innate immune cells and epithelial cell [11, 12]. This process is called structural feature...
recognition. Damage-associated molecular patterns (DAMPs; e.g., high mobility group box 1 (HMGB1), S100A8 (MRP8, calgranulin A) and S100A9 (MRP14, calgranulin B)), are molecules resulting from stressed cells that, once released, follow a similar path. PAMPs are either released by an infecting alive bacterium or ‘translocated’ from the gut lumen to blood, while DAMPs are released from tissues where necrosis and pyroptosis take place (liver and extrahepatic organs (not shown)).

Whichever the origin of these molecular patterns, their recognition by PRRs results in the production of a broad variety of inflammatory molecules (cytokines, chemokines and lipids), vasodilators and of reactive oxygen species, particularly in phagocytes. Intense systemic inflammation may cause collateral tissue damage (a process called immunopathology) and subsequently organ failures (hypothesis 1). Extrahepatic tissue damage can result in the release of DAMPs, which may perpetuate or accentuate PAMP-initiated and DAMP-initiated systemic inflammatory response (not shown) [11, 13].

Patients with cirrhosis and ascites have a vulnerable renal function long time attributed to effective hypovolemia due to peripheral arterial vasodilation [9]. It is now clear that decompensated cirrhosis is characterized by a systemic proinflammatory and pro-oxidant milieu playing a major role in the pathogenesis of multiorgan dysfunction. In patients with cirrhosis and portal hypertension, a peripheral arterial vasodilation, mainly occurring in the splanchic circulatory area, endangers effective volaemia [10]. Qualitative and quantitative changes in the intestinal microbiota and impairment in intestinal mucosal barrier, translocation of bacteria or bacterial products, and local inflammation and release of inflammatory vasoactive mediators is likely the initial sequence of events leading to splanchic arterial vasodilatation in cirrhosis. With the progression of the disease, bacterial translocation increases, inflammation become systemic and effective hypovolemia worsens. Activation of the hypothalamic–pituitary–adrenal axis, widespread release of norepinephrine (NE) in the sympathetic nervous system terminals, increased adrenal secretion of epinephrine (E), activation of the renin–aldosterone system and increased release of antidiuretic hormone (ADH) are the main homeostatic responses to restore arterial pressure, leading to renal fluid retention, which accumulates as ascites, dilutional hyponatremia and hepatorenal syndrome (HRS) as the most relevant consequences.

The well-established indications for the use of albumin in patients with decompensated cirrhosis rely on this pathophysiological background and mainly aim at restoring effective volaemia or preventing its deterioration. Serum albumin in decompensated cirrhosis undergoes structural and functional abnormalities endangering its non-ontocit properties such as antioxidant, scavenging, immune-modulating and endothelium protective functions. As a result, due to both qualitative (hypoalbuminemia) and qualitative changes, the amount of circulating ‘effective’ albumin can be dramatically reduced. The pleiotropic non-ontocit properties of albumin make it a potential multitarget agent for a mechanistic treatment of decompensated cirrhosis. It has recently provided evidence that long-term albumin administration to patients with decompensated cirrhosis improves survival, prevents complications, eases the management of ascites and reduces hospitalizations, thus being cost-effective [14, 15]. However, variant results indicate that further investigations are needed, aiming at confirming the beneficial effects of albumin, clarifying its optimal dosage and administration schedule and identify patients who would benefit most from long-term albumin administration.

Albumin, the most abundant protein in human serum, has an important role in both maintaining fluid distribution in the body and potentially regulating immune response by binding and inactivating pro-inflammatory molecules. In advanced liver disease, the synthesis of albumin in the liver is disturbed and both the quantity and functionality of albumin are substantially reduced [16]. Treating patients with advanced liver disease with albumin infusions might improve both their ability to respond to infectious threats such as SBP and their ability to restore adequate renal blood flow. Current clinical guidelines for albumin use in decompensated cirrhosis recommend the use of intravenous albumin infusions for management of ascites-related symptoms and paracentesis (removal of ascitic fluid) and for the management of SBP, renal dysfunction and variceal bleeding. Routine albumin use is not recommended for the management of non-SBP infections [9].

Spontaneous bacterial peritonitis (SBP) is diagnosed via cell count and differential of ascitic fluid obtained by paracentesis demonstrating an elevated polymorphonuclear leukocyte (PMN) count (≥ 250 cells/mm³). Treatment focuses on appropriate antibiotic therapy. A third-generation cephalosporin is the treatment of choice as they are typically effective in covering the three most common isolates from infected ascitic fluid: Escherichia coli, Klebsiella pneumonia, and Streptococcus pneumonia [18]. Intravenous albumin administration is often added to the management of these patients but the utility for improving morbidity and mortality is questionable. The benefit of albumin infusion in SBP is not entirely known, although multiple possible mechanisms have been identified. Albumin has been demonstrated to mitigate endotoxemia, block lipopolysaccharide-stimulated neutrophil activity, and modulate nitric oxide activity, mitigating systemic vasodilatation and capillary leak [19]. Sort, et al. [20]. Proved that for select patients, the addition of IV albumin (1.5g/kg) given within 6 hours of diagnosis of SBP reduces the incidence of renal failure and in-hospital mortality in patients with cirrhosis with SBP. Xue, et al [21]. In Chin J Dig Dis in 2002 published a study which conclusion was that the addition of intravenous albumin to an antibiotic regimen may reduce the incidence of renal impairment and mortality in cirrhotic patients with SBP.

The 2012 AASLD Guidelines, based largely on the trial by Sort, et al. [20], recommend that patients with ascitic fluid PMN counts greater than or equal to 250 cells/mm³ and clinical suspicion of SBP, who also have a serum creatinine >1 mg/dL, blood urea nitrogen >30 mg/dL, or total bilirubin >4 mg/dL should receive intravenous albumin (1.5 g/kg) within 6 hours of detection and 1.0 g/kg on day 3. (Class IIa, Level B)

Conclusions

The use of intravenous albumin in addition to antibiotics in the treatment of patients with SBP and concomitant azotemia or hyperbilirubinemia is a lifesaving intervention of critical importance in the emergency department. As the published data and AASLD recommend administration within six hours of diagnosis, this intervention falls firmly in the hands of ED providers. It is recommended timely administration of 1.5 g/kg of albumin in addition to antibiotics in all patients presenting to the emergency department diagnosed with SBP who also have a serum creatinine >1 mg/dL, BUN >30 mg/dL, or total bilirubin >4 mg/dL. Long-term albumin administration to patients with decompensated cirrhosis improves survival, prevents complications, eases the management of ascites and reduces hospitalizations, thus being cost-effective. However, variant results indicate that further investigations are needed, aiming at confirming the beneficial effects of albumin, clarifying its optimal dosage and administration schedule and identify patients who would benefit most from long-term albumin administration.
References