Review

Role of Albumin in Spontaneous Bacterial Peritonitis: Indications, Side-Effects and Outcome

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Abstract

The most prevalent bacterial infection in cirrhotic patients is spontaneous bacterial peritonitis. Hospitalized patients with cirrhosis and ascites have an incidence that ranges between 10% and 30%, making it one of their primary complications. Since it may lead to kidney failure, hepatic encephalopathy, gastrointestinal bleeding, hypervolemic hyponatremia, the development of acute or chronic liver failure, systemic sepsis, so the outcomes in patients with spontaneous bacterial peritonitis are poor. Early antibiotic treatment is essential for bacterial spontaneous peritonitis. It is advised to utilize albumin in addition to antibiotics for some high-risk patients who have spontaneous bacterial peritonitis. The purpose of this research is to review the available information about the role of albumin in spontaneous bacterial peritonitis: indications, side-effects and outcome. Albumin is a plasma volume expander and is responsible for decreasing inflammatory response mediators such nitric oxide and the proinflammatory cytokines tumour necrosis factor-alpha and interleukin-6 because of this property it has a beneficial role in spontaneous bacterial peritonitis. Intravenous albumin administration has also been demonstrated to enhance systemic hemodynamic and renal function among spontaneous bacterial peritonitis patients. This effect is mediated by both an increase in cardiac function and a decrease in arterial vasodilatation Albumin along with the antibiotics is safe and effective in management of spontaneous bacterial peritonitis. It reduces the risk of renal complications and mortality. Although further research for standardizing the dosage and duration of albumin is needed.

Keywords: *spontaneous, bacterial, peritonitis, albumin, infection*

Introduction

Spontaneous bacterial peritonitis (SBP), which accounts for roughly 10% to 30% of bacterial infections in hospitalized patients, is characterized as bacterial infections that happen in patients with cirrhosis and ascites without any substantial intraperitoneal infection. Because of alterations in the intestinal bacterial population and mucosal barriers, SBP occurs in patients with liver cirrhosis. Furthermore, the compromised host immune system is unable to eliminate the foreign bodies and their by-products. Gram-negative bacteria, like Escherichia coli and Klebsiella species, are the most frequent causes of SBP, however infections with Gram-positive bacteria are on the rise. After paracentesis, ascites with greater than 250 polymorphonuclear leukocyte/mm^3 are indicative of SBP (1). As per numerous studies in literature, SBP affects 10%–30% of hospitalized patients with cirrhosis and ascites as well as 3.5% of outpatients, with a 20%–40% in-hospital mortality rate. Kidney failure, hepatic encephalopathy, gastrointestinal haemorrhage, hypervolemic hyponatremia, development of acute and chronic liver failure, systemic sepsis, and poor survival may all be driven by SBP (2).

A high rate of renal impairment and mortality has been documented in patients with cirrhosis who develop SBP. Modifications in systemic hemodynamics that result in a reduction in the effective arterial blood volume may be associated with renal failure. Albumin which is a plasma volume expander may help high-risk SBP patients with serum bilirubin levels over 68.4 mol/L, blood urea nitrogen levels above 10.7 mmol/L, or serum creatinine levels above 88.4 mol/L reduce renal impairment and death (3). The protein albumin is most prevalent in the human circulatory system. Its physiological functions include osmotic pressure management, the binding and transport of different ligands, as well as anti-inflammatory and antioxidant properties. In order to increase the delivery and activity of diuretics in the kidneys and to prevent circulatory damage following large-volume paracentesis, albumin has established roles as a diuretic adjunct. Albumin's capacity to increase intravascular volume and bind proinflammatory chemicals is thought to make it useful in these circumstances (4-6).

The positive effects of albumin on renal function and survival in cirrhotic individuals with SBP may be mediated by a number of different pathways. Beyond the increase in plasma oncotic pressure that causes plasma expansion and an increase in cardiac output, individuals suffering from SBP treated with albumin also observe decrease in arterial vasodilatation. After administration of albumin to SBP patients, inflammatory response mediators such nitric oxide and the proinflammatory cytokines tumour necrosis factor-alpha and interleukin-6 decreased. Albumin binds to a wide range of molecules and acts as a scavenger (7). For high-risk patients with baseline laboratory results including serum creatinine >1 mg/dL, blood urea nitrogen >30 mg/dL, or total bilirubin >4 mg/dL, albumin treatment is advised within six hours of diagnosis (8). The purpose of this research is to review the available information about the role of albumin in SBP: indications, side-effects and outcome.

Methodology

This study is based on a comprehensive literature search conducted on October 4, 2022, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the information about role of albumin in SBP: indications, side-effects and outcome. There were no restrictions on date, language, participant age, or type of publication.

Discussion

SBP is attributed to in-hospital mortality rates of 20%–40% unrelated to infection and mortality rates of up to 70% and 80%, respectively, at one and two years without transplantation. The mortality risk is highest in individuals with SBP who also have concurrent renal failure, which occurs in 30%–40% of patients. Albumin infusion is a component of the standard treatment for acute renal failure and SBP. As per current recommendations, albumin should be administered to all SBP patients at doses of 1.5 g/kg on day one and 1 g/kg on day three in order to prevent the onset of hepatorenal syndrome. However, there are still a lot of unanswered problems for clinicians who want to enhance the level of care given to patients with ascites. First, there is ongoing discussion on albumin's advantages for individuals with low-risk SBP. Second, it is unknown what minimal effective albumin dose is required to prevent renal failure in SBP. Given the price of albumin and the possibility of complications from volume overload, such as respiratory distress, proper dosing is vital (9).

Indications of albumin in SBP

Currently, albumin is used to treat cirrhosis in three primary ways. The first would be when large-volume paracentesis is performed, typically when more than 4-5L of ascites are drained, in the treatment of tight or recalcitrant ascites in order to prevent post-paracentesis dysfunction. It is formally advised when bilirubin is greater than 4 mg/dL or creatinine is greater than 1 mg/dL in cases of SBP to prevent renal impairment and increase survival. Using it in conjunction with terlipressin appears to be the most effective treatment plan for type I hepatorenal syndrome. Therefore, is very pertinent and advantageous in the management of these issues in the cirrhotic patient (10). Despite the paucity of reliable evidence, all treatment guidelines for SBP advocate for albumin infusions in addition to antibiotics, at least for individuals at risk for acute renal injury (11).

Effectiveness of albumin in SBP

Findings of a retrospective cohort study showed that the incidence of acute kidney injury and fatality dramatically decreased, and the appropriateness of the ordered albumin regimen increased when the albumin order was limited to high-risk SBP patients. In both the pre-order set and the post-order set, the incidence of acute kidney injury was 63.93% and 33.33%, respectively (p= 0.01). Mortality rates in the pre-order set and post-order set were respectively, 36.07% and 7.41% (p = 0.005). In the pre-order set and post-order set, there were 24.59% to 40.74% of patients who received albumin within 6 hours (p = 0.14) respectively (8). Results of a meta-analysis showed that in the control groups, renal impairment occurred among 30.6%, as opposed to 8.3% of subjects in the albumin-treated groups. A decrease in renal impairment following albumin infusion was associated with a pooled odds ratio of 0.21 (95% confidence interval, 0.11-0.42). The odds ratios for renal impairment during albumin therapy ranged from 0.19 to 0.30 for each study, 35.4% of individuals died, compared to 16% of albumin-treated patients. The pooled odds ratio for decreased mortality following albumin infusion was 0.34. Clinical trials indicated that albumin infusion averted renal impairment and decreased mortality in SBP patients (12).

Elloumi et al. reported in their retrospective study that in 87.8% of cases, cefotaxime was the first intravenous antibiotic used, while ofloxacin was used in 6.1% of cases, and 85.7% of cases had favourable results. Within 18 months, 18.3% of patients developed hepatorenal syndrome. However, even with albumin perfusion, the creatinine level rose in 20.4% of patients. The six-month survival rate was 81.8%, and the immediate mortality was 4%. Even when albumin was administered at a low dose during SBP, renal failure and hepatorenal syndrome did not occur as frequently as reported in the literature. These findings in light of financial constraints may indicate the implementation of such a procedure for SBP or the selection of high-risk individuals who require albumin perfusion during SBP (13). Results of a study by Sort et al. concluded that treatment with intravenous albumin in addition to an antibiotic lowers the risk of renal impairment and death in patients with cirrhosis and SBP compared to treatment with an antibiotic alone (14).

Chen et al. described in their study that in cirrhotic patients with SBP, combination therapy with albumin and antibiotics can significantly (p<0.01) lower plasma levels of tumour necrosis factor-alpha and interleukin-6, as well as levels of endotoxin, tumour necrosis factor-alpha, and interleukin-6 in ascitic fluid. The plasma and ascitic fluid levels of nitric oxide products considerably increased in individuals with SBP without the addition of albumin to an antibiotic regimen (p=0.005 and p=0.004, respectively). The findings show that the anti-inflammatory properties of albumin are linked to a decrease in tumour necrosis factor-alpha and nitric oxide products levels in both plasma and ascitic fluid. Patients with cirrhosis with SBP are advised to get an albumin infusion continuously for three days while also receiving antibiotic medication at the time of SBP diagnosis (15).

In cirrhotic patients with SBP, intravenous albumin treatment has also been demonstrated to enhance systemic hemodynamic and renal function. This effect is mediated by both an increase in cardiac function and a decrease in arterial vasodilatation. More significantly, compared to antibiotic treatment alone, the use of albumin along with SBP treatment resulted in a significantly lower 3-month death rate. The positive impact of albumin infusion on SBP is primarily attributed to its anticancer effects, while it may also be a result of its anti-inflammatory, immune-stimulating, and scavenger activities (16). Choi et al. concluded in their prospective randomized study that in terms of treating SBP, large volume paracentesis combined with intravenous albumin was just as successful as diuretics with similar mortality. For the treatment of tense or refractory ascites in cirrhotic patients with SBP, large volume paracentesis with intravenous albumin may be practical (17).

Sanglodkar et al. suggested in their study that instead of the recommended high dosage albumin of 1.5 g/kg on

day 1 and 1 g/kg on day 3, administration of 20 g albumin per day together with antibiotics is a viable alternative also it is necessary to conduct additional multicentric studies to determine the appropriate dose of albumin to administer in SBP in order to enhance haemodynamic and lessen renal impairment (18). SBP is associated with a significant risk of acute kidney injury, hepatorenal syndrome, and death even with appropriate and prompt antibiotic treatment. Patients with basal blood bilirubin levels greater than 4 mg/dL, or 68 mol/L, or serum creatinine levels more than 1 mg/dL, or 88 mol/L, in particular, were observed to benefit from albumin. Albumin remains the gold standard of therapy since other plasma expanders have not, to date, consistently demonstrated to be as efficacious as albumin (19). Similarly, Abd elaal et al. concluded in their study that when compared to other regimens, the treatment of SBP with cefotaxime and an albumin infusion based on body weight produced the best results (20).

Administration of human albumin solutions has been proven to be advantageous in patients having large-volume paracentesis, or who have hepatorenal syndrome or SBP, due to their oncotic and non-oncotic qualities. In advanced cirrhosis, albumin reduces the severity and risk of infections while enhancing immune cell performance. By delaying the emergence of complications, enhancing quality of life, also likely enhancing survival, its long-term use can alter the course of decompensated cirrhosis patients. But albumin therapy's dosage, duration, and frequency need to be justified (21). It is generally known that albumin infusions can help avoid the decline in renal function brought on by large-volume paracentesis, SBP, and established hepatorenal syndrome when used in conjunction with a vasoconstrictor. Some of these indications are backed up by the findings of randomized studies, but others are just based on clinical experience and haven't been demonstrated in prospective investigations. The use of albumin is debatable due to the absence of well-designed trials, the expensive cost of albumin, the lack of a distinct survival benefit, and the worry of spreading undiagnosed infections. A contemporary example of how albumin can work through processes other than its oncotic impact is the molecular adsorbent recirculating system, which is also referred to as albumin dialysis (22). The current literature is very limited in defining the role of albumin therapy among SBP patients. Research in future including prospective clinical studies, randomized trials, case-control studies are necessary to elaborately study and compare the role of albumin in management of SBP additionally discuss side-effects and complications associated with the albumin administration since current studies are very scarce and mostly have discuss complications in non- SBP infections.

Conclusion

The use of albumin therapy in SBP patients has been studied because of albumin's capacity to increase intravascular volume and bind inflammatory cytokines. Administration of albumin along with the antibiotics among SBP patients is safe and highly effective especially in high-risk patients with increased renal markers but further research is however required for the standardization of its dosage, duration and frequency in clinical settings.

Disclosure

Conflict of interest

There is no conflict of interest

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Data availability

Data that support the findings of this study are embedded within the manuscript.

Author contribution

All authors contributed to conceptualizing, data drafting, collection and final writing of the manuscript.

References

1. Song DS. [Spontaneous Bacterial Peritonitis]. The Korean journal of gastroenterology = Taehan Sohwagi Hakhoe chi. 2018;72(2):56-63.

2. Duah A, Nkrumah KN. Prevalence and predictors for spontaneous bacterial peritonitis in cirrhotic patients with ascites admitted at medical block in Korle-Bu Teaching Hospital, Ghana. The Pan African medical journal. 2019;33:35.

3. Narula N, Tsoi K, Marshall JK. Should albumin be used in all patients with spontaneous bacterial peritonitis? Canadian journal of gastroenterology = Journal canadien de gastroenterologie. 2011;25(7):373-6.

4. Peters Jr T. Serum albumin. Adv Protein Chem. 1997;45:153-203.

5. Laffi G, Gentilini P, Romanelli RG, La Villa G. Is the use of albumin of value in the treatment of ascites in cirrhosis? The case in favour. Digestive and liver disease : official journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver. 2003;35(9):660-3.

6. Ginès P, Titó L, Arroyo V, Planas R, Panés J, Viver J, et al. Randomized comparative study of therapeutic paracentesis with and without intravenous albumin in cirrhosis. Gastroenterology. 1988;94(6):1493-502.

7. Poca M, Concepción M, Casas M, Alvarez-Urturi C, Gordillo J, Hernández-Gea V, et al. Role of albumin treatment in patients with spontaneous bacterial peritonitis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2012;10(3):309-15.

8. Ebied AM, Rattanasuwan T, Chen Y, Khoury AP. Albumin Utilization in Spontaneous Bacterial Peritonitis. Journal of pharmacy practice. 2022;35(4):546-50.

9. Afinogenova Y, Tapper EB. The efficacy and safety profile of albumin administration for patients with cirrhosis at high risk of hepatorenal syndrome is dose dependent. Gastroenterology report. 2015;3(3):216-21.

10. Alves de Mattos A. Current indications for the use of albumin in the treatment of cirrhosis. Annals of hepatology. 2011;10 Suppl 1:S15-20.

11. Roux D, Moreau R, Dreyfuss D. Albumin infusion in spontaneous bacterial peritonitis: another brick off the wall? Annals of intensive care. 2018;8(1):99.

12. Salerno F, Navickis RJ, Wilkes MM. Albumin infusion improves outcomes of patients with spontaneous bacterial peritonitis: a meta-analysis of randomized trials. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2013;11(2):123-30.e1.

13. Elloumi H, Sabbah M, Bibani N, Trad D, Elleuch N, Gargouri D, et al. Effect of low dose albumin administration in spontaneous bacterial peritonitis on renal function and survival. Arab journal of gastroenterology : the official publication of the Pan-Arab Association of Gastroenterology. 2019;20(4):205-8.

14. Sort P, Navasa M, Arroyo V, Aldeguer X, Planas R, Ruiz-del-Arbol L, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. N Engl J Med. 1999;341(6):403-9.

15. Chen TA, Tsao YC, Chen A, Lo GH, Lin CK, Yu HC, et al. Effect of intravenous albumin on endotoxin removal, cytokines, and nitric oxide production in patients with cirrhosis and spontaneous bacterial peritonitis. Scandinavian journal of gastroenterology. 2009;44(5):619-25.

16. Thévenot T, Bureau C, Oberti F, Anty R, Louvet A, Plessier A, et al. Effect of albumin in cirrhotic patients with infection other than spontaneous bacterial peritonitis. A randomized trial. Journal of hepatology. 2015;62(4):822-30.

17. Choi CH, Ahn SH, Kim DY, Lee SK, Park JY, Chon CY, et al. Long-term clinical outcome of large volume paracentesis with intravenous albumin in patients with spontaneous bacterial peritonitis: a randomized prospective study. Journal of gastroenterology and hepatology. 2005;20(8):1215-22.

18. Sanglodkar U, Jain M, Vargese J, Kedarisetty C, Venkataraman J. Clinical audit to determine efficacy of daily infusion of low dose of 20% albumin in combination with antibiotics in patients with spontaneous bacterial peritonitis. Clinical and experimental hepatology. 2019;5(4):301-7.

19. Marciano S, Díaz JM, Dirchwolf M, Gadano A. Spontaneous bacterial peritonitis in patients with cirrhosis: incidence, outcomes, and treatment strategies. Hepatic medicine : evidence and research. 2019;11:13-22.

20. Abd Elaal MM, Zaghloul SG, Bakr HG, Ashour MA, Abdel-Aziz-El-Hady H, Khalifa NA, et al. Evaluation of different therapeutic approaches for spontaneous bacterial peritonitis. Arab journal of gastroenterology : the official publication of the Pan-Arab Association of Gastroenterology. 2012;13(2):65-70.

21. Jagdish RK, Maras JS, Sarin SK. Albumin in Advanced Liver Diseases: The Good and Bad of a Drug! Hepatology (Baltimore, Md). 2021;74(5):2848-62.

22. Lee JS. Albumin for end-stage liver disease. The Korean journal of internal medicine. 2012;27(1):13-9.