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Albumin Administration in Patients With Spontaneous Bacterial Peritonitis at a Tertiary Hospital: A Retrospective Clinical Analysis

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Purpose Albumin is recommended for the treatment of spontaneous bacterial peritonitis (SBP) in patients at high risk for mortality. We assessed adherence to guidelines for administration of albumin for SBP in clinical practice at a private tertiary care hospital.

Methods A retrospective clinical analysis of all cases of SBP diagnosed at a tertiary referral center from January 1, 2006, to December 31, 2012, was performed. Patients were identified electronically and manually validated. The appropriateness of albumin administration for treatment of SBP was assessed in all patients in whom mortality risk could be established and separately for patients who did or did not meet published trial exclusion criteria.

Results A total of 57 patients diagnosed with SBP were identified, 43 of whom had sufficient data available to assess mortality risk. Of the 17 patients at high risk for mortality, 11 (65%) were treated with albumin. This number increased to 83% when only those eligible for published trials were considered. Of the 26 patients at low risk for mortality, 8 (31%) were treated with albumin. The rate of appropriate treatment for low-risk patients did not change when trial exclusion criteria were applied.

Conclusions In the setting studied, approximately one-third of low-risk patients were inappropriately treated with albumin. Conversely, albumin administration in high-risk patients is lacking to some extent, especially in more medically complex patients. Appropriate albumin administration in SBP can significantly impact quality and cost of care. (*J Patient-Centered Res Rev.* 2015;2:51-55.)

Keywords albumin, administration, dosage, bacterial infection, peritonitis, complications

Spontaneous bacterial peritonitis (SBP) arises from acute bacterial infection of the ascitic fluid. By expanding intravascular volume, intravenous albumin infusion has been shown to prevent renal failure and decrease mortality in patients with SBP. As such, separate clinical guidelines presented by the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases (AASLD) recommend that patients with SBP receive albumin,[1,2] but original trial results and other retrospective and subgroup analyses suggest that albumin should be reserved for patients at highest risk for renal failure and death.[3,4] This suggestion was confirmed in a 2012 study of SBP patients evaluating the efficacy of albumin in high-risk patients, defined as those with elevated blood urea nitrogen (BUN) ≥ 11 mmol/L and/or bilirubin ≥ 68 μmol/L. Poca et al.[5] demonstrated that albumin therapy increased survival of patients with high-risk SBP episodes, but it does not seem to be necessary for patients at low risk for death. As such, AASLD clinical guidelines suggest that albumin should be administered to patients with SBP who are at high risk for mortality, i.e. serum creatinine ≥ 1 mg/dL, BUN ≥ 30 mg/dL or total bilirubin ≥ 4 mg/dL.[2]

The benefits of albumin administration in high-risk SBP episodes are clear, yet evidence from an Italian health care system suggests that appropriate balance of efficacy and cost can only be achieved via implementation of institutionally supported rational albumin prescription guidelines.[6] Although a comprehensive assessment of appropriate use of albumin performed across 53 U.S. institutions in 2003

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found that use was inappropriate more than 50% of the time,[7] a similar study focused on assessing compliance with guidelines for albumin administration in the context of SBP in clinical practice, to our knowledge, has not been conducted in a U.S. tertiary care setting. Herein, we report a case series of patients admitted to Saint Joseph's Hospital (Marshfield, WI) for SBP and describe patterns of risk, albumin administration and outcomes of interest, including renal failure and mortality, among treated and untreated patients.

METHODS

The study was approved by the Marshfield Clinic Research Foundation Institutional Review Board, with waiver of informed consent. An observational study was performed to establish a case series of patients diagnosed with SBP by retrospective chart review at St. Joseph's Hospital from January 1, 2006, to December 31, 2012. SBP was defined as ascitic fluid with polymorphonuclear cell count > 250/mm^3 and no evidence of secondary peritonitis. Patients between the ages of 18 and 80 years at time of diagnosis were included and categorized based on mortality risk and whether or not they met exclusion criteria defined by clinical trials of albumin administration for SBP reported in the literature.[3,8,9] To date, trials of albumin administration in SBP have utilized strict exclusion criteria based on factors that might influence short-term patient outcomes, essentially excluding more medically complex patients. These criteria were recorded in the current study in order to assess the influence these factors may have on the propensity of clinicians to follow albumin administration guidelines based on risk level.

In the literature, clinical trial exclusion criteria include gastrointestinal bleeding or compromised heart function at diagnosis; any neoplasm, human immunodeficiency virus or other infection; antibiotic treatment, increase in diuretic dose or large-volume paracentesis within one week; hepatic encephalopathy; and pneumonia, urinary tract infection or endocarditis at diagnosis.[3,8,9] Patients also were categorized as being at low or high risk for mortality, with high risk defined as BUN ≥ 11 mmol/L (30 mg/dL) or bilirubin ≥ 68 μmol/L (4 mg/dL).[2] Outcomes related to renal failure and mortality were assessed by appropriateness of albumin treatment, and whether or not published clinical trial exclusion criteria were met.

Renal failure was defined using reported laboratory measurements for serum creatinine and BUN. Changes in serum creatinine were considered indicative of renal failure using the RIFLE (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease) criteria, defined as a 1.5-fold increase in serum creatinine over baseline levels within 7 days, or the AKIN (Acute Kidney Injury Network) criteria, defined as an increase in serum creatinine by 0.3 mg/dL or ≥ 1.5-fold over baseline within 48 hours. To qualify as having renal failure, changes in BUN also must have occurred, including a more than 50% increase from pretreatment levels to > 30 mg/dL.

Potential SBP cases were identified electronically and manually validated for inclusion in the case series. Relevant data were manually abstracted by study investigators from the combined electronic medical records of Marshfield Clinic/Saint Joseph's Hospital after electronic identification of potential subjects. Albumin administration according to clinical guidelines was assessed in all patients in whom risk could be assessed and separately for patients who did or did not meet published trial exclusion criteria.

RESULTS

We identified a total of 57 patients diagnosed with SBP during the 7-year study period. Sufficient data were available to assess mortality risk in 43 patients (Table 1). Of the 17 patients at high risk for mortality, 11 (65%) were treated with albumin. Of the 26 patients at low risk for mortality, 8 (31%) were treated with albumin.

After removing all patients who did not meet the exclusion criteria used to enroll patients in the randomized controlled trials reported in the literature, 15 patients remained. These 15 patients are those who would have met all inclusion and exclusion criteria for clinical trial participation as reported in the literature. The remaining 28 patients met clinical trial inclusion criteria for eligibility but had one or more of the described exclusions, suggesting they were more medically complex. When clinical trial inclusion and exclusion criteria were applied, a higher percentage of high-risk patients were treated with albumin appropriately. Of 6 high-risk patients, 5 (83%) were treated with albumin. However, the rate of appropriate treatment did not significantly change

Table 1. Cases of spontaneous bacterial peritonitis (2006–2012) by mortality risk and albumin treatment

Trial criteria met?	BUN (mg/dL)	Bilirubin (mg/dL)	Body surface area, m^2			Renal failure
			Baseline	48 hours	7 days	
High risk, albumin-treated						
Yes	11	17.2	0.7	0.7	0.6	No
Yes	73	0.6	3.9	4	3.6	No
Yes	47	1.9	5.1	2.9	4.1	No
Yes	14	10.1	3.9	1.2	NA	No
Yes	7	4.5	0.5	NA	0.5	No
No	55	4.2	2.4	1	0.7	No
No	24	5	0.6	0.8	0.7	Yes
No	13	22.1	0.7	0.7	NA	No
No	69	0.4	3.1	3.7	0.4	No
No	29	6.4	1.4	NA	NA	No
No	115	4.3	3.2	2.8	2.2	No
High risk, no albumin						
Yes	34	1.8	1.8	1.8	1.4	No
No	43	2.6	1.5	1	0.7	No
No	34	2.7	1.5	1.4	1.3	No
No	30	2.6	0.6	0.7	1	Yes
No	30	0.2	1.4	1.1	1.7	No
No	7	7.9	0.7	0.7	0.8	No
Low risk, no albumin						
Yes	4	2.4	0.4	0.4	0.4	No
Yes	6	1.5	0.4	0.4	0.4	No
Yes	20	1.6	0.9	1.1	0.7	No
Yes	27	2.7	0.8	0.8	NA	No
Yes	14	3.1	0.8	0.8	0.8	No
Yes	14	1.8	1.3	NA	NA	No
No	9	3.1	0.9	NA	0.8	No
No	14	2.1	0.9	NA	0.9	No
No	25	1.3	1.3	1.5	1.7	No
No	29	0.4	1.2	NA	NA	No
No	24	1.1	1.2	1.4	NA	No
No	9	0.6	0.9	0.9	0.8	No
No	13	2.5	0.9	NA	1.1	No
No	5	2.8	0.9	NA	0.8	No
No	13	1.3	0.7	0.6	0.6	No
No	14	1.8	0.8	1.3	0.9	Yes
No	7	1.9	0.5	0.4	0.8	Yes
No	9	0.6	0.5	0.4	0.5	No
Low risk, albumin-treated						
Yes	17	1.7	1.1	0.9	1.3	No
Yes	18	1.2	1.4	NA	1.4	No
Yes	11	3.4	0.7	0.8	1.1	No
No	20	1.3	1.1	1.5	2.3	Yes
No	15	3.6	1.3	0.9	0.8	No
No	23	2.3	1.8	0.7	0.6	No
No	23	0.3	1.1	1.1	0.9	No

BUN, blood urea nitrogen.

Table 2. Renal failure and mortality in patients with spontaneous bacterial peritonitis by mortality risk and albumin treatment

Mortality risk/albumin treatment	Renal failure	Mortality	Mortality due to renal failure
High risk/albumin-treated, n=11	1 (9.1%)	5 (45.4%)	1 (9.1%)
High risk/no albumin, n=6	1 (16.7%)	3 (50.0%)	1 (16.7%)
Low risk/no albumin, n=18	2 (11.1%)	6 (33.3%)	0
Low risk/albumin-treated, n=8	1 (12.5%)	4 (50.0%)	1 (12.5%)

in trial-eligible low-risk patients, as 3 of 9 (33%) low-risk patients were treated with albumin.

As shown in Table 2, renal failure was uncommon in patients with SBP regardless of mortality risk or albumin treatment, and few deaths were attributable to renal failure. All 3 patients in whom mortality was attributable to renal failure were considered medically complex, as they did not meet clinical trial eligibility criteria (Table 1).

DISCUSSION

The recommendation for the administration of albumin in SBP has been in place since 1999,[3] and since then, many randomized controlled trials and a recent meta-analysis have supported the efficacy of albumin administration in high-risk patients.[4] In the meta-analysis, the incidence of renal impairment was 30.6% in the control groups and 8.3% in groups given albumin. Renal impairment and mortality were significantly reduced after albumin infusion. The salutary effects of albumin infusion were remarkably consistent from trial to trial.[4] As such, albumin administration is recommended by the AASLD for the treatment of SBP in patients at high risk for mortality.

In our clinical practice, we found that albumin administration in high-risk patients is lacking to some extent, especially when more complex patients, who would have been excluded from published clinical trials, are considered. This is consistent with the finding that renal failure tended to occur only in those patients who did not meet trial exclusion criteria, regardless of mortality risk or albumin administration, suggesting that clinical guidelines do not apply as well in this more medically complex population often seen in routine clinical practice. In these cases, renal failure may not be the result of SBP itself but could have been attributable to other causes, such as gastrointestinal bleeding, sepsis or other comorbidities that would have otherwise precluded trial inclusion.

In contrast to patients at high risk for mortality, albumin administration is not recommended for patients with low mortality risk.[2] In the patient population described here, approximately one-third of low-risk patients were treated with albumin. It is possible this is the result of a lack of awareness of the distinction between low- and high-risk patients in the clinical guidelines. Importantly, this may be of particular cost concern[6] and may also expose patients to the risks associated with transfusion of blood products, such as risk of viral disease transmission and potential effects on drug elimination.[10]

In general, mortality due to renal failure was uncommon following SBP, regardless of albumin administration. However, failure to follow risk-based albumin administration guidelines presents an important issue related to quality and cost of care. Evidence from clinical practice suggests the best cost-benefit ratio for albumin therapy is achieved when it is used only in circumstances in which there is clinical evidence of efficacy and avoided in instances when clinical evidence suggests that administration is futile.[8] Considerable success in this respect was noted by Mirici-Cappa and colleagues, who used a multistep approach to systemwide guideline adoption, including multidisciplinary adoption of a consensus document, use of an albumin order form with restatement of recommendations at time of prescription, and regular distribution of information to clinicians regarding local albumin prescription practices.[6]

CONCLUSION

Given the expense of albumin and the large volume necessary for administration, strict regulation of albumin administration in patients with spontaneous bacterial peritonitis is warranted to ensure ineffective albumin infusion is minimized.

Patient-Friendly Recap

- Albumin is used to treat patients with the abdominal infection spontaneous bacterial peritonitis.
- Clinical guidelines and other reports indicate the effectiveness of albumin depends greatly on whether the patient is at high or low risk for mortality.
- The authors found that, while unnecessary, administering albumin to low-risk patients is common in real-life clinical practice.
- Identifying and eliminating inappropriate albumin use could lower health care costs of treating patients with this infection.

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Conflicts of Interest

None.

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