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Washington University Emergency Medicine Journal Club
Albumin for Patients With SBP or Large-Volume Paracentesis

Vignette

You are caring for a fifty year old gentleman with a history of non-alcoholic steatohepatitis with cirrhosis who presents to the emergency department (ED) with increased abdominal distension, shortness of breath, and fevers. His abdomen is distended and tense with mild diffuse tenderness. His temp is 38.7 C, BP is 103/60, HR is 89, and SpO2 is 99% on room air. You check his labs and find a WBC of 13.4, baseline anemia, a creatinine of 1.2, and an INR of 1.4. His chest x-ray reveals small lung volumes without infiltrates or pulmonary edema. A bedside ultrasound reveals a large amount of ascites. You decide to perform both a therapeutic paracentesis to relieve pressure on his diaphragm and improve his respiratory complaints, and send fluid to the lab for cell count, differential, gram stain, and culture given your concern for spontaneous bacterial peritonitis (SBP).

You manage to drain just over 8 liters of fluid, for which the patient is quite thankful. The fluid gram stain reveals abundant polymorphonuclear cells (PMNs) with no organism seen. The cell count reveals 15,000 nucleated cells, of which 89% are PMNs. You feel confident that the patient has SBP and order a dose of cefotaxime. You are admitting the patient to the medicine service when the resident suggests that you administer albumin. She tells you that the American Association for the Study of Liver Diseases (AASLD) recommends albumin administration both following large-volume paracentesis and in the management of select patients with SBP. You follow the resident's recommendations, but are curious what the evidence actually shows. After your shift you decide to begin your literature search.

PICO Question #1
Population: Adult patients with cirrhosis and tense ascites undergoing large volume paracentesis
Intervention: Intravenous albumin
Comparison: None
Outcome: Death, renal impairment, circulatory dysfunction, hyponatremia

PICO Question #2
Population: Adult patients with cirrhosis and spontaneous bacterial peritonitis
Intervention: Intravenous albumin + antibiotics
Comparison: Antibiotics alone
Outcome: Death, renal impairment, circulatory dysfunction, hyponatremia

Search Strategy

Two MEDLINE searches were conducted via PubMed. A search was performed using the terms albumin AND "spontaneous bacterial peritonitis" which resulted in 230 citations (http://tinyurl.com/l2zy2se). Of these, one systematic review and one

large randomized controlled trial were chosen. An additional search was conducted using the terms albumin and paracentesis (http://tinyurl.com/kfau542). This resulted in 414 citations, from which two systematic reviews were chosen.

Article 1: Bernardi M, Caraceni P, Navickis RJ, Wilkes MM. Albumin infusion in patients undergoing large-volume paracentesis: a meta-analysis of randomized trials. Hepatology. 2012 Apr;55(4):1172-81. Answer Key.

Article 2: Sort P, Navasa M, Arroyo V, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. N Engl J Med. 1999 Aug 5;341(6):403-9. Answer Key.

Article 3: Salerno F, Navickis RJ, Wilkes MM. Albumin infusion improves outcomes of patients with spontaneous bacterial peritonitis: a meta-analysis of randomized trials. Clin Gastroenterol Hepatol. 2013 Feb;11(2):123-30. Answer Key.

Article 4: Kwok CS, Krupa L, Mahtani A, et al. Albumin reduces paracentesis-induced circulatory dysfunction and reduces death and renal impairment among patients with cirrhosis and infection: a systematic review and meta-analysis. Biomed Res Int. 2013;2013:295153. Answer Key.

Bottom Line

Ascites is one of the many complications associated with hepatic cirrhosis, and is associated with a poor prognosis (D'Amico 2006). Ascitic fluid can accumulate to the extent that it impairs functional status, and current guidelines recommend a large volume paracentesis for patients with tense ascites. When such large volumes of ascitic fluid are removed, fluid shifts and a decreased systemic vascular resistance can potentially lead to circulatory dysfunction, hyponatremia, and renal impairment (Lindsay 2014). The administration of intravenous albumin can theoretically reduce the risk of these complications, though this practice remains controversial (Manzocchi 2012, Caraceni 2013).

Two systematic reviews and meta-analyses published on the use of albumin following large volume paracentesis found similar results (Bernardi 2012, Kwok 2013). The use of albumin was shown to significantly reduce the risk of circulatory dysfunction, with a number needed to treat (NNT) of 2, and the risk of hyponatremia, with a NNT of 8. For these outcomes, albumin was shown to outperform other volume expanders as well. Albumin was not, however, shown to reduce mortality, renal impairment, ascites recurrence, or hospital readmission. While this evidence suggest some benefit to albumin administration, the two outcomes for which albumin demonstrated an improvement are of unclear clinical relevance. As a result, it is difficult make a strong recommendation either for or against albumin administration in patients undergoing large volume paracentesis. The current recommendation from the American Association for the Study of Liver Disease (AASLD) is to consider the administration of albumin (6-8 g/L of fluid removed) for patients undergoing removal of greater than 5 liters. This recommendation is appropriately given a low grade (IIa/C).

With regards to albumin administration in patients with SBP, the evidence is more compelling. A meta-analysis of 4 randomized controlled trials comprising 288 patients found significant reductions in both the risk of renal impairment (OR 0.21, 95% CI 0.11-0.42) and mortality (OR 0.34, 95% CI 0.19-0.60) with NNTs of 4 and 5, respectively. The included studies were, admittedly, of only moderate quality, with only one of them being blinded. The largest of these trials (Sort 1999), which included nearly half of the patients in the meta-analysis, independently demonstrated significant reductions in renal impairment (OR 0.21) and both in-hospital and 90-day mortality (ORs of 0.26 and 0.41, respectively). This study was not blinded, and more importantly was limited by a difference in baseline bilirubin levels between the two group: the mean bilirubin in the control group was 6 ± 1 compared to 4 ± 1 in the group that received albumin. This difference is important, as the study demonstrated on multivariate logistic regression that elevated bilirubin levels were independently predictive of a higher risk of both renal impairment and death.

Despite this limitation, the AASLD recommendation is to administer albumin (1.5 g/kg within 6 hours of diagnosis of SBP followed by 1.0 g/kg on day 3) in patients with a serum creatinine > 1 mg/dL OR BUN > 30 mg/dL OR bilirubin > 4 mg/dL. It should be noted that the limited administration based on these laboratory abnormalities is based on a single observational cohort study, and seems somewhat arbitrary.

Both therapeutic and diagnostic paracentesis are common procedures in emergency medicine, and the diagnosis and initial management of SBP fall well within our practice parameters. Given the increased boarding times observed in many EDs, it is prudent that the emergency physician be aware of treatment modalities that require initiation within the first several hours of patient care. As a result, it seems reasonable to begin the administration of albumin to patients with SBP concomitantly with antibiotics while the patient is still in the ED, as this has been shown to decrease the risk of both renal impairment and mortality. It is also reasonable to consider albumin infusion in patients undergoing large volume paracentesis (more than 5 liters of ascitic fluid removed), though the evidence in support of this is much less compelling.