Plasma volume expansion with albumin reduced renal impairment and death in cirrhosis and spontaneous bacterial peritonitis

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;341:403-9.

Question

In patients with cirrhosis and spontaneous bacterial peritonitis, does plasma volume expansion with albumin prevent renal impairment and reduce mortality?

Design

Randomized (allocation concealed*), unblinded,* controlled trial with 90-day follow-up.

Setting

7 university hospitals in Spain.

Patients

126 patients who were 18 to 80 years of age (mean age 61 y, 64% men) and had cirrhosis and spontaneous bacterial peritonitis or polymorphonuclear cell count ≥ 250/mm³ in ascitic fluid. Exclusion criteria were antibiotic use during the week before diagnosis, other infections, shock, gastrointestinal bleeding, ileus, grade 3 or 4 hepatic encephalopathy, cardiac failure, organic nephropathy, HIV, any other disease affecting short-term prognosis, serum creatinine level > 3 mg/dL (265 µmol/L), or potential causes of dehydration present for ≤ 1 week before diagnosis. Follow-up was 100%.

Intervention

Patients were allocated to intravenous cefotaxime and albumin (n = 63) or intravenous cefotaxime alone (n = 63). Cefotaxime was given at doses of 2 g every 6 hours, 1 g every 6 hours, 1 g every 8 hours, and 1 g every 12 hours for serum creatinine levels of < 1.5 mg/dL (133 µmol/L), 1.5 to 2.0 mg/dL (133 to 177 µmol/L), > 2.0 to 2.5 mg/dL (177 to 221 µmol/L), and > 2.5 mg/dL (221 µmol/L), respectively. The albumin dose was 1.5 g/kg of body weight for the first 6 hours and 1 g/kg on day 3.

Main outcome measures

Renal impairment and death.

Main results

Analysis was by intention to treat. Fewer patients in the cefotaxime-and-albumin group than in the cefotaxime-alone group developed renal impairment (P = 0.002), died during hospitalization (P = 0.01), or died by 3 months (P = 0.03) (Table).

Conclusion

In patients with cirrhosis and spontaneous bacterial peritonitis, plasma volume expansion with albumin reduced the development of renal impairment and death.

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*See Glossary.

Cefotaxime (Cef) and albumin (Alb) vs Cef alone for spontaneous bacterial peritonitis in patients with cirrhosis†

Outcomes at 90 d	Cef + Alb	Cef	RRR (95% CI)	NNT (CI)
Renal impairment	10%	33%	71% (37 to 88)	5 (3 to 11)
In-hospital death	10%	29%	67% (25 to 86)	6 (4 to 19)
Death	22%	41%	46% (8 to 69)	6 (3 to 37)

†Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

Commentary

In patients with advanced chronic liver disease, reversible renal failure is usually caused by hypovolemia (e.g., gastrointestinal bleeding) and less frequently by nephrotoxic agents (e.g., aminoglycosides). Irreversible renal failure, a manifestation of end-stage liver disease with > 80% mortality, is confirmed only by the exclusion of reversible factors. In this study by Sort and colleagues, volume expansion with intravenous albumin, combined with antibiotics for spontaneous bacterial peritonitis, prevented irreversible renal failure and reduced mortality more than antibiotics alone. An important omission, however, is information relating to noncolloid volume repletion in the patients who received antibiotics alone. In these patients, hypovolemia was confirmed because of increased plasma renin activity. Hypovolemia commonly accompanies infection in cirrhosis and further reduces the decreased systemic vascular resistance, mean arterial pressure, and central venous pressure.

Two key issues emerge from this study. First, it is clear that volume repletion, when combined with antibiotic therapy for patients with spontaneous bacterial peritonitis, prevents renal impairment and reduces mortality. The second issue, which is also the basis of this study, is whether intravenous albumin should be recommended for volume replacement. This conclusion is less clear because systemic hemodynamic data or specific details about volume replacement in the control group are lacking. The fact that albumin infusions were superior to crystalloid or plasma expanders in preventing circulatory dysfunction after therapeutic paracentesis (1) does not justify its use in spontaneous bacterial peritonitis. Albumin is expensive and tends to be in short supply; thus, recommendations about its use in spontaneous bacterial peritonitis should be unequivocally substantiated.

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Reference

1. **Gines A, Fernandez-Esparrach G, Monescillo A, et al.** Randomized trial comparing albumin, dextran 70, and polygeline in cirrhotic patients with ascites treated by paracentesis. Gastroenterology. 1996;11:1002-10.