

Role of Albumin Peritoneal Dialysis for Bilirubin Removal after Complicated Liver Transplant

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Abstract

Background: Hyperbilirubinemia has been implicated to have nephrotoxic and hepatotoxic effects. Thus, removal of excessive bilirubin in patients with severe jaundice and renal failure could potentially benefit the recovery of hepatic and renal function. In experimental animal and anecdotal reports in humans, albumin containing peritoneal dialysis (PD) maybe successful in removing bilirubin.

Methods: We utilized albumin-enriched (4 - 8.4 g/L) PD in a patient with primary hepatic allograft dysfunction with severe jaundice and renal failure.

Results: Plasma and peritoneal concentrations of bilirubin (total/direct) before initiation of PD were 23.9 / 14.8 mg/dl and 4.1 / 2.5 mg/dl, respectively. After addition of 8.4 g of albumin / L of PD fluid, the concentrations were 32.4 / 21.3 mg/dl and 0.1 / 0.1 mg/dl, respectively.

Conclusions: There was no significant benefit of this therapy in improving hyperbilirubinemia. However, a higher concentration of albumin in PD fluid might have been more effective.

INTRODUCTION

ROLE OF ALBUMIN PERITONEAL DIALYSIS FOR BILIRUBIN REMOVAL AFTER COMPLICATED LIVER TRANSPLANT

Mild to moderate hyperbilirubinemia frequently occurs within the first postoperative week of liver transplantation. This is due to "functional cholestasis", a temporary and reversible state that usually requires no specific therapy. However, severe jaundice with serum bilirubin levels > 30 mg/dl usually indicates severe allograft dysfunction and is frequently associated with hemodynamic instability, encephalopathy, pulmonary and renal failure (1). Uncomplicated jaundice per se does not cause multiple organ failure, however it may be an important contributing factor in the presence of other insults such as infections, transplant rejection and surgical complications. In vitro studies have demonstrated multiple toxic effects of bilirubin on cell respiration, membrane integrity and transport functions. Although the primary cause of renal failure in

hepatorenal syndrome is intense renal vasospasm leading to renal hypoperfusion, it is thought that toxic tubular damage due to accumulation of bilirubin and bile salts within the tubules may also play a role (2). Moreover, hyperbilirubinemia has also been implicated to impair immune response and have neurotoxic and hepatotoxic effects (2,3).

In view of these toxic effects, it would seem prudent to remove the excessive bilirubin and bile salts. For this, various therapies have been utilized including phototherapy, plasmapheresis and plasma separation with bilirubin adsorption (4), which in selected cases have led to successful removal of bilirubin and clinical improvement. A few animal studies and anecdotal reports in humans suggest that peritoneal dialysis may be an attractive route for removal of bilirubin. Hereby we report a case of hepatic allograft dysfunction with severe jaundice and an attempt to remove bilirubin via albumin-enriched peritoneal dialysis.

CASE REPORT

A 64-year-old white male with end stage liver disease secondary to nonalcoholic steatohepatitis received an orthotopic liver transplant. He had significant blood loss intraoperatively requiring multiple transfusions. His postoperative course was complicated by hepatic artery thrombosis for which re-exploration was performed which led to bile duct injury necessitating biliary drain placement. Due to hemodynamic instability and respiratory failure, the patient had a prolonged stay in the intensive care unit. His hospital course was further complicated with multiorganism sepsis including multidrug resistant pseudomonas, hepatic dysfunction, and renal failure due to hemodynamically mediated acute tubular necrosis necessitating renal replacement therapy.

Although he was in a very positive fluid balance with a significant generalized edema and ascites, fluid removal was rather challenging due to his hemodynamic instability even with continuous venovenous hemofiltration. Thus, he was initiated on peritoneal dialysis (PD), which provided continuous dialysis and fluid removal, as well as the possibility of removal of some of the excessive bilirubin that had accumulated due to his hepatic allograft failure. His PD prescription constituted a total of 12 liters of 1.5% Dianeal solution over 24 hours, with 1 liter exchange every 2 hours. Bilirubin removal was studied on 2 different concentrations of albumin in the PD fluid. Albumin was added to 1.5 % Dianeal during the first 2 days, whereas albumin-free Dianeal was used for the subsequent 2 days. Plasma and peritoneal bilirubin concentrations are shown in table 1. We did not find any significant bilirubin removal with PD with or without the addition of albumin.

Figure 1

Table 1: Serum and peritoneal fluid bilirubin concentration before and after initiation of peritoneal dialysis with and without albumin enrichment

	Serum bilirubin (mg/dl) (total / conjugated)	Peritoneal fluid bilirubin (mg/dl) (total / conjugated)
Day 0: Pre PD initiation	23.9 / 14.8	4.1 / 2.5
Day 1: PD fluid with 4.2 g albumin / L	29 / 19.1	1.6 / 0.9
Day 2: PD fluid with 8.4 g albumin / L	32.4 / 21.3	0.1 / 0.1
Day 3: No albumin in PD	30.4 / 19.3	Not available
Day 4: No albumin in PD	29.9 / 19.2	2.6 / 1.4

The patient was diagnosed with primary allograft nonfunction and a liver biopsy showed mild cholestasis. His hospital course was further complicated by an acute myocardial infarction, acute pancreatitis, ventilator associated pneumonia and multiorganism sepsis which eventually led to his demise.

DISCUSSION

Hyperbilirubinemia is an independent risk factor for increased mortality. In 1940s, it was shown that bilirubin formed complexes with albumin, each molecule of albumin binding 2 molecules of bilirubin at pH 7.4, and that 1 gram of albumin binds 15 mg of bilirubin in vitro (5). These observations were followed by experimental evidence suggesting that protein enriched peritoneal dialysis increases the clearance of bilirubin in rats suffering from obstructive jaundice (6). This was further supported by case reports from Grollman et al. (7) and Hobolth et al. (8), demonstrating that measurable amounts of indirect as well as direct bilirubin could be extracted by PD, when the dialyzing fluid contained albumin (4-5 gm/dl). These preliminary reports prompted us to utilize albumin enriched PD, with the goal to provide the patient with renal replacement therapy and the additional benefit of improving hyperbilirubinemia. In contrary to the earlier observations and consistent with the reports of Shoshkes et al. (9) and Krebs et al. (10), we did not find PD an effective therapy for removal of bilirubin. We feel the discrepancy may be due to the lower concentration of albumin we used in our PD solution.

CONCLUSIONS

Our results suggest that PD with the addition of albumin at the concentration used in our patient (4.2 – 8.4 g/L) does not result in any significant bilirubin removal. Further studies with higher albumin concentration (up to 50 g/L) are needed to resolve this important clinical question.

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