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The Use of Plasma Expanders in Preventing Paracentesis-Induced Circulatory Dysfunction: A Brief Review

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Abstract: ***Ascites is a common complication of liver cirrhosis. Annually, 10% of cirrhotic patients with ascites will develop refractory ascites, which requires large-volume paracentesis (LVP) as the first-line therapeutic procedure. LVP is considered as a safe method; however, it may induce an impairment of circulatory function termed paracentesis-induced circulatory dysfunction (PICD). Plasma volume expanders have been shown to be effective in the prevention of PICD. In this review, we discuss the use of plasma expander in preventing PICD.***

Keywords: circulatory dysfunction, large volume paracentesis, plasma expanders, refractory ascites

1. Introduction

Ascites is one of the most common complication of liver cirrhosis, with an annual incidence of 5-10% in compensated cirrhosis [1]. Annually, 10% of cirrhotic patients with ascites will develop refractory ascites, which is associated with a poor prognosis. In addition to sodium and fluid restriction, large volume paracentesis (LVP) is a common therapeutic procedure in managing ascites, particularly in patient with massive ascites and refractory ascites [2].

LVP is the first-line treatment, as it is effective, faster and easy to perform, and associated with fewer adverse outcomes. However, LVP may induce an impairment of circulatory function that has been termed paracentesis-induced circulatory dysfunction (PICD) [3]. PICD usually occurs after large volume paracentesis (more than 5 liters) and associated with rapid reaccumulation of ascites, hyponatremia, renal impairment, and shorter survival [4].

2. Definition and Pathophysiology of PICD

PICD is a disorder characterized by marked activation of the renin-angiotensin axis secondary to the further increase of an already established arteriolar vasodilatation. PICD is a common and potentially harmful complication of large volume paracentesis. It develops in up to 80% of cirrhotic patients with tense ascites who are not infused with plasma expanders after large volume paracentesis. The occurrence of PICD was associated with worsening of renal function, reacummulation of ascites, hyponatremia, and diminished survival [5], [6]. Definitive diagnosis of PICD was made through laboratory result, defined as an elevation in plasma renin activity (PRA) of more than 50% from the pretreatment level to a level greater than 4 ng/mL/h on the 6th day after paracentesis [3], [6], [7].

The exact mechanism of PICD is not yet fully understood. Dynamics of paracentesis (the rate of ascitic fluid removal), mechanical modifications due to abdominal decompression, and release of vasodilator molecules, such as nitric oxide, from vascular endothelium are thought to play a significant role in development of PICD [3], [8]. Other available evidence suggests that the acute reduction of high intra-abdominal pressure after paracentesis promotes the accentuation of arteriolar vasodilation and results in PICD [7].

PICD was thought to be caused by fluid shifting following paracentesis, which results in decreased circulating volume. Another study concluded that decreased systemic vascular resistance, secondary to increased nitric oxide synthesis, plays an important role in PICD. Increased cardiac output may lead to decreased systemic vascular resistance through short-term downregulation of sympathetic nervous system and renin release caused by activation of cardiac volume receptor. Hypovolemia due to arteriole vasodilatation causes prolong activation of sympathetic nervous system and renin-angiotensin-aldosterone pathway. Increased plasma renin activity (PRA) is characteristic of PICD [7], [8].

3. Evidence Supporting The Use of Plasma Expanders in Preventing PICD

Plasma volume expanders have been shown to be effective in the prevention of PICD. The rationale for using plasma expanders after paracentesis is to refill the dilated vascular space after paracentesis, thereby preventing the subsequent activation of vasoconstrictor systems [3]. Without plasma volume expansion, hemodynamic and hormonal changes after LVP have been extensively reported in previous studies [7]. Albumin has been widely known as one of plasma expansion agents. However, since it is derived from human plasma and the cost is relatively high, its availability in many countries is limited [5], [7]. A number of randomized clinical trials have investigated whether albumin can be replaced by less-expensive plasma expansion agents in therapeutic paracentesis to prevent the occurrence of PICD.

First study conducted by Planas et al. in 1990 assigning 88 patients to receive either intravenous albumin or dextran-70 at the same dose of 8g per liter of ascitic fluid removed.

Neither treatment group showed significant changes in renal and serum electrolytes. A significant increase in plasma renin activity and aldosterone concentration was observed in 51% of patients treated with dextran-70 and in only 15% of patients treated with albumin. These results indicated that although dextran-70 is less efficacious than albumin in protecting cirrhotic patients treated with LVP from the decrease in effective intravascular volume, it appears to be capable of preventing the renal and electrolyte complications induced by paracentesis [9].

A study conducted by Garcia-Compean et al. in 2002 has evaluated the use of dextran-40 versus albumin as prevention of PICD. Sixty-nine cirrhotic patients were randomized to receive either dextran-40 infusion or albumin infusion after LVP. Plasma renin activity and aldosterone concentrations increased in both groups 48h after LVP, but they were more marked in those received dextran-40 infusion. They concluded that dextran-40 was not as efficacious as albumin for preventing PICD [10]. Gines et al. conducted another study comparing the effectiveness of albumin, dextran-70, and polygeline. A total of 289 cirrhotic patients were randomized to those three groups. PICD occurred more frequently in patients treated with dextran-70 (34.4%) or polygeline (37.8%) than in those receiving albumin (18.5%). The author suggested that albumin is the best plasma expander to prevent PICD [11].

A meta-analysis supported those findings, which claimed that albumin was more effective in reducing risk of PICD to 15% [12], and this is probably related to its prolonged half-life (21 days) [3]. However, albumin was better than other plasma expansion agents only when a large volume of ascites was removed. In contrast, when a low volume of ascites (<5L) was drained, the incidence of PICD was low (about 10%) irrespective of the type of plasma expander used [3].

The American Association for the Study of Liver Diseases also recommend the administration of albumin about 6-8 gram per liter of ascites evacuated [6]. Comparison of different dose of albumin was evaluated in study conducted by Alessandra et al. in 2011. Seventy cirrhotic patients treated with LVP were randomized to receive either 4g intravenous albumin per liter of ascites removed of 8g of albumin per liter of ascites removed. The incidence of PICD, hyponatremia, and renal impairment on the 6th day after paracentesis was similar between both groups. After 6 months of follow up, rates of survival and recurrence of ascites requiring LVP were not different between the two groups. The author concluded that treatment with half doses of albumin was effective in preventing PICD and its related complications, with a significant cost reduction [8]. However, large controlled studies comparing recommended doses of albumin versus low doses are still needed.

Paracentesis also induces arteriolar vasodilation which plays a major role in initiating the decrease in arterial blood volume; therefore, the use of vasoconstrictor agent may be effective. The effectiveness of terlipressin, a vasopressin analogue and a potent vasoconstrictor, was evaluated in a randomized pilot study compared to albumin. Twenty patients were enrolled and randomly assigned to receive either terlipressin (3 mg) or albumin (8 g/l of removed ascites). The author concluded that terlipressin may be as effective as intravenous albumin in preventing a decrease in effective arterial blood volume in patients with cirrhosis treated by paracentesis [13].

Midodrine, an oral α-adrenoceptor agonist, was also compared with albumin in cirrhotic patients with tense ascites for the prevention of PICD. Fifty patients were randomly assigned to be treated with either midodrine or albumin after LVP. Those receiving midodrine showed a marked increase of plasma renin activity and plasma aldosterone concentration compared to those receiving albumin therapy. That pilot study suggested that midodrine in a fixed short-term dose is not as effective as intravenous albumin in preventing PICD [14].

4. Conclusion

PICD occurs as a complication of paracentesis and is associated with a high incidence of morbidity and mortality. PICD is a clinically silent syndrome but is associated with faster reacummulation of ascites, hyponatremia, renal impairment, and shorter survival. Plasma volume expansion is the only proven treatment to prevent the condition. A number of plasma expansion agents are available, with albumin as the most recommended choice in cirrhotic patients undergoing large volume paracentesis.

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