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EFFECTS OF TOTAL VOLUME PARACENTESIS FOR TENSE ASCITES ON PORTAL AND VARICEAL HEMODYNAMICS IN PATIENTS WITH CIRRHOSIS

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Chapter I

INTRODUCTION

INTRODUCTION

ASCITES FORMATION IN CIRRHOSIS

Ascites is of Greek derivation (askos) and refers to a 'bag' or 'sack'. The word is a noun that describes pathological fluid accumulation within the peritoneal cavity.[1] Ascites is the most common of the major complications of cirrhosis. Approximately 50% of the patients with 'compensated' cirrhosis develop ascites during 10 years of observation. The development of fluid retention in the setting of cirrhosis is an important landmark in the natural history of chronic liver disease.[2] Approximately 50% of patients with ascites succumb in two years.[3]

The fluid sequestrated in the peritoneal cavity is not a static collection; there is a continuous movement of fluid and solutes in and out of the peritoneal cavity.[4] Once formed, ascitic fluid can exchange with blood through an enormous capillary bed under the visceral peritoneum. This plays a vital dynamic role, sometimes actively facilitating transfer of fluid into the ascites and sometimes retarding it.[5] Meanwhile, the amount of fluid that accumulates, reflects a balance between rates of formation and absorption through the peritoneal membrane.[4] Normally, the peritoneal membrane is covered with a continuous layer of flattened

mesothelial cells which have many open intercellular channels (approximately 50 nm wide) on the antiluminal surface. Also, in some areas, tight junctions between adjacent cells are absent resulting in the formation of stomas and the basement membrane has homogenous openings, allowing direct contact between the peritoneal cavity and the lymphatic network.[6] In cirrhosis, peritoneal membrane thickening may slow the rate of absorption of ascitic fluid.[7]

Factors Involved in Ascites Formation in Cirrhosis:

The formation of ascites in cirrhosis is the final consequence of a combination of abnormalities in renal function, overactivity of vasoconstrictor and antinatruiretic systems which are responsible for sodium and water retention, and alterations in portal and splanchnic circulations, which facilitates the accumulation of retained fluid in the peritoneal cavity.[8] Nevertheless, lowered plasma oncotic pressure due to hypoalbuminemia as a result of liver disease as well as, to dilutions due to extravascular volume expansion, probably a contributing factor but is of lesser importance[4].

I. Sodium and water retention:

The main pathogenic factor of ascites and edema formation in cirrhosis is sodium retention, which causes expansion of the extracellular fluid volume and results eventually in ascites and/or edema formation.[8] Renal sodium retention accompanying cirrhosis is primarily attributable

to enhanced tubular reabsorption mainly along the proximal tubule rather than to alterations in the filtered load of sodium.[9,10] Persistent increase in renal vascular resistance prevents the rise in interstitial pressure responsible for driving fluid into the proximal tubular lumen. Moreover, intrarenal redistribution of plasma flow with shift of blood from the cortex to medulla would be associated with decreased sodium excretion.[11] A number of intrarenal and extrarenal factors are involved in the increased sodium reabsorption, the most important being hyperaldosteronism due to increased renal secretion and decreased metabolic degradation[12] and enhanced renal sympathetic nerve activity.[13,14] In the meantime, the existence of sodium retention in cirrhotic patients with ascites despite normal or increased release of atrial natriuretic peptide,[15,16] may suggest the presence of a reduced renal responsiveness to atrial natriuretic peptide in these patients.[17]

Also, an impairment in the renal capacity to excrete water occurs frequently in cirrhotic patients with ascites and usually follows sodium retention in the natural course of the disease. The clinical consequences of this abnormality are an increase in total body water and in severe cases, dilutional hyponatremia.[8] The pathogenesis of water retention in cirrhosis is complex and involves several factors, including; a reduced delivery of filtrate to the ascending limb of the loop of Henle and the

diluting segment of the nephron,[18] reduced renal synthesis of prostaglandins[19] and increased non-osmotic secretion of antidiuretic hormone which is considered the most important factor in the pathogenesis of water retention in cirrhosis.[20,21]

A vasoconstriction of the renal circulation is, also, a common finding in patients with cirrhosis and ascites. Because renal vasoconstriction in cirrhosis occurs in the absence of morphological changes in the kidney, an imbalance between the vasoconstrictor systems and intrarenal prostaglandins could result in unrelenting renal vasoconstriction.[8] Eicosanoids with vasoconstrictor effects may, also, participate in the reduced renal perfusion in cirrhosis.[22] Moreover, the enhanced release of endothelin (an endothelium derived peptide with a marked vasoconstrictor activity) from the hepatic and/or splanchnic circulation and within the kidney in cirrhosis may contribute to renal vasoconstriction.[23]

II. Alterations in hepatic and splanchnic circulations:

The existence of cirrhosis causes marked structural abnormalities in the liver which result in a severe disturbance in the hepatic and splanchnic circulations.[8] Cirrhosis of the liver is a process of progressive destruction and regeneration of the hepatic parenchyma characterized by

increased connective tissue deposition and marked distortion of parenchymal and vascular architecture and hence, hepatic venous outflow obstruction.[24] Meanwhile, there is a recent evidence suggesting that the increase in intrahepatic vascular resistance in cirrhosis may be attributed to the enhanced contractility of perisinusoidal stellate cells in response to endothelin[25] and the diminished nitric oxide (NO) release in sinusoidal endothelial cells as a result of altered function of endothelial cell nitric oxide synthase.[26] The increased intrahepatic vascular resistance causes marked effects on the portal venous system and also on the arterial side of the splanchnic circulation. On the venous side, the main changes consist of the development of portal hypertension and formation/opening of porta-systemic collaterals with shunting of blood from portal to systemic circulation. On the arterial side, there is a marked arterial vasodilatation[27] which increases portal venous inflow and contributes to the increased portal pressure in the portal venous system. All these changes in the hepatic and splanchnic microcirculation predispose to ascites formation by increasing the filtration of fluid into the peritoneal cavity.[28]

Based on the microvascular changes in cirrhosis, one would predict that the protein content of ascitic fluid of cirrhosis would be high as a