Cardiac output Changes in Hepatorenal Syndrome

Thesis

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List of Abbreviations

Abbreviation	*Title*
ADH	Antidiuretic hormone.
ALF	Acute liver disease.
EAV	Effective arterial volume.
ENOS	Endothelial NO synthase.
ESLD	End stage liver disease.
GFR	Glomerular filtration rate.
HRS	Hepatorenal syndrome.
LVEF	Left ventricular ejection fraction.
MELD	The Model for End Stage Liver Disease.
NO	Nitric oxide.
NSAIDS	Nonsteroidal anti-inflammatory drugs.
PHT	Portal hypertention.
PRA	Plasma rennin activity.
RAS	Renin-angiotensin system.
RBF	Renal blood flow.
RRT	Renal replacement therapy.
SBP	Spontaneous bacterial peritonitis.
SNS	Sympathetic nervous system.
SVR	Systemic vascular resistance.
TIPS	Transjugular intrahepatic portosystemic shunt.
TNF	Tumor necrosis factor.

Introduction

Liver cirrhosis is associated with a wide range of cardiovascular abnormalities. These abnormalities include hyperdynamic circulation characterized by an increase in cardiac output and a decrease in peripheral vascular resistance**(Waleed Al Hamoudi et al., 2006).**

A complex interplay between the splanchnic, systemic, and renal circulation takes place once portal hypertension is established. In the initial stages of cirrhosis (compensated state), in the process of progressive vasodilation, both intravascular volume and cardiac output increase to maintain hemodynamic homeostasis. With progression to decompensated cirrhosis there is more vasodilation, and cardiac output still increases. This high-output state eventually cannot maintain perfusion pressure, and renal blood flow decreases**(Cardenas andGines, 2006).**There seems to be a complex and bidirectional interaction between the heart and the kidneys, and different observations have suggested that a type of cardiac dysfunction known as cirrhotic cardiomyopathy significantly contributes to the pathophysiology of hepatorenal syndrome (HRS**) (Krag A et al., 2011).**

The reduction of the effective arterial blood volume and renal failure in patients with cirrhosis and refractory ascites are

consequences of not only progressive arterial vasodilatation but also cardiac systolic dysfunction**(Vincente Arroyo et al., 2007,Ruiz-del-Arbol L. et al., 2005, Krag Aet al., 2011).**

Recent studies suggest that the development of HRS occurs in the setting of a reduction in cardiac output, indicating that the progression of circulatory and renal dysfunction in cirrhosis is caused not only by splanchnic vasodilation but also by a reduction in cardiac output. This finding suggests that HRS may be the consequence of a fall in cardiac output in the setting of marked splanchnic vasodilation**(Vincente Arroyo et al., 2007,Ruiz-del-Arbol L. et al., 2005, Krag A,et al., 2010).**

Aim of the study

The aim of this study is to evaluate cardiac output changes in patients with hepatorenal syndrome in comparison to patients with decompensated cirrhosis and ascites and patients with compensated liver cirrhosis.

Hepatorenalsyndrome

Introduction:

Hepatorenal syndrome (HRS) is a distinct form of renal failurecharacterized bysevere renal vasoconstriction that occurs in the setting of severe liver disease.HRS is the most frequent fatal complication of cirrhosis, because nearly half of patients die within 2 weeks of this diagnosis**(Fig.1)(Nguyen et al., 2007).**The annual incidence of HRS is estimated at 8% to 40% in cirrhosis(**Fernandez et al., 2007)**.The Model for End Stage Liver Disease (MELD) score in patients with cirrhosis and ascites parallels the risk of developing HRS**(Fernandez et al., 2007).**Onset of ascites in patients with MELD scores of about 10 is associated withan 8% and 11% risk of HRSat 1 and 5 years, respectively**(Planaset al. 2006).**If the MELD score approaches 18 nearly40% of patients develop HRS within 1year(**Fernandez et al., 2007)**.

Common high-risk scenarios for HRS include diuretic-resistantascites, severe hyponatremia or coagulopathy, and a MELD score greaterthan 18. Profound jaundice is often present, but HRS can develop in patients with minimal hyperbilirubinemia (**Fernandez et al., 2007)**.

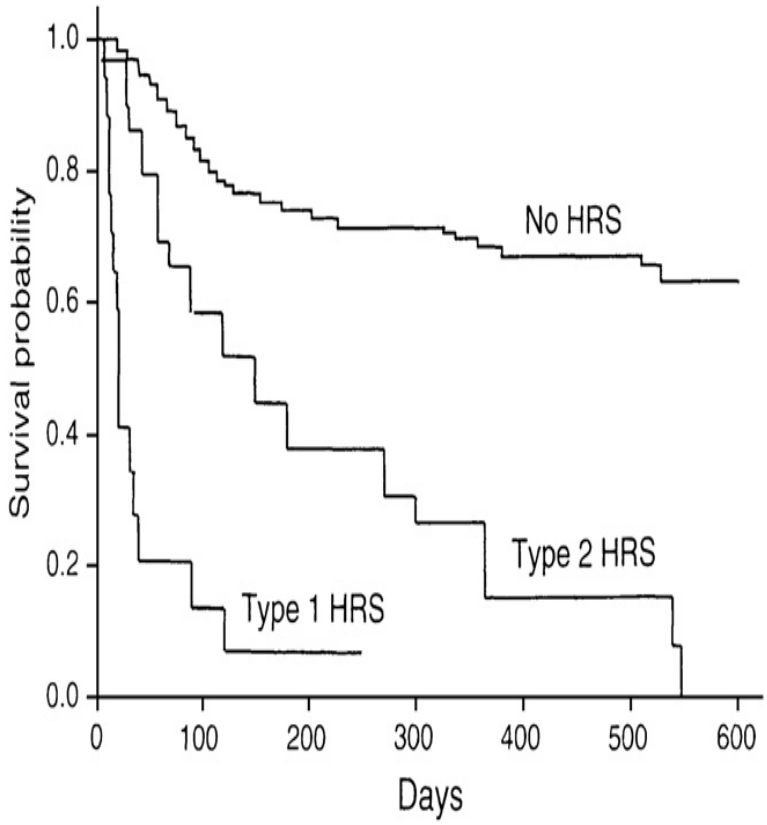

Figure 1: Impactof hepatorenal syndrome on survival**(Arroyo et al.,2007).**

In HRS, the histological appearance of the kidneys is normal, and the kidneys often resume normal function following liver transplantation. This makes HRS a unique pathophysiological disorder that provides possibilities for studying the interplay between vasoconstrictor and vasodilator systems on the renal circulation **(Lau et al., 2011).**

Pathophysiology of Hepatorenal Syndrome:

The hallmark of HRS is renal vasoconstriction, although the pathogenesis is not fully understood. Multiple mechanisms are probably involved and include interplay between disturbances in systemic hemodynamics, activation of vasoconstrictor systems, and a reduction in activity of the vasodilator systems. The hemodynamic pattern of patients with HRS is characterized by increased cardiac output, low arterial pressure, and reduced systemic vascular resistance.Renal vasoconstriction occurs in the absence of reduced cardiac output and blood volume, which is in contrast to most clinical conditions associated with renal hypoperfusion (**Arroyo et al., 2007).**

Precipitatingfactors of HepatorenalSyndrome:

Bacterial infection, especially spontaneous bacterial peritonitis (SBP), is a common precipitating factor for HRS **(Arroyo et al.,2007)**. SBP and other infections augment the production of vasoactive cytokines and other factors which further increase nitric oxide synthesis thereby aggravating splanchnic vasodilatation.

Reductions in effective arterial volume resultingfrom over diuresis, vomiting, varicealhemorrhage,diarrhea (aggravated by

lactulose use), large volume paracentesis without concomitant albumin administration, etc may also precipitate HRS.

Use of nonsteroidal anti-inflammatoryagents (NSAIDs) may contribute to the development of HRS by inhibitingrenalvasodilatoryprostaglandin synthesis**(Ginés and Schrier, 2009)**.

Classification of the hepatorenal syndrome**(Medical Clinics Of North America,2008).**

Type 1: cirrhosis with rapidly progressive acute renal failure**.**

Type 2: cirrhosis with subacute renal failure.

Type 3: cirrhosis with types 1 or 2 HRS superimposed on chronickidney disease (diabetic nephropathy, chronic glomerulonephritis, hypertensive nephropathy, and others) or acute renal injury (acute tubular necrosis and other causes).

Type 4: fulminant liver failure with HRS.

Type 1 hepatorenal syndrome:

In type 1 HRS the serum creatinine level doubles to greater than 2.5 mg/ dL within 2 weeks**(Arroyo et al., 2007).**The key features of type 1 HRS are its rapid progression and high mortality, with a median survival of only 1 to 2 weeks**(Fig.1)(Arroyo et al.,2007).**

Type 2 hepatorenal syndrome

In type 2 HRS, the serum creatinine increases slowly and gradually during several weeks or months with a reciprocal gradual reduction in glomerular infiltration rate (GFR).The median survival of type 2 HRS is about 6 months, significantly longer than for type 1**(Alessandria et al., 2005).**Many patients with type 2 HRS eventually progress to type 1 HRS because of a precipitating factor. The clinician should distinguish between type 1 and type 2 HRS. Theformer is associated with a rapidly fatal prognosis. Type 1 HRS must beurgently managed, with elimination of precipitating factors and evaluationfor liver transplantation. In contrast, type 2 HRS permits less franticevaluation and therapy**(Alessandria et al., 2005)**.

Type 3 hepatorenal syndrome: coexistent kidney diseaseand hepatorenal syndrome

A recent study found that 85% of end-stage cirrhotics had intrinsic renal disease on renal biopsy **(McGuire et al.,2007).** Patients with pre-existing renal disease do not meet the traditional diagnostic criteria for HRS**(Salerno et al., 2007)**. Because they canalso develop HRS from circulatory derangements found in