Management of Organ Dysfunction Assosciated with end Stage Liver Disease

Essay

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in Critical Care Medicine

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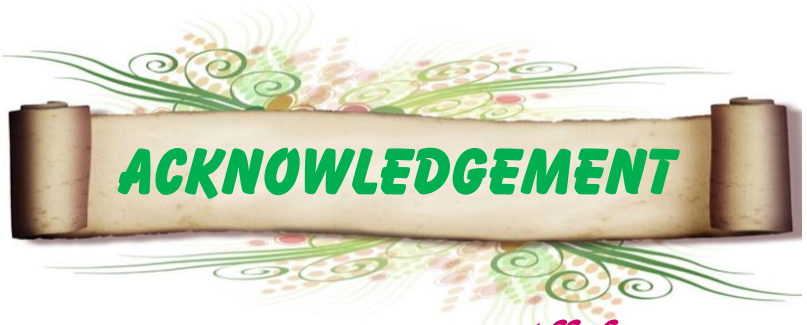

First of all, all gratitude is due to **Allah** *almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.*

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Last but not least, I dedicate this work to my family, whom without their sincere emotional support,

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List of Abbreviations

AAA : Aromatic amino acid

ACEI : Angiotensin-converting enzyme inhibitors

AChE : Acetylcholinesterase

ADQI : Acute Dialysis Quality Initiative

ARDS : Acute respiratory distress syndrome

BCAA : Branched-Chain Amino Acids

BNP : B-type natriuretic peptide

cAMP : Cyclic adenosine monophosphate

CCM : Cirrhotic cardiomyopathy

CHE : Covert hepatic encephalopathy

CO : Carbon monoxide

CRP : C-reactive protein

ECMO : Extracorporeal membrane oxygenation

EF : Ejection fraction

eNOS : Endothelial nitric oxide synthase

ET : Endothelin

ETBR : Endothelin B receptors

FPSA : Fractionated plasma separation and adsorption

GABA : Gamma-aminobutyric acid

GFR : Glomerular filtration rate

GLS : Global longitudinal strain

HO : Heme oxygenase

HPS : Hepatopulmonary syndrome

IAC : International ascites club

iNOS : Inducible NO synthase

IPVD : Intrapulmonary vascular dilatation

LOLA : L-ornithine l aspartate

LPS : Lipopolysaccharide

LT : Liver transplantation

LVDD : Left ventricle diastolic dysfunction

MAA : Macroaggregated albumin

MARS : Molecular absorbent recirculating system

MELD : Model for end-stage liver disease

MHE : Minimal hepatic encephalopathy

MRI : Magnetic resonance imaging

NO : Nitric oxide

NOS : Nitric oxide synthase

OHE : Overt hepatic encephalopathy

OPTN : Organ Procurement Transplant Network

RAAS : renin–angiotensin–aldosterone system

SBP : Spontaneous bacterial peritonitis

SIBO : Small intestinal bacterial overgrowth

SIRS : Systemic inflammatory response syndrome

SOD : Superoxide dismutase

TIPS : Transjugular intrahepatic portosystemic shunt

TTE : Transthoracic echocardiogram

UNOS : United Network for Organ Sharing

V/Q : Ventilation-perfusion

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Introduction

The liver is the largest organ in the body and is critical to a number of metabolic, regulatory and detoxification processes. These include the production of bile, metabolic processing of nutrients, synthesis and regulation of plasma proteins and glucose, and biotransformation of drugs and toxins **(Diehl-Jones and Askin, 2002)**.

Patients with cirrhosis and portal hypertension are at risk of the development of multiorgan dysfunction as hepatorenal syndrome, hepatopulmonary syndrome, hepatic encephalopathy and cirrhotic cardiomyopathy **(Gines et al., 2012)**.

The average survival for type 1 Hepatorenal syndrome (HRS) patients was one month for a Model for end-stage liver disease (MELD) score ≥ 20 and the average survival For type 2 HRS was 11 months for a MELD score < 20 and three months for a MELD score ≥ 20 **(Wong, 2012)**.

Hepatopulmonary syndrome (HPS) is characterized as a triad: liver disease, intrapulmonary vascular dilatation

and arterial hypoxemia. HPS is reported to be present in 4% to 32% of adult patients with end-stage liver disease and in 9%-20% of children. The established 5-year survival rate was 23% for HPS patients and 67% for patients without HPS. Another study showed that 33%-40% of HPS patients died within 2.5-4 years. Approximately 85%-100% of patients with HPS undergoing LT have an improvement in oxygenation within 1 year **(Tumgor, 2014)**.

Overt hepatic encephalopathy has been shown to have a poor prognosis independent of severity of liver disease. One study evaluating hospitalized patients with OHE found that 1 year survival probability was 42% and 23% at 3 years. Similarly past studies have also found 1 year survival to be 20%–40% with 3 year survival of 15% **(Suraweera et al., 2016)**.

Cirrhotic cardiomyopathy is a cardiac dysfunction presented in patients with cirrhosis. The prognosis is difficult to establish in patients with cirrhosis due to the concomitant liver and cardiac function progressive deterioration **(Møller et al., 2013)**.

Aim of the Essay

The aim of the essay is to throw the light on organ dysfunction associated with end stage liver disease and discuss recent trends in management.

Pathophysiology of Organ Dysfunction Associated with end Stage Liver Disease

The hepatocytes, which account for approximately 80% of the total liver cell mass, have essential physiological functions, such as the regulation of carbohydrate and lipid metabolism, and the clearance and inactivation of drugs, ethanol, toxins, and various hormones and vasoactive substances. A very important function of hepatocytes is the synthesis of plasma proteins, including albumin, C-reactive protein (CRP), fibrinogen, complement, and coagulation factors **(Møller and Bendtsen, 2015).**

When the liver is exposed to toxic substances such as drugs, alcohol, and hepatitis B or C virus, and autoimmune diseases, fibrogenesis increases and initiates the cirrhotic process along with the development of regenerative nodules through activation of the hepatic stellate cells into myofibroblast-like cells with contractile, proliferative, and fibrogenic properties (Fig 1). It is this cell type that is primarily responsible for the deposition of extracellular scar matrix in the Space of Disse in the liver. Sustained fibrogenesis leads to cirrhosis, which is

characterized by a distortion of the liver parenchyma and a reduction in vascular architecture **(Lee and Friedman, 2011).**

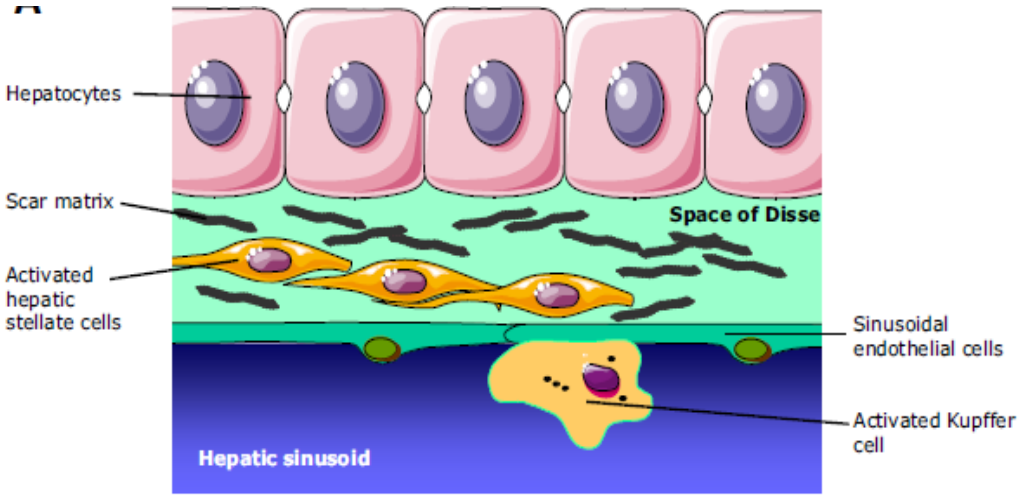

Figure 1: Histopathology of liver cirrhosis **(Møller and Bendtsen, 2015).**

The disease course in patients with cirrhosis is characterized by several phases. For a long period, the clinical presentation is silent, and the patients may not experience any major clinical events. This stage of the disease is usually referred to as ‘‘compensated cirrhosis.’’ After a longer or shorter silent period, the liver function may progressively deteriorate with a rapid decrease in life expectancy **(D’amico et al., 2014)**.

From a clinical point of view, these patients may develop ascites, bleeding from esophageal varices,

encephalopathy, cardiopulmonary dysfunction, and renal failure. This phase is referred to as ‘‘decompensated cirrhosis.’’ There are strikingly different survival outcomes between patients with compensated and decompensated cirrhosis **(Bajaj et al., 2014)**.

From a pathophysiological point of view, the amount of fibrosis in the liver may increase and thereby adversely affect the splanchnic hemodynamic homeostasis with an increase in the portal pressure as a result **(Lee and Friedman, 2011).**

The combination of portal hypertension with portosystemic shunting and increased hepatocellular dysfunction may lead to increased circulating levels of vasodilators, which may induce splanchnic vasodilatation and reduced systemic vascular resistance **(Møller and Bendtsen, 2015).**

The translocation of bacterial products from the gut may further augment the splanchnic and arterial vasodilatation that leads to a number of hemodynamic changes and, ultimately, to a universal hyperdynamic syndrome **(Matuchansky, 2014).**