Cholestatic liver dysfunction in Critically ill patient

An Essay
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Abbreviations

ACG ..... American College of Gastroenterology

AFLP ..... Acute fatty liver of pregnancy

ALP ..... Alkaline phosphatse

ALT ..... Alanine amino transferase

ARDS ..... Acute respiratory distress syndrome

AST ..... Aspartate amino transferase

BSEP ..... Bile salt export pump

CCK ..... Cholecystokinin

DIC ..... Disseminated intravascular coagulation

DILI ..... Drug induced liver injury

DJS..... Dubin-Johnson syndrome

ERCP ..... Endoscopic Retrograde Cholangio-pancreato-graphy

G6PD ..... Glucose-6-phosphate dehydrogenase

GGT ..... Gamma-Glutamyl Transpeptidase

HAART .... Highly active antiretroviral therapy

HES ..... Hydroxyethyl starch

HLI..... Hypoxic liver injury

ICU ..... Intensive care unit

IL ..... Interleukin

INF-ɣ ..... Interferon-ɣ

iNOS ..... Inducible nitric oxide synthase

IGF-1 ..... Insulin-like growth factor 1

KC ..... Kupffer cells

LCHAD .... Long-chain 3-hydroxyacyl-coenzyme A dehydrogenase

LCTs ..... Long chain triglycerides

LFTs ..... Liver Function Tests

LPS ..... Lipopolysaccharide

LT ..... Liver transplantation

MCTs ..... Medium chain triglycerides

MODS ..... Multiple organ dysfunction syndrome

MRCP ..... Magnetic resonance cholangiopancreato-graphy

MV ..... Mechanical ventilation

NASH ..... Nonalcoholic steatohepatitis

NO ..... Nitric oxide

NRH ..... Nodular regenerative liver hyperplasia

OCP ..... Oral contraceptive pills

PBC ..... Primary biliary cirrhosis

PEEP ..... Positive end-expiratory pressure

PNAC ..... Parenteral nutrition associated cholestasis

PNALD ..... Parenteral Nutrition Associated Liver Disease

PSC..... Primary sclerosing cholangitis

RBC ..... Red blood cell

SGOT ..... Serum glutamic pyruvate transaminase

SGPT ..... Serum glutamate oxaloacetic transaminase

SIRS ..... Systemic inflammatory response syndrome

SSC-CIP ... Secondary sclerosing cholangitis in critically ill patient

TGF- β ..... Transforming growth factor-β

TNF ..... Tumor necrosis factor

TNF-α ..... Tumor necrosis factor-α

TPN ..... Total Parenteral Nutrition

VBDS ..... vanishing bile duct syndrome

Abstract

In critically ill patient technical and medical progress in intensive care medicine has increased survival rates of patients with life-threatening injuries. However, as critically ill patients survive more, new ICU-acquired diseases have emerged. One of thsese disease is cholestatic liver dysfunction which is associated with increased morbidity and mortality at the ICU.

Cholestatic liver dysfunction is basically characterized by impaired bile formation and transportation.. The serum concentrations of conjugated bilirubin is the most commonly measured.

Causes can be classified into hepatocellular that include metabolic causes like total parentral nutrition, shock, sepsis, and drug induced liver injury, obstructive causes like mechanical ventilation and post operative causes.

Theses patients can present with different scenarios, so good assessment of these patients is important for diagnosis and proper treatment.

Interpretation of liver function tests in relation to clinical condition of the patient and imaging studies are the most important tools in diagnosis. Treatment of the underlying cause is the main step in the plan of treatment.

Conclusion: This study illustrated the main causes of cholestatic liver dysfunction in critically ill patient and the recent updates in diagnosis and treatment.

Key words: Cholestatic liver dysfunction

INTRODUCTION

Liver dysfunction is a frequent finding in critically ill patients. According to the clinical and laboratory presentation, it can be divided into two major patterns: cholestatic dysfunction and jaundice on the one hand and hypoxic liver injury (HLI), which is also known as ischemic hepatitis or shock liver on the otherhand. About 20%of the patients develop cholestasis and10% suffer from HLI during their stay at the intensive care unit **(Kramer et al., 2007).**

Both cholestatic jaundice and HLI are associated with increased morbidity and mortality at the ICU. However, apart from the usage of bilirubin in several prognostic scores, clinical impact of liver dysfunction in critical illness has been underrepresented in critical care literature for years. Traditionally, hepatic dysfunction and jaundice are regarded as late features in critical illness. However, findings demonstrated that liver cell necrosis and cholestasis are usually early findings in life threatening conditions and major risk factors for complications and increased mortality in patients at the ICU **(Vincent, 1995).**

Hypoxic liver injury is usually defined by three clinical cornerstones: an acute setting of cardiac, circulatory or respiratory failure, a sharp but transient increase in serum aminotransferase levels to at least 20 times the upper limit of

normal, and exclusion of other potential causes for increased aminotransferase levels like viral or drug induced hepatitis **(Henrion, 2003).**

Cholestasis is the most common feature of liver dysfunction at the intensive care unit. **Kramer et al. (2007)** reported the occurrence of early hepatic dysfunction defined by bilirubin levels greater than 2 mg/dl – in up to 20% of a large cohort of critically ill patients within 48 h after ICU admission**.**

Cholestatic liver dysfunction is basically characterized by impaired bile formation and transportation. A general distinction of cholestasis can be drawn between the extrahepatic form that is mainly a consequence of mechanical obstruction and consecutive decreased bile flow, and the intrahepatic form usually because of functional alterations at the hepatocellular level **(Sherlock, 1997).**

As cholestasis of critical illness is mainly the consequence of functional alterations at the hepatocellular level, it is usually reversible. Only a small subset of patients develops biliary fibrosis and liver cirrhosis because of progressive secondary sclerosing cholangitis (SSC) mainly as a consequence of septic shock, trauma and acute respiratory distress syndrome **(Ruemmele, 2009).**

Currently, the clinical awareness of bile acids is continuously increasing. They may indicate alterations of hepatic biotransformation and cholestatic dysfunction at an earlier stage during the course of the disease. Furthermore, they may offer new therapeutic options for targeted therapies **(Vanwijngaerden, 2011).**

AIM OF THE ESSAY

The purpose of this essay was to throw light on the cholestatic liver dysfunction in critically ill patient regarding to its pathophysiology, etiology and management.

Chapter (1):

LIVER FUNCTION AND PATHOPHYSIOLOGY OF CHOLESTASIS

The liver is a vital organ located in the upper right quadrant of the abdomen, below the diaphragm. It has a wide range of functions as detoxification of various metabolites, protein synthesis, and the production of biochemicals which is necessary for digestion **(Abdel-Misih et al., 2010).**

The liver plays a major role in metabolism with numerous functions in the human body including regulation of glycogen storage, plasma protein synthesis, hormone production, decomposition of red blood cells and detoxification. Also it is an accessory digestive gland and produces bile which is an alkaline compound aids in digestion via the emulsification of lipids. The gallbladder is a small pouch that is found just inferior to the liver and stores bile produced by the liver **(Tortora et al., 2008).**

The liver's highly specialized tissue containes hepatocytes that regulate a wide variety of biochemical reactions like the synthesis and breakdown of small and complex molecules that are necessary for normal vital functions. Total number of liver functions vary, but

textbooks generally cite it being around 500 **(Zakim et al., 2002).**

Structure:

The liver is a reddish-brown wedge-shaped organ with four lobes of unequal size and shape. A human liver normally weighs 1.44–1.66 kg **(Cotran et al., 2005).** It is the heaviest internal organ and the largest gland in the body. It's located in the right upper quadrant of the abdominal cavity just below the diaphragm to the right of the stomach and overlies the gallbladder **(Tortora et al., 2008).**

The liver recieves blood from the hepatic artery and the portal vein. The hepatic artery carries oxygenated blood from the aorta and the portal vein carries blood rich in digested nutrients from the gastrointestinal tract and also from the spleen and pancreas.

The functional units of the liver are lobules which are made up of millions of hepatic cells (hepatocytes) which are considered to be the basic metabolic cells. Theses lobules are held together by a fine dense irregular fibroelastic tissue layer. The whole surface of the liver is covered with a serous coat derived from peritoneum and this has an inner fibrous coat (Glisson's capsule) to which it's firmly adhered. The fibrous coat is formed of areolar tissue and follows the vessels and ducts to support them **(Tortora et al., 2008).**