Anesthetic Management for Patients with Hyperbilirubinemia

Essay

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Shaymaa Tareq Ali

المعالجة التخديرية للمرضى ذوى ارتفاع نسبة صفراء الدم

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توطئة للحصول على درجة الماجستير فى التخدير

مقدمة من

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Abstract

Background: Hyperbilirubinaemia is defined as a bilirubin concentration above the normal laboratory upper limit of 19 μmol/l. Jaundice occurs when bilirubin becomes visible within the sclera, skin, and mucous membranes, at a blood concentration of around 40 μmol/l. It is the commonest presentation of patients with liver and Biliary disease.

Aim of the work: The study aims to evaluate the safe perioperative anesthetic practice and management for patients with hyperbilirubinaemia.

Methodology: The liver is the largest internal organ in the body and it plays a critical role in the homeostasis of many physiologic systems, including nutrient and drug metabolism, synthesis of plasma proteins and hemostatic factors, and detoxification and elimination of many endogenous and exogenous substances .

The normal total serum bilirubin levels is less than 1.5mg/dl (<25 mmol/L) and reflects the balance between bilirubin production and excretion .

Conclusion: Based on large retrospective studies, patients with cirrhosis who are undergoing abdominal surgery, especially those in CPT class C, appear to have an increased risk of perioperative death. Elective surgery in these individuals should be avoided, if possible, in favor of less invasive procedures . Post operative pain relief can be challenging. The role of regional techniques is very much restricted by the high incidence of coagulation defects. Non-steroidal anti-inflammatory medications and their association with increased risk of GI bleeding, platelet dysfunction and nephrotoxicity. Paracetamol is sometimes used.

Keywords: Anesthetic Management, Patients Hyperbilirubinemia

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List of Abbreviations

BAEPs	Brainstem auditory evoked potentials
BDG	Bilirubin diglucuronide
BMG	Bilirubin monoglucuronide
BSP	Sulfbromophthalein
CN	Crigler-najjars syndrome
CTP	Child turcotte pugh
DJS	Dubin-johnson syndrome
ER	Endoplasmic reticulum
G6PD	Glucose-6-phosphate dehydrogenase
GABA	G-amino butyric acid
GPA	Glycophorin a
GS	Gilbert's syndrome
GST	Glutathione s-transferase
HPS	Hepatopulmonary syndrome
ICG	Indocyanine green
IPVD	Intrapulmonary vascular dilation
LFT	Liver functions tests
MELD	Model for end stage liver disease
MRP2	Multidrug resistance protein
OATPC	Organic anion transporting protien
PBC	Primary biliary cirrhosis
PPHTN	Portopulmonary hypertension
PSC	Primary sclerosing cholangitis

List of Abbreviations

RhAG	Rh-associated antigen
SOFA	Sequential organ failure assessment
TOE	Transoesophageal echocardiography
tPA	Tissue plasminogen activator
TRALI	Transfusion-related acute lung injury
UDP	Uridine diphospho-glocuronyl transferase
UGT1A1	Uridine diphospho-glucuronyl transferase a1
vWF-Ag	Von willebrand factor antigen

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INTRODUCTION

Hyperbilirubinaemia is defined as a bilirubin concentration above the normal laboratory upper limit of 19 μmol/l. Jaundice occurs when bilirubin becomes visible within the sclera, skin, and mucous membranes, at a blood concentration of around 40 μmol/l. It is the commonest presentation of patients with liver and Biliary disease ***(Beckingham and Ryder, 2001).***

Bilirubin metabolism takes place in three phases- prehepatic intrahepatic and posthepatic. Dysfunction in any of these phases may lead to jaundice. According to the type of bilirubin, hyperbilirubinaemia is either conjugated or unconjugated. Unconjugated hyperbilirubinaemia results from excessive heme metabolism either from hemolysis or reabsorption of a large hematoma. Hemolytic anemias result from abnormal red blood cell survival times due to membrane abnormalities (e.g. Hereditary spherocytosis) or enzyme abnormalities (e.g. glucose - 6- phosphate dehydrogenase deficiency) ***(Roche and Kobos, 2004).***

Patients with liver disease have multisystem organ dysfunction that leads to physiological perturbations from hyperbilirubinaemia to severe coagulopathy and metabolic disarray. Patient-specific risk factors, clinical scoring systems, and surgical procedures stratify perioperative risk for these patients. The anaesthetic management of patients with hepatic dysfunction involves consideration of impaired drug metabolism,

hyperdynamic circulation, perioperative hypoxaemia, bleeding, thrombosis and hepatic encephalopathy ***(Kiamanesh et al., 2013)***.

Obstructive jaundice represents the commonest cause of post hepatic hyperbilirubinaemia, it is most commonly due to choledocholithiasis. Surgery in patients with obstructive jaundice is generally considered to be associated with a higher incidence of complications and mortality. However, appropriate preoperative evaluation and optimization can greatly contribute to a favorable outcome ***(Wang and Yu, 2014)***.

AIM OF THE WORK

The study aims to evaluate the safe perioperative anesthetic practice and management for patients with hyperbilirubinaemia.

PHYSIOLOGY OF BILIRUBIN

Basic principles of bilirubin metabolism:

Bilirubin is a metabolite of heme, a compound that serves to coordinate iron in various protiens. Very recently, bilirubin has been shown to possess important role as an antioxidant, but it also serves simply as a mean to excrete unwanted heme, derived from various heme-containing protiens such as hemoglobin and myoglobin. Bilirubin and its metabolites are also notable for the fact that they provide color to the bile and stool, and to a lesser extent, the urine ***(Sticova and Jirsa, 2013)***.

Role and significance:

It is important for the body to be able to excrete bilirubin as it is potentially toxic. Certain diseases rises due to excessive levels of bilirubin in the bloodstream can lead to accumulation of bilirubin in the brain due to its ability to cross the blood-brain barrier, a condition known as kernicterus. The development of this condition impairs brain function and can be fatal if left untreated. Bilirubin is also notable for its yellow coloration.Accumulation of this substance in the blood is the basis of jaundice, or a yellow discoloration of the skin and eyes which is a common symptom of liver disease ***(Johnson et al., 2009)***.

Pathway of bilirubin synthesis and metabolism:

Bilirubin derives from two main sources. The majority (80 %) of the bilirubin formed in the body comes from the heme released from the senescent red blood cells. The reminder originates from various heme-containing protiens found in other tissues especially the liver and muscles ***(Maisels et al., 2004)***.

- **Celluar heme metabolism:**

Bilirubin is produced by a two stage reaction that takes place in cells of the reticulo-endothelial system, including phagocytes, the Kuppfer cells of the liver, and cells in the spleen and bone marrow. Heme is taken up into these cells and acted on by the enzyme heme oxygenase, liberating the chelated iron from the heme structure and releasing an equimolar amount of carbon monoxide, which is excreted through the lungs. The reaction yields a green pigment known as biliverdin.

BILIVERDIN is then acted on by the enzyme biliverdin reductase, again releasing a molecule of carbon monoxide and producing the yellow bilirubin. Although it contains two propionic acid side chains, the structure of bilirubin is highly compacted by hydrogen bonding.This renders the molecule essentially insoluble in aqueous solutions at neutral pH ***(Sedlak and Snyder, 2004)***.

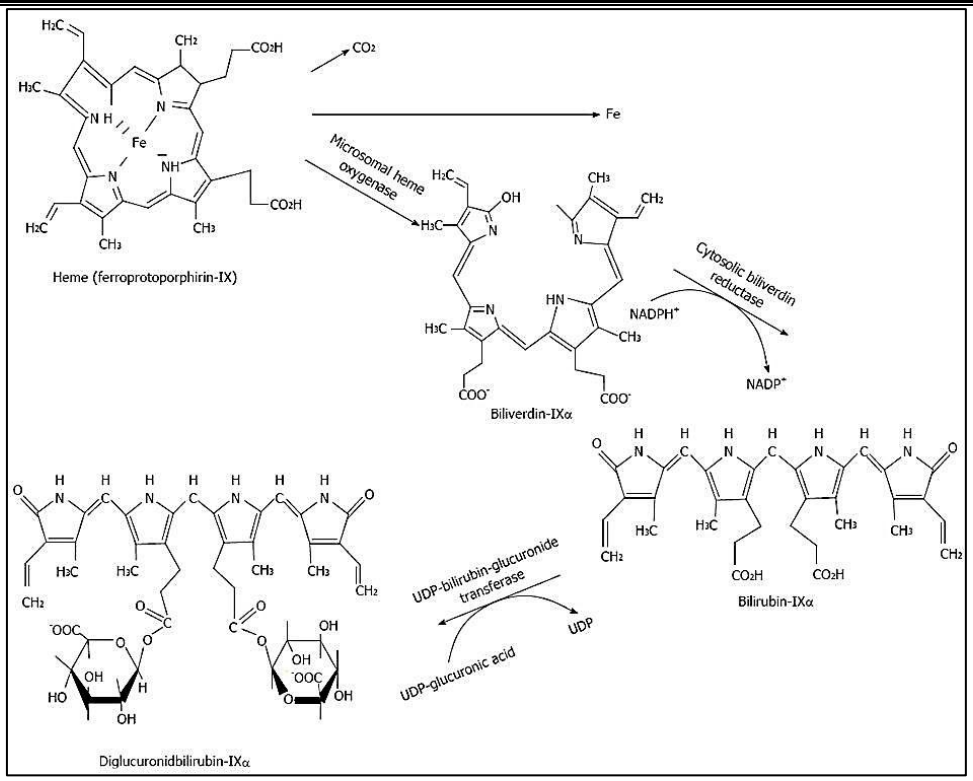

Fig. (1): Formation of bilirubin from heme ***(Reshetnyak, 2013).***

Bilirubin is released into the plasma and is taken up by albumin, which serves to transport this molecule throughout the body. The binding affinity of this unconjugated bilirubin for albumin is extremely high, and under normal conditions,there is essentially no free unconjugated bilirubin in the plasma.When the bilirubinladen albumin reaches the liver, the high permeability of the hepatic microcirculation allows the complex to enter the space of Disse such that it encounters the basolateral aspect of hepatocytes. At this site, bilirubin is taken up by a specific transport mechanism to enter the hepatocyte. However, this process is relatively inefficient, with the first pass clearance of