Perioperative liver protection

Protocol for an essay

Submitted for partial fulfillment of Master degree in anesthesiology

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1. INTODUCTION;

Estimates suggest as many as 10% of all patients with advanced liver disease will undergo surgery in the last 2 years of their lives. In addition the number of successful liver transplantation has increased dramatically over the last few years more and more patients with post-transplant liver dysfunction may require further surgical intervention . even seemingly healthy patients without clinical signs of liver impairment may present with subtle liver dysfunction as seen in about 1 in 700 patient with a pre test classification of American society of anesthesiology physical status classification (A.S.A.1) admitted for elective surgery ***(schemel, 1976)***. Knowledge and evaluation of preoperative liver impairment is extremely important ,as the extent of peri-operative liver injury caused by ischemia ***(Gujral et al., 2001)*** . as well as on preexisting liver diseases such as cirrhosis is ***(Kurokawa et al. , 1996)*** or acute hepatitis ***(Tanaka et al. , 1993)*** hepatic ischemia and subsequent liver dysfunction is associated with a profound deterioration in prognosis ***(Maynard et al., 1997)*** because of the central role of the liver in the metabolic and immunological response to stress ***(Pannen and Robotham, 1995)*** the increased mortality seen after per operative liver failure is most likely due to progression to multiple organ failure ***(Jarrar et al., 1999).*** Preexisting hepatic dysfunction poses a great risk even for non hepatic surgery .as shown by higher blood transfusion requirements , longer hospital stays , more complication and increased mortality rate of 16.3 % in patient with cirrhosis compared to 3.5 % in controls ***(Delolmo et al., 2003).***

2. AIM OF WORK;

The aim of this work is to review the current medical literature addressing the subject of peri-operative liver protection to help in a detailed understanding of the underlying path-physiology , evaluation and preoperative optimization which is crucial to be done by expert anesthetic team to avoid peri-operative liver insult.

3. METHOD OF STUDY AND MATERIALS; Literature review.

To identify English-language randomized, controlled trials exploring the peri-operative liver protection, MEDLINE, through Pub Med and EMBASE, was searched using the key words liver protection and peri-operative management Studies collected were current through December 2008, January, February ,march ,April and may 2009.

4. CONTENTS;

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- PREOPERATIVE CONSIDERATIONS AND ASSESSMENT
- QUANTIFIED RISK ASSESSMENT
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  - General anesthesia
  - Regional anesthesia
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5. REFERENCES

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1- المقدمة

الإحصائيات ترجح أن ما يقارب من 10% من جميع مرضى الكبد ذوي الحالات المتقدمة سوف يخضعون للجراحة في أخر عامان من حياتهم بالإضافة أن عدد عمليات زراعة الكبد الناجحة قد زاد بشكل كبير خلال الأعوام القلية الماضية مما ترتب عليه أن المزيد والمزيد من المرضى ذوي الأضطرابات فيما بعد الزراعة قد يكونوا بحاجة إلي المزيد من العمليات الجراحية, حتى المرضى الأصحاء اللذين لا يبدون أي علامة إكلينيكية علي اعتلال الكبد من الممكن أن يتم تقديمهم باضطرابات كبدية غير ظاهرة بنسبة واحد إلي 700 مريض كما تم تقسيمهم بواسطة الجمعية الأمريكية للتخدير وذلك عند قيامهم بعمليات غير عاجلة.

معرفة وتقسيم الاعتلال الكبدي فيما حول العمليات هام للغاية لأن درجة إصابة الكبد فيما حول العمليات والذي تسبب بواسطة القصور الدموي بالإضافة إلي أمراض الكبد السابق تواجدها كتليف الكبد أو الألتهاب الكبدي الحاد أو القصور الدموي للكبد وما يتبعه من اعتلال كبدي يصاحبة تدهور حاد في تطورات المرض .

نظراً للدور الرئيسي للكبد في الاستجابات الايضية والمناعية للإجهاد فان زيادة معدل الوفيات بعد الفشل الكبدي فيما حول العمليات علي الأغلب نتيجة إلي فشل وظائف الأعضاء المتعدد.

الأعتلال الكبدي السابق تواجده يحتوي علي خطورة كبيرة حتي بالنسبة إلي العمليات غير الكبدية كما أتضح من زيادة نسبة الاحتياج إلي نقل الدم, أطاله فترة الاقامة بالمستشفيات, زيادة التعقيدات وزيادة معدل الوفيات.

2- هدف العمل :-

الهدف من هذا العمل هو مراجعة المقالات الطبية الحالية التى تناولت موضوع وقاية الكبد فيما حول العمليات للمساعدة على الفهم المفصل للفسيولوجيا المرضية,التقييم والوصول إلي أفضل الأوضاع فيما حول العمليات والذي يعد ضروري للقيام به بواسطة فريق تخدير ذو خبرة لتجنب إصابة الكبد فيما حول العمليات .

3- أسلوب الدراسة :-

مراجعة طبية لموضوع وقاية الكبد فيما حول العمليات باستخدام عوامل البحث على شبكة المعلومات والعديد من المراجع وذلك في خلال أشهر ديسمبر 2008 يناير فبراير مارس ابريل مايو 2009 .

4- المحتويات :-

أ- مقدمة .

ب . الاهتمامات والتقييم فيما قبل العملية

ج . تقسيم الخطورة

د . الاعتبارات التخديرية والمعالجة خلال العملية:

تخدير عام

تخدير موضعي

معالجة الدنياميكة الدموية

هـ . التأهيل التقدمي

م . العناية فيما بعد العملية

ن . ملخص

و . مراجع

ي . ملخص عربي

INTRODUCTION

Estimates suggest that as many as 10% of all patients with advanced liver disease will undergo surgery in the last 2 years of their lives ***(Garrison et al., 1984).*** In addition, the number of successful liver transplantations has increased dramatically over the last few years. More and more patients with post-transplant liver dysfunction may require further surgical intervention. Even seemingly healthy patients without clinical signs of liver impairment may present with subtle liver dysfunction, as seen in about 1 in 700 patients with a pre-test classification of American Society of Anesthesiology physical status classification (ASA-1) admitted for elective surgery ***(Schemel, 1976)***. In general, the liver has a substantial functional reserve because of its dual blood supply: portal-venous (75%) and hepatic-arterial (25%). Hence, clinical manifestations of liver damage occur only after considerable injury ***(Haranath et al., 2006).***

Knowledge and evaluation of pre-operative liver impairment is extremely important, as the extent of peri operative liver injury caused by ischemia and reperfusion depends primarily on the duration of ischemia ***(Gujral et al., 2001)*** as well as on pre-existing liver diseases, such as cirrhosis, acute hepatitis, and end-stage liver disease ***(Kurokawa et al., 1996)***. The most common causes of

advanced liver disease are viral infection (hepatitis C and B), alcohol abuse, autoimmune disease, drugs or toxins, metabolic disorders (e.g., involving alpha-1 antitrypsin, hemochromatosis, copper), and biliary tract diseases ***(Haranath et al., 2006).***

Anesthesia and surgery are known to have decompensatory effects on patients with compromised liver function, and previous publications have reported greater morbidity and mortality in patients with cirrhosis undergoing nonhepatic procedures. Retrospective investigations have identified multiple clinical and laboratory variables that contributed to increased perioperative morbidity and mortality rates in cirrhotic patients who underwent abdominal surgery. Moreover, it has been shown that there is a correlation between the number of risk factors identified by multivariate analyses and the rate of peri-operative complications**.** Hepatic ischemia and subsequent liver dysfunction also is associated with a profound deterioration in prognosis ***(Picker et al., 2008)***.

Because of the central role of the liver in the metabolic and immunological response to stress as the liver is vital for protein synthesis, glucose homeostasis, bilirubin excretion, and toxin removal, the increased mortality seen after peri-operative liver failure is most likely due to progression to multiple organ failure ***(Jarrar et al., 1999).*** Pre-existing hepatic dysfunction poses a great risk even for

nonhepatic surgery, as shown by the higher blood transfusion requirements, longer hospital stays, more complications and increased mortality rate in patient with cirrhosis compared to controls.

A detailed understanding of the underlying path-physiology and thorough evaluation and pre-operative optimization by expert anesthetic teams is, therefore, crucial to avoid perioperative liver insults.

AIM OF WORK

The aim of this work is to review the current medical literature addressing the subject of peri-operative liver protection to help in a detailed understanding of the underlying pathophysiology, evaluation and preoperative optimization which is crucial to be done by expert anesthetic team to avoid peri-operative liver insult.

PREOPERATIVE CONSIDERATION AND ASSESSMENT

Liver disease can vary in severity from sub-clinical to end-stage liver disease (ESLD), with life threatening, multi-organ multi- system failure. Anaesthetic and operative risks are related to the severity of liver dysfunction, so thorough pre-operative assessment is essential for safe peri-operative care. A good understanding of the pathophysiology of hepatic dysfunction and multiorgan changes due to liver impairment is vital for assessment of operative risk ***(Picker et al., 2008).***

Impaired liver function gives rise to effects directly attributable to the failing liver itself and also to indirect effects expressed via other organ systems. Effects directly attributable include hypoglycaemia, lactic acidosis, hypermetabolism, azotemia and impaired urea synthesis. Jaundice appears when serum bilirubin exceeds 35 µmol/l and defects in cholesterol metabolism together with intra-hepatic cholestasis may lead to production of poor quality bile and malabsorbtion of fat and fat-soluble vitamins. There is reduced synthesis of proteins such as albumin, clotting factors, thyroid binding globulin and pseudo-cholinesterase. Impaired hormone biotransformation, reduced production of modulator proteins and reduced protein binding lead to increased circulating levels of hormones such as insulin, thyroxine, aldosterone and

oestrogen. Impaired hormone modulation, failure to clear by-products of metabolism, activation of cytokines and release of vasoactive substances from the damaged liver result in patho-physiological changes in many organ systems ***(Ginsburg, 2003).***

Cardiovascular changes:

Most patients with advanced liver disease have a normal or even supernormal ejection fraction judged by echocardiography. Thus, physicians previously assumed that cardiac function was normal in most patients with liver disease. However, further investigation has uncovered multiple problems in cardiac performance that place patients at risk of heart failure ***(Mandell and Tsou, 2008).*** This part will explore the pathophysiology of cardiovascular changes in patients with end-stage liver disease, but before that we should know that cardiovascular diseases (C.V.D.) process in cirrhotic can occur as one of the following categories ***(Karasu et al., 2004).***

I. CVD That Occurs as Part of a Systemic Disease Process that Also Involves the Liver

The classic systemic disease processes that involve both the heart and the liver. It includes hemochromatosis, Wilson's disease and glycogen storage diseases that involve the liver. Other systemic disease processes that also affect the liver include amyloidosis, sarcoidosis, AIDS and to a

lesser extent after chronic hepatitis B and chronic hepatitis C. The hepatic and cirrhotic problems found in patients with these diseases represent components of these systemic disease processes involving the liver and the heart.

II. C.V.Ds in Cirrhotic Patients That Occur Independent of the Co morbid Hepatic Disease

Atherosclerotic CVD, rheumatic valvular heart disease and particularly coronary artery disease are common problems seen in the clinic. As such these diseases also involve cirrhotic. These diseases present with no difference in cirrhotic as compared to noncirrhotic with chest pain, angina, myocardial infarction, and congestive heart failure.

III. Myocardial Dysfunction Occurring as a Consequence of the Hepatic Disease Not Associated With a Systemic Disease Process

Cardiovascular function which is frequently impaired in cirrhotic patients has a direct relationship with the degree of hepatic dysfunction defined by either the Child-Pugh score or the Model for End Stage Liver Disease (MELD) score. This CVD process is characterized by hemodynamic changes termed "the hyper dynamic syndrome" and has been reported to occur in more than 30% of cirrhotic patients ***(Karasu et al., 2004).***

A- The hyper dynamic syndrome:

The components of this syndrome include an increased cardiac output, increased heart rate, vascular volume, reduced arterial pressure, reduced systemic vascular resistance and impaired renal perfusion. The hyper dynamic circulatory consequences of this syndrome can lead to morphologic alterations in the heart to include right atrial and right ventricular dilatation ***(Karasu et al., 2004).*** Left atrial dilatation has been reported also but left ventricular dilatation does not occur presumably as a consequence of the reduced systemic vascular resistance ***(Kelbaek et al., 1984).*** Experimental data obtained in animals and to a lesser degree in man has shown that an excess production of nitric oxide plays a major role in the initiation and maintenance of the hyperdynamic state of the cirrhotic patient ***(Sogni et al., 1995; Bomzon and Blendis, 1994)***. Nitric oxide however, is not the sole factor responsible for the hyperdynamic state. Other factors such as increased levels of endotoxin, tumor necrosis factor, bile acids, glucagon and others in the plasma contribute to the phenomenon. The increase in these later substances is generally not a result of increased production as is the case with nitric oxide but rather occurs as a consequence of a reduced hepatic clearance of these factors ***(Schulz et al., 1995; Kleber et al., 1992).***

B- Body Fluid Composition in Liver Disease:

Approximately 2/3 of the total body water is normally contained in the intracellular compartment while the remaining one third is distributed in the intravascular and intercellular space. At any one point within a cardiac cycle, most of the total blood volume is found in the systemic veins with only 10% in the splanchnic circulation ***(Schrier, 2007)***. The distribution of total body fluid is altered by liver disease. Sodium and water are retained by the kidneys and this increases the amount of total body fluid. Fluid shifts into the intracellular compartment, which expands to accommodate the increased volume ***(Arroyo and Jimenez, 2000).*** In disease, this compartment commonly holds 3/4 or more of the total body water ***(Eisenhut, 2006).*** Protein-rich fluid moves into the body cavities as disease worsens. This causes ascites and pleural or pericardial effusion ***(Cardenas and Arroyo, 2003).*** As disease progresses, total blood volume increases but the relative amount of blood in the systemic circulation falls. Rather, blood moves into splanchnic (gut) circulation as it expands due to portal hypertension. Tissue oxygenation is therefore impaired. These changes are initiated by the development of portal hypertension. Portal hypertension causes vasodilatation and new blood vessel formation in the splanchnic circulation ***(Bosch and Garcia, 2005)***. An increase in the number of small slow transit blood vessels in the gut increases the capacitance of the splanchnic