Section A -Research paper

Anesthetic Effect of Sevoflurane and Propofol on Elevated Liver Enzymes

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Article History: Received: 11.06.2023 **Revised:** 08.07.2023 **Accepted:** 19.07.2023

Abstract:

Propofol and sevoflurane are widely used in clinical anesthesia, and both have been reported to exert a protective effect in liver function.

Keywords: Sevoflurane, Propofol, Liver Enzymes.

DOI: 10.53555/ecb/2023.12.1172

Introduction:

Most surgical procedures result in small elevations in serum liver biochemical test levels, whether performed under general, spinal, or epidural anesthesia. In patients without underlying liver disease, minor postoperative increases in serum aminotransferase, alkaline phosphatase, or bilirubin levels are not clinically important. Surgery, on the other hand, can hasten hepatic decompensation in patients with underlying liver disease, especially those with compromised hepatic synthetic function. The intensity of the operation is related to the operational risk **(1)**.

In patients with elevated liver enzyme levels, anesthesia and surgery may deteriorate liver function; thus, choosing anesthetics with less hepatotoxicity may be critical in these patients. Preoperative evaluation is critical for elective procedures to ensure a proper risk benefit calculation for elective surgery and to direct optimization. The emphasis of postoperative treatment should be on patient rehabilitation and close monitoring for liver decompensation. Non-hepatic surgery is more common in general and occurs often in the course of acute care surgery **(2)**.

Preoperative assessment and treatment of patients with chronic liver disease begin with a detailed preoperative history and physical examination and it is important to assess for the presence and severity of liver disease. Aside from recognizing the risk factors for liver disease (blood transfusions, tattoos, illegal drug usage, sexual promiscuity, family history of liver disease,

alcoholism, travel history, and a review of prescription or over-the-counter medications), it's also necessary to evoke any prior history of decompensation, such as ascites, edema, or hepatic encephalopathy, variceal bleeding, or anesthesia related complications **(3).**

A full blood count, coagulation profile, liver function tests, serum electrolytes, and creatinine should be included in a minimum range of blood tests. Cirrhotic patients often experience coagulopathy, electrolyte disruptions, and renal dysfunction, all of which have clear perioperative consequences **(3).**

Nutrition screening, which includes SGA and anthropometric measurements, is effective in detecting malnutrition early and initiates the entire nutrition care process. It is therefore important for appropriate nutrition policies and protocols to be implemented so that all patients with chronic liver diseases are monitored closely from a nutritional standpoint **(4)**.

Individualized dietary support and fluid therapy plans can be used for perioperative therapy in patients with liver diseases, taking into account the patient's needs, disease process features, liver function, and gastrointestinal tract tolerance **(4)**.

Risk stratification:

The Child-Pugh classification and the model for end-stage liver disease (MELD) score are valuable methods for predicting peri-operative morbidity and mortality in patients. Child A patients are acceptable candidates for elective procedures with special intra-operative care. Child B should undergo pre-operative optimization to convert to Child A, and Child C or with a MELD score greater than 20, are at a high risk for anesthesia, and should be postponed to elective surgeries **(5)**.

Table (1): Child Turcotte–Pugh (CTP) classification **(1)**

A. Classification				**B. Interpretation**		
Clinical parameter	**1 point**	**2 points**	**3 points**	**Points**	**Class**	**Mortality**
Total bilirubin (mg/dL)	<2	2–3	>3			
Serum albumin (g/dL)	>3.5	2.8–3.5	<2.8			
INR	<1.7	1.7–2.3	>2.3			
Ascites	None	Mild	Moderate to severe	5–6	A	10%
Hepatic encephalopathy	None	Grade I or II	Grade III or IV	7–10	B	30%
				10–15	C	76–82%

Scores such as the Child-Turcotte-Pugh (CTP) and the model for end-stage liver disease (MELD) can be used to determine the severity of liver disease. The MELD estimate, as opposed to CTP, which provide a more accurate assessment of peri-operative morbidity and mortality since it is based solely on objective data. However, it has been proposed that CTP and MELD scores work together to provide a more precise measure of liver dysfunction and decompensation **(6)**.

An evidence-based guideline done in France according to a risk assessment for non-hepatic surgery, converting a Child C patient to a Child B patient prior to surgery can improve post-surgery survival so that coagulopathy and thrombocytopenia should be treated with vitamin K replacement, fresh-frozen plasma (FFP), and likely cryoprecipitate transfusions to get the prothrombin time down to within 3 s of normal and to achieve a goal of platelet counts >50 000/mm^3 **(1)**

Even in patients with CTP class B, emergency surgery has a 4 to 5 times higher mortality rate, and such operations, like cardiac surgeries with cardiopulmonary bypass, should be avoided **(7)**.

If necessary, emergency operations should be delayed, and semi-elective surgery should be planned with meticulous medical management. Getting older, as well as the presence and severity of comorbidities may provide additional clue in assessing the perioperative morbidity and mortality **(7)**.

In general, propofol is favored as a narcotic over benzodiazepines. Sufentanil and remifentanil are the opioids of choice for liver insufficiency. Since the muscle relaxants vecuronium and rocuronium are only metabolized by the liver, they should be avoided. In patients with liver disease, atracurium and cisatracurium are favored because they are not metabolized by the liver **(1)**

An evidence based guideline done in India recommends that anesthetics can reduce hepatic blood flow by 30–50%; therefore: isoflurane, desflurane, sevoflurane, and propofol are recommended for patients with liver disease because they cause less disruption in hepatic arterial blood flow than other inhaled anesthetics **(1)**

Intraoperative anesthetic management:

A systematic review on perioperative evaluation and management of patient with cirrhosis concluded that the overall intraoperative objectives are to preserve hepatic blood flow and oxygen supply while minimizing exposure to hepatotoxic drugs to prevent more liver harm **(2)**.

According to the Intravenous Hypnotic Regimens (IHR) in patients with liver disease guideline, opioids are successfully used in patients with liver diseases, and fentanyl is the medication of choice for these patients when used at an average dose, as liver oxygen content and liver blood flow are not impaired **(2)**.

Analgesics are often metabolized in the liver and removed by the kidneys. To avoid drug accumulation in patients with liver disease, lower opioid doses with longer interval periods should be used. Long-acting opioids like morphine and mepiridine should be avoided, but shorter-acting opioids like fentanyl are well tolerated when given in small doses and titrated to effect. Avoid mepiridine in patients with liver disease because of reduced clearance and increasing the risk of seizures. Morphine has been shown to have reduced clearance and improved oral bioavailability in patients with liver disease, and it should be avoided to prevent accumulation and increased risk of adverse reactions. If morphine is needed, the intervals between doses should be increased **(1)**.

For patients with liver failure, a few opioids are favored. At lower doses and longer dosing times, tramadol should be used with caution. Fentanyl is the safest drug because it does not have a toxic metabolite and it does not normally need dosage changes **(8)**.

Rocuronium and vecuronium, amino steroid neuromuscular agents, are metabolized in part by the liver, and their term of action can be extended in liver failure **(3)**.

Peripheral nerve stimulators should be used to titrate these drugs to impact. Atracurium and cis-atracurium, two benzylisoquinolinium neuromuscular agents, are unaffected by liver disease. Succinylcholine is metabolized by plasma cholinesterase, a liver enzyme; despite the fact that succinylcholine has a long time of action, it is not clinically important **(3)**.

In cases of advanced liver cirrhosis, the dose of intravenous anesthetic agent thiopental should be decreased and propofol is the preferred intravenous anesthetic agent **(9)**.

Normal monitoring of arterial blood gases, lactate, glucose, electrolytes, and coagulation status is recommended for all patients, as recommended by the Association of Anaesthetists of Great Britain and Ireland (AAGBI), but intrusive monitoring of both arterial and central venous pressure are recommended for major surgery and regular monitoring of arterial blood gases, lactate, glucose, electrolytes, and coagulation status are also recommended for major surgery. It's also a good idea to keep track of patients core body temperature, neuromuscular block, and urine production **(10)**.

Postoperative anesthetic management:

An evidence based guideline on surgery in patients with liver disease concluded that urine output must be monitored carefully as intra-operative fluid shift can lead to poor renal perfusion which if not detected early and treated aggressively can lead to acute renal failure. In these patients, it is important to monitor the CVP, pulse, BP, and oxygen saturation continuously **(6)**.

An evidence-based guideline on non-hepatic abdominal surgery in patients with cirrhotic liver disease suggested that many of the postoperative cirrhotic patient's treatment techniques are similar to those used before surgery: avoid liver-metabolized drugs, control intravascular volume, avoid metabolic disturbances, and use lactulose for hepatic encephalopathy (HE) and opioid-

induced constipation. If the patient will remain null per os (NPO), parenteral feeding should be started as soon as possible **(6)**.

Opioid-induced constipation should be avoided with the use of laxatives, and these patients should be closely monitored for symptoms of sedation and encephalopathy. In patients who are intolerant to opiates due to advanced disease and a high risk of HE, regional analgesia in the form of local infiltration or transverse abdominis plane block is a choice. Only after coagulopathy has been corrected with INR 100 000/mm^3, epidural analgesia can be considered **(10)**.

According to a Spanish guideline on the outcome of abdominal surgery in patients with cirrhosis, postoperative management should preferably be done in the intensive care unit (ICU), at least for the first 24 h, particularly in Child-Turcott-Pugh (CTP) B and C. It's crucial to monitor for potential complications, which vary depending on the severity of the liver cirrhosis (LC) and the type of operation **(11)**.

Any drug that is nephrotoxic should be avoided. Starting oral feeding as soon as possible is recommended to help avoid spontaneous bacterial peritonitis (SBP). Following surgery, the patient's liver, renal, and coagulation profiles, as well as blood sugar levels, should be closely monitored to diagnose early liver or renal failure. Any decline in liver or renal function could indicate sepsis, and broad-spectrum antibiotics should be given to these patients with a low threshold. **(11)**.

Effect of Sevoflurane and Propofol on Elevated Liver Enzymes

The halogenated inhalational anaesthetics have been linked to idiosyncratic liver injury for more than 50 years with presentation ranging from asymptomatic alanine transaminase (ALT) elevations to fatal hepatic necrosis. This injury is usually recognized when it results in fulminant hepatitis, however authors have reported that milder cases of hepatitis are quite common with transaminases of 5 to 22 times the upper limit in 1% of patients **(12)**.

The estimated incidence of volatile anaesthetic drug induced liver injury is 3%. The overall incidence of significant liver injury after halothane was estimated at 1 per 15,000 initial exposures, and probably 1 per 1000 repeated exposures, particularly if the re-exposure was within 28 days. As a result of this, the Committee on Safety of Medicines recommended that repeated exposure to halothane within a period of three months should be avoided unless there are overriding clinical circumstances. Consequent to this, its use has been replaced by other halogenated anaesthetics including enflurane (1972), isoflurane (1981), desflurane (1993) and sevoflurane (1995) **(12)**.

Sevoflurane seems to be a suitable anaesthetic for patients with previous exposure to other halogenated anaesthetics or hepatic disease. Studies have also demonstrated that sevoflurane may be a viable option for anaesthesia in large size surgeries and liver transplants, where postoperative liver dysfunction could be detrimental to patients. It is further reassuring that sevoflurane may

even exert a protective effect on hepatic ischemia/reperfusion injury, which is a frequently encountered problem in hepatic surgery **(13)**.

Total intravenous anaesthesia with propofol is expected to have a lower risk of direct liver damage from anaesthetic metabolites but its use has been associated with rare instances of idiosyncratic acute liver injury. In addition, prolonged high dose propofol therapy (doses greater than 4 mg/kg/hour for more than 48 hours) can lead to "Propofol infusion syndrome" which is marked by bradyarrhythmias, metabolic acidosis, rhabdomyolysis, hyperlipidemias and an enlarged or fatty liver **(12)**.

A few studies have investigated the effects of different types of anesthetic agents, especially intravenous versus inhalational agents, on postoperative liver function after non-hepatic surgery, but the effects have remained unclear **(14)**.

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