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Anesthesia for patients with liver disease

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INCIDENCE OF POSTOPERATIVE HEPATIC COMPLICATIONS

Surgical stress, particularly laparotomy, in patients with liver disease carries high mortality rate. For example, a 30 day mortality rate after laparotomy with liver biopsy, in patients with liver disease was approaching 30%[1,2]. The presence of acute viral hepatitis, alcoholic hepatitis, ascites, or prolongation in prothrombin time by more than 2.5 seconds increased 30 day mortality to 85-95%[2]. More recent studies suggest an improvement: overall perioperative 30-day mortality was reported as 11.6%; perioperative complication rate remains at the level of 30%[3]. Factors associated with perioperative complications and mortality includes male gender, the presence of ascites, diagnosis of cirrhosis, an elevated creatinine concentration, chronic obstructive pulmonary disease, perioperative infection, upper gastrointestinal bleeding, presence of intraoperative hypotension and some others[3].

PATHOPHYSIOLOGY OF HEPATIC DISEASE

For practical clinical purposes, anesthesiologists may divide patients with liver disease into two large heterogeneous groups: 1) those with parenchymal liver disease, including acute and chronic viral hepatitis, hepatic cirrhosis (with or without portal hypertension), and some other disorders; 2) those with cholestasis, including obstruction of extrahepatic biliary pathway.

Parenchymal liver disease is usually associated with a hyperdynamic state which is characterized by a decreased vascular resistance (peripheral vasodilation, increased arterio-venous shunting); increased circulating blood volume and cardiac output; maintained arterial blood pressure, filling pressures, and hear rate (deterioration is late); possible cardiomyopathy, decreased arterio-venous oxygen content difference and increased venous oxygen content; decreased responsiveness to catecholamines; increased splanchnic (except the liver), pulmonary, and skin blood flows; decreased portal blood flow to the liver: maintained or increased hepatic arterial blood flow; and maintained or decreased renal blood flow.

Hypoxemia is often associated with severe hepatic disease and results from a right-ward shift of the oxyhemoglobin dissociation curve, ventilation/perfusion abnormalities (impaired hypoxic pulmonary vasoconstriction), hypoventilation resulting from ascites, decrease in pulmonary diffusing capacity resulting from an increase in extracellular fluid, and right-to left shunt across the lungs due to : a) a spider angiomas in the lungs, b) portapulmonary venous communications c) humoral factors (vasodilation secondary to nitric oxide, glucagon, ferritin, vasointestinal polypeptide, etc). Anemia, leucopenia, thrombocytopenia and coagulopathy often accompany hepatic disease. Encephalopathy, renal dysfunction, including hepatorenal syndrome, and ascites are also common.

While providing anesthesia for patients with liver disease, the concept of oxygen supply-demand relationship in the liver should be kept in mind. Therefore, the main rule is to maintain adequate pulmonary ventilation and cardiovascular function, including cardiac output, blood volume, and perfusion pressures. Arterial hypotension, drug induced or due to inadequate blood volume replacement or relative overdose of inhalational anesthetics should be avoided because vasodilation and a decrease in perfusion pressure, accompanied by a decrease in blood velocity, could lead to an increase in oxygen extraction in all tissues, including the preportal area. Decreased blood velocity and increased oxygen extraction result in a decrease in venous oxygen content, in this case, in portal venous blood. A decrease in portal blood oxygen content and/or flow is usually accompanied by a compensatory increase in hepatic arterial

blood flow. This prevents ischemic induced hepatic injury which is rare after arterial hypotension in normal individuals. However, in patients with severe liver dysfunction, the autoregulatory ability of hepatic arterial blood flow to increase might be diminished or abolished. Therefore, in patients with severe hepatic disease, hepatic arterial blood flow does not increase when portal blood flow and/or oxygen content in portal venous blood are decreased. This could lead to a decrease in hepatic blood and oxygen supply, with subsequent hepatic oxygen deprivation. Thus, the lesson is clear: arterial hypotension as well as states of reduced cardiac output should be avoided. More detailed description of pathophysiology of hepatic disease, relevant to anesthesiologist, is available elsewhere[4].

ANESTHETIC MANAGEMENT

Regional anesthesia might be used when possible in patients with advanced liver disease. Coagulopathy should be considered as a contraindication to some types of regional anesthesia. Keeping in mind the comparative pharmacology of inhalational anesthetics, it seems that halothane should be avoided because this anesthetic leads to the most prominent decrease in hepatic blood and oxygen supply and postoperative hepatic dysfunction. In addition, immunologically mediated severe postoperative halothane hepatitis may follow halothane anesthesia. Isoflurane seems to be a better choice if an inhalational technique is selected[6-8]. More recently introduced volatile anesthetics, servoflurane and desflurane, have not been studied that thoroughly as halothane and isoflurane. However, a few studies suggest that both of them probably can be used safely in patients with liver disease; a few indirect comparisons of servoflurane and desflurane with isoflurane and halothane might suggest that servoflurane could have some advantages over other volatile anesthetics as it concerns effect of the anesthetics on the liver[5,9-14]. Further studies are required to make definite conclusions. Whatever the conclusion in this regard might be, it appears at present that the differences between these volatile anesthetics (namely isoflurane, desflurane and servoflurane) are minimal. Nitrous oxide has been used in patients with advanced hepatic disease for many years, and so far has not been incriminated in increased anesthesia related hepatic postoperative complications. However, a well-known sympathomimetic effect of nitrous oxide and some possibilities of jeopardizing oxygenation render the routine use of nitrous oxide in patients with advanced liver disease undesirable according to some experts. It is important to remember that long surgical operations under anesthesia with nitrous oxide might result in the accumulation of nitrous oxide in the intestinal lumen with subsequent intestinal distension.

Opioids can also be used successfully in patients with hepatic disease despite certain pharmacological consequences (decreased clearance and prolonged half-life); fentanyl should probably be considered the opioid of choice. Interestingly, fentanyl does not decrease hepatic oxygen and blood supply nor does it prevent increases in hepatic oxygen requirements when used in relatively moderate doses[7,8]. Therefore, the hepatic oxygen supply-demand relationship during anesthesia with fentanyl is not much better than that during anesthesia with isoflurane[8]. Opioids can induce spasm of sphincter Oddi; however, the incidence does not exceed 3%. Spasm of sphincter Oddi induced by opioids can be successfully treated with many different drugs, including atropine, naloxone, glucagon, nitroglycerin, volatile anesthetics, and others. It seems at present that anesthetic management using inhalational agents (isoflurane, desflurane or sevoflurane) alone or in combination with small doses of fentanyl can be considered as the anesthetic management of choice provided that adequate pulmonary ventilation, cardiac output, and arterial pressure are maintained.

When administering drugs, one must appreciate the substantially changed pharmacokinetics. For example, the half-life of lidocaine in patients with liver disease may be increased by more than 300%, for diazepines by more than 100%, etc. For drugs binding to albumin, the volume of distribution can be decreased and therefore the dose of the drug should be decreased (e.g. sodium pentothal). On the other hand, the volume of distribution of many drugs can be substantially increased (for different reasons, including an increase in gamma globulin, edema), dictating a necessity to increase the first effective dose of the drug. However, owing to a decrease in hepatic blood flow and hepatic metabolic and excretory functions, as well as impaired renal function, the clearance of such a drug can be decreased and therefore the effect can be prolonged (e.g. d-tubocurarine, pancuronium). It seems that advanced hepatic disease does not significantly affect the pharmacokinetics of vecuronium, although some dose-dependent pharmacokinetic alterations have been observed. Actually, any muscle relaxant can be used in patients with advanced liver disease. Atracurium has a theoretic advantage because its metabolism is not dependent on liver function. Therefore, it is not surprising that the clearance and elimination half-life of atracurium in patients with impaired hepatic and/or renal function is not particularly different from those who have normal hepatorenal function. However, the volumes of distribution are larger, and, accordingly, the distribution half-lives are shorter in patients with severe hepatorenal dysfunction compared with normal individuals. Titration of any relaxant according to the transcutaneous nerve stimulation monitoring is beneficial because the degree of hepatic dysfunction affects the degree of pharmacokinetic disorders and there-

fore, again, the best way to avoid complications is to titrate drugs against effects.

Renal function must be maintained by administering proper fluid load (volume and content) and diuretics if needed. The parameters of controlled ventilation should be carefully selected in order to avoid an unnecessary increase in intrathoracic pressure which may impede venous return thereby decreasing cardiac output. Monitoring of the coagulation state during surgery can be important. The treatment should be based on the results of hematologic monitoring and may include administration of platelets, fresh frozen plasma, cryoprecipitate and sometimes epsilon-amniocaproic acid. It appears that adequate ventilation and circulation is the key to successful anesthesia for patients with advanced liver disease.

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