Lesson 245: PreAnesthetic Assessment of the Patient With Portal Hypertension

PREANESTHETIC ASSESSMENT

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LEARNING OBJECTIVES

At the end of this activity, the participant should be able to:
1. Describe the physiology of the hepatic circulation.
2. Explain the hepatic arterial buffer response.
3. List the possible causes of portal hypertension.
4. Discuss the pathophysiology of liver disease and subsequent portal venous hypertension.
5. Recognize the clinical signs and symptoms of portal hypertension.
6. Describe an effective preoperative evaluation and assessment of the patient with portal hypertension.
7. Identify intraoperative areas of potential concern when a patient has chronic liver disease and elevated portal pressures.
8. Assess the relationship between liver disease and portal hypertension, and describe the effects of these conditions on the cardiovascular, pulmonary, renal, and nervous systems and the blood.
9. Discuss the benefits and risks of commonly used anesthetic agents in patients with hepatic insufficiency.
10. Outline anesthetic management of the patient with portal hypertension.

CASE HISTORY

A 42-year-old man weighing 97 kg, with portal hypertension and liver cirrhosis secondary to long-term alcohol intake, presented for an emergency appendectomy. A review of systems revealed ascites, gynecomastia, splenomegaly, and petechiae. Basic laboratory values were as follows: hemoglobin, 10.8 g/dL; hematocrit, 31.7 g/dL; sodium, 128 mEq/L; albumin, 1.9 g/dL. The prothrombin time was elevated, at 14.5 seconds, as was the partial thromboplastin time, at 34.2 seconds.

ood flows to the liver in 2 independent circulatory systems: the portal venous system and the hepatic arterial system. These vascular networks allow the adequate perfusion and oxygenation of hepatocytes, in addition to the delivery of nutrient-rich blood, which is detoxified and metabolized by the liver. Total blood flow to the liver accounts for approximately 25% of the cardiac output. Most (75%) of the blood flow to the liver is through the portal venous system, which drains the large and small intestines, spleen, and pancreas. The portal venous system is a unique venous system in that it begins and ends in capillary beds (Figure 1). It allows nutrient-rich, poorly oxygenated blood to enter the hepatic sinusoids, where body metabolism is regulated. The portal system is characterized by low perfusion pressures, typically between 5 and 10 mm Hg, and by the absence of intravascular resistance. The major site of resistance to the portal flow is at the hepatic sinusoids, which are lined by highly permeable fenestrated epithelium. Dysregulation of the portal venous flow, with increased perfusion pressures, results in the amplification of fluid flow into the (extravascular) space of Disse.4

The hepatic arterial system delivers oxygen-rich blood to the liver and accounts for approximately 25% of the total circulation in the liver. The hepatic artery delivers blood under much higher perfusion pressures than those in the portal circulation. Most of the resistance to arterial flow is centered around the hepatic arterioles. The intrahepatic blood flow, also unique, is best described in terms of the liver lobule. The center of each lobule contains a tributary of the hepatic vein. At each corner of the lobule, the portal triad is present. The portal triad consists of 3 vessels: a branch of the hepatic artery, a branch of the portal vein, and an interlobular bile duct.6 Nutrient-rich blood from the portal veins filters through the hepatic sinusoids, allowing nutrients and toxins alike to enter the perisinusoidal hepatocytes. Highly oxygenated blood from the hepatic artery courses through the liver, filters along beds of capillaries, and empties via the hepatic vein into the inferior vena cava.BILE ACIDS AND WASTES ELIMINATED BY THE LIVER

Bile acids and wastes eliminated by the liver empty into bile canaliculi,7 which in turn empty into the interlobular bile ducts. The bile acids and wastes are ultimately stored in the gallbladder. Bile is excrated by periodic contractions of the gallbladder, from which bile flows into the duodenum. According to the described pattern, the flow of bile and blood within the liver lobule is bidirectional (Figure 2, page 34). Unique to the hepatic blood flow is a phenomenon called the hepatic arterial buffer response.8 This mechanism allows continuous regulation of the hepatic perfusion. When the portal flow decreases, the hepatic arterial flow increases, and vice versa. The vascular buffer is mediated by adenosine, a metabolite. Studies have shown that even when the portal flow is maintained at a constant rate, a decrease in the pH or oxygen concentration of the portal venous blood will increase the hepatic arterial flow.9 According to the current and prevalent understanding of the process, adenosine is produced by hepatocytes. When the portal flow decreases, the accumulation of adenosine causes the hepatic arterioles to dilate, so that relatively constant perfusion pressures are maintained.10


Figure 2. The distribution of blood and bile along the portal triad.9

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Abnormalities arising in either circulatory system result in a profound dysfunction of the overall fluid status. Increases in the portal venous pressure cause fluid transudates to leak into the abdominal cavity. The third spacing of fluid can be extreme in individuals with any pathology that affects the hepatic circulation.11

Physiology of Liver Function

The liver performs many tasks critical to survival. It is the major site of detoxification, effectively neutralizing harmful substances and preparing them for excretion. Biliverdin, a product of heme metabolism, is sequestered in the liver, where it is conjugated and eliminated. Another vital function of the liver is to regulate blood glucose levels. The liver is the site of gluconeogenesis, glycogen formation and storage, fatty acid oxidation, cholesterol synthesis, deamination of amino acids, urea formation, and protein synthesis. Other critical actions of the hepatocytes include the storage of vitamins and iron, synthesis of necessary coagulation factors, and production of bile.

Because the liver serves as the major site of detoxification, its condition is of paramount importance in pharmacologic considerations. Drug conjugation and metabolism can be substantially altered by liver pathology or abnormal hepatic perfusion. For example, glucuronide concentration is increased in many patients with advanced liver disease and cirrhosis,12 and they are therefore less responsive to the administration of cholecystochannels.13 These factors must be taken into consideration—especially intraoperatively—when patients with liver or portal flow pathology are being treated.

Pathophysiology of Portal Hypertension

The portal venous flow can be characterized by Ohm’s law (AP = Q × R), where AP is the pressure gradient, Q is portal venous flow, and R is resistance to flow.14 Pathologic conditions that disrupt either Q or R will effectively increase portal venous pressures. In reality, increases in splanchnic flow (Q) rarely contribute significantly to overall increases in portal pressures. Clinically, portal hypertension is almost always a result of increased resistance to flow.24

The causes of portal hypertension are commonly classified according to whether resistance occurs at prehepatic, intrahepatic, or posthepatic sites.14 Intrahepatic resistance can be further classified as presinusoidal, sinusoidal, or postsinusoidal.14

The most common cause of portal hypertension is hepatic cirrhosis, a disorder of intrahepatic (sinusoidal) resistance.15 Cirrhosis can be secondary to many conditions, including chronic viral hepatitis, alcoholic toxicity, Wilson’s disease, and hemochromatosis. Less common causes of parenchymal liver disease include sarcoidosis, schistosomiasis, myelofibrosis, and hepatocarcinoma from vinyl chloride or other chemicals. Alcoholic cirrhosis is a common cause of portal hypertension. Medications and toxins can cause both parenchymal and non-parenchymal injury to the liver, with resultant portal hypertension.25

Portal hypertension is often characterized by a hyperdynamic circulatory state; cardiac output is typically increased. The etiology of these changes is not well understood, although peripheral arterial vasodilation may play a role.26 As previously mentioned, the serum glucagon levels are invariably increased, in turn decreasing the physiologic responsiveness to cholecystokinin. Vasopressin may prove to be a better vasoconstrictor in patients with liver disease and portal hypertension.27 Massive ascites may impede adequate venous return—elevation of the diaphragm by ascitic fluid decreases thoracic volume and increases intrathoracic pressure, thereby decreasing venous return and cardiac output.24

Respiratory Complications

Portal hypertension complicated by ascites may cause pulmonary hyperventilation (increased closing volume leading to gas trapping). In addition, an increased amount of interstitial fluid can decrease the diffusion capacity across the capillary–alveolar membrane28; hypoxia may result.

Preoperative Assessment

A preoperative evaluation of the patient is critical for determining the severity of liver pathology and identifying comorbidities. A pertinent medical history of complications—such as esophageal varices and ascites—should be elicited. The patient’s history of previous surgeries or anesthetic complications is particularly relevant. It is important for the anesthesiologist to know of previous adverse effects of anesthetic drugs or other pharmacologic agents. Pharmacologic avoidance is clearly the best way to manage an adverse drug reaction, but in the anesthetic setting, this is clearly not possible. Physical examination may reveal an abdominal fluid wave, splenomegaly, hepatomegaly, icterus, feto hepaticus, asterixis, and other signs of portal hypertension. In some cases, it can be helpful to drain the ascitic fluid if it is causing significant respiratory distress.

Laboratory Testing

Blood testing that includes a complete metabolic panel is useful to ascertain the degree of liver dysfunction, in addition to abnormalities of other organs and physiologic systems. Typically, elevated aspartate aminotransferase and alanine aminotransferase levels are indicative of hepatocellular injury—although patients who have chronic liver disease with cirrhosis often present with low levels of transaminases.29 The level of alkaline phosphatase can be elevated, especially in patients with disease involving the hepatobiliary system. Alkaline phosphatase is also present in bone, intesti
Liver transplantation is considered when the patient’s overall clinical picture deteriorates significantly, and when certain laboratory values become critical. Specifically, the international normalized ratio (INR) of total bilirubin level, and plasma creatinine level are combined in a special formula to calculate what is known as the MELD (model for end-stage liver disease) score. The MELD score, among other factors, is used to ensure that livers available for transplant are given to those patients with the most severe liver disease.

Another pertinent blood and serum laboratory tests for the preoperative assessment include the prothrombin time, serum protein analysis, and renal profile. The prothrombin time evaluates the hepatic synthesis of coagulation factors. It is elevated not only in patients with severe liver dysfunction, but also in those with vitamin K deficiency (including that secondary to ileal resection and steatorrhea) or taking warfarin. The risk for bleeding increases dramatically when the INR exceeds 4.0 to 6.0—although the absolute risk for bleeding remains fairly low, <5% cases per 1,000 patients per day.

Because the intravenous administration of vitamin K can be complicated by anaphylactoid reactions, and subcutaneous administration by cutaneous reactions, the oral administration of vitamin K is preferred. A dose of 1 to 2.5 mg of oral phytonadione (phyloquinone, or vitamin K₃) reduces the INR range from between 5.0 and 9.0 to between 2.0 and 3.0 within 24 to 48 hours. For patients with an INR >10.0, a dose of vitamin K should be repeated at intervals of 7 to 14 days until variceal obliteration occurs (usually 2-4 sessions).

Surgical Intervention

Surgical care includes the placement of decompressive shunts, devascularization procedures, and liver transplantation. The selective shunt is the most commonly used decompressive operation for refractory variceal bleeding. It is used primarily in patients who present with refractory bleeding and continue to have good liver function. The shunt decompresses the gastroesophageal varices through the short gastric veins, the splenic, and the hepatic vein to the left renal vein. Portal hypertension is maintained in the splanchic and portal venous system; the shunt maintains portal flow to the liver. A decompressive shunt provides better long-term maintenance of some portal flow and liver function with a lower incidence of encephalopathy (10%-15%) than does a total shunt. The operation causes ascites because the retroperitoneal lymphatics are diverted.

Preoperative Pharmacology

The administration of drugs to the patient with portal hypertension will necessarily depend on the extent of pathology found in the liver. If hypoalbuminemia is present, the doses of drugs bound by serum proteins should be smaller than those normally recommended for adults. If ascites is present, the risk for gastric reflux and aspiration is increased. Preme dication with nonpeptidyl type 2 (H₂) receptor antagonists may be indicated. In patients with acute hepatic failure, only surgery designed to correct a life-threatening situation should be considered. Depressant or sedative drugs are not required in these patients. Nitrous oxide may be sufficient to provide analgesia and total amnesia in such critically ill patients.

Intraoperative Care

Several critical areas must be considered with regard to intraoperative care.

Fluid Replacement

Proper fluid management, with the use of large-bore intravenous lines, is paramount, especially as third-space losses may be extreme. In addition to the routine use of patient monitors, arterial pressure measurements may be obtained and central venous pressure waveforms examined, depending on circumstances. Typically, large catheters are placed for urinary measurement, depending on the duration of surgery.

Pharmacology

Liver dysfunction can profoundly alter normal drug metabolism. While hepatic pathology can decrease the efficacy of some drugs, it will increase the potency and duration of action of others. During the formulation of an anesthetic plan, the metabolism of individual agents should be investigated. The mechanism of action of halothane—classically known for its hepatotoxicity—is postulated to occur in one of the following 3 ways:

1. Production of toxic metabolites
2. Depression of hepatic glucose production
3. Immunologic hypersensitivity

In their study of the effects of halothane administration, Stock and Strunn concluded that halothane is unlikely to occur after a one-time dose. In the past, providers had to be aware of potential toxicity of the agent and the risk for hypoperfusion of the liver during anesthesia with halothane. The newer anesthetic agents used now are much safer, with fewer toxic effects.

Preoperative anesthetics were chosen to be good choices for the anesthetic management of patients with liver disease and portal hypertension. Thus far, investigators have not been able to consistently demonstrate a relationship between the use of these agents and hepato toxicity. In this regard, sevoflurane has not been associated with dose-dependent liver injury. Desflurane, the inhalational agent that is most minimally metabolized, should prove to be the anesthetic of choice for this subpopulation. However, if regional anesthesia techniques are an option, they are a safe alternative provided that the systemic blood pressure is well maintained.

Measurement of the hepatic venous pressure is used to guide medical therapy aimed at reducing portal hypertension. The measurement is taken frequently during the patient’s period of general anesthesia. Because most drugs used for general anesthesia reduce the hepatic blood flow, it would be anticipated that the hepatic venous pressure is also altered. In a prospective, randomized study, Mandell et al examined the effects of 2 frequently used anesthetics on the hepatic venous pressure to determine if pressure measurements taken during general anesthesia were similar to awake values. They studied 21 patients with hepatitis C, excluding those with hepatofugal flow and portal vein thrombosis. The free and wedged hepatic venous pressures were measured in all patients—awake, during sedation, and after anesthesia—in whom a cephalic or femoral catheter was used. Desflurane reduced the pressure difference between the portal and systemic circulations. This effect can result in errors in assessments.

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ing the success of medical therapy of portal hypertension. Propofol had less effect than desflurane on the pressure difference between the portal and systemic circulation.

The role of the liver in clearing muscle relaxants must be considered when one of these drugs is selected for administration to a patient with cirrhosis of the liver. Succinylcholine is an acceptable option, although severe liver disease can decrease plasma cholinesterase activity sufficiently to produce a modestly prolonged action.\(^{32}\) The increased volume of distribution that accompanies cirrhosis may result in the need for larger initial doses of nondepolarizing muscle relaxants to produce the required plasma concentration, but the resulting neuromuscular blockade can be prolonged if the drugs are eliminated via hepatic clearance mechanisms. Hepatic dysfunction does not appear to alter the elimination half-time of atracurium.\(^{33}\) All factors considered, intermediate-acting muscle relaxants, especially atracurium, would seem to be the preferred agents for producing skeletal muscle paralysis in patients with severe liver disease.

**Intraoperative Challenges**

Complications related to the stress of surgery are likely to develop in patients with significant incapacity of the liver. The worsening of hepatic injury because of poor oxygenation, anemia, or hypovolemia can be prevented by following standard measures. Because fluid extravasation into the abdominal cavity can be extreme, fluids are administered and levels maintained aggressively. Patients are observed and monitored postoperatively for normalization of their vital signs and common laboratory indices.

**Management of the Case Presented**

In the case presented, tannomide, metoclopramide, and sodium citrate were administered to the patient preoperatively. Two large-bore intravenous cannulae were placed, and fresh-frozen plasma (dose of 15 cc/kg) was delivered. A rapid-sequence induction and intubation was performed with propofol and succinylcholine, and rapid desaturation was noted at the time of intubation. The oxygen saturation quickly returned to normal after the patient was successfully intubated.

4. The Model for End-Stage Liver Disease (MELD) score:
   a. attempts to ensure a more equitable distribution of livers available for transplant
   b. is calculated from the international normalized ratio (INR), total bilirubin, and plasma creatinine
   c. identifies those patients requiring a liver transplant
   d. All of the above are correct.

5. The clinical signs and symptoms of hepatic encephalopathy do not usually include:
   a. feteric hepatitis (musty odor of the breath)
   b. asthenia
   c. indolent, sedated serum ammonia levels, confusion
   d. increased production of coagulation factors

6. The prothrombin time:
   a. is calculated from the international normalized ratio (INR), total bilirubin, and plasma creatinine
   b. increases with vitamin K deficiency
   c. decreases with vitamin K deficiency
   d. valvular obstruction within the portal system
   e. None of the above is correct.

7. Electrolyte disturbances in portal hypertension are most likely to be associated with:
   a. increased production of aldosterone
   b. excretion of potassium by the renin–angiotensin system
   c. decreased levels of serum glucagon
   d. hypernatremia related to dehydration

8. Which of the following is true regarding portal hyperten-
   sion and pharmacologic intervention?
   a. Valproate has not been associated with decreased hepatic
   b. A patient with a cirrhotic liver usually requires increased
   c. The levels of serum proteins have little effect on the
   d. Ascorbic increases the risk for gastric reflux and aspiration

9. Most cases of portal hypertension are caused by:
   a. systemic hypertension
   b. arteriovenous fistula formation with resultant decreased
   c. decreased levels of serum glucagons
   d. Ascorbic increases the risk for gastric reflux and aspiration

10. Hepatorenal syndrome is associated with portal hyper-
    a. intrinsic morphologic renal abnormalities
    b. polyuria
    c. an unknown etiology
    d. obstruction within the collecting system