Liver Disease and Anesthesia for Liver Surgery

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Hepatic Anatomy

- Vascular supply
  - HBF ~25% of cardiac output (100-130 ml/min/100g)
  - 25% flow and 50% oxygen supply from hepatic artery
  - 75% flow and 50% oxygen from portal vein
  - Portal venous blood is first supplied to visceral organs and is relatively deoxygenatated and rich with nutrients
  - Portal venous tributaries connect with the systemic circulation in various places that receive little flow due to normally low portal pressures (6-10 mmHg)
  - Blood bathes hepatocytes in the liver via sinusoids and drains collectively via multiple hepatic veins into the IVC

Disclosure Statement

- I do not have relevant financial relationships with commercial interests related to the content of this presentation.

Hepatic Arterial Buffer Response

- A microvascular regulatory system in the liver to modify blood flow
- Reciprocal variation of hepatic arterial flow and portal venous flow
- Adenosine is constantly produced by hepatocytes in the periarteriolar regions of the liver and is typically washed out by relatively large portal venous flow
- Reduction of portal blood flow keeps some adenosine in the vicinity of hepatic arterioles and promotes vasodilation and increased flow
- This system can provide a reserve to account for up to 50% of portal venous flow – protects from ischemic insults since arterial flow has higher oxygen content

Overview

- Hepatic anatomy and normal physiology
- Hepatic and hepatobiliary disease
- Cirrhosis/End stage liver disease and systemic effects
- Anesthetic considerations for patients with liver disease
- Anesthetic considerations for patients undergoing liver surgery (resection)

Hepatic Blood Flow (cont'd)

- Extrinsic control of hepatic blood flow is via modulation of arterial and venous tone and resistance to flow
- Alpha-adrenergic stimulation will both change the amount of blood available to the liver and the egress of blood from the venous side. This leads to reduction in the blood flow to the liver and blood volume present in the sinusoids (important for function as a reservoir)
- Beta stimulation allows for vasodilation and the opposite effect.

Hepatic Anatomy (cont'd)

- Zones of parenchyma:
  - Zone 1 – Periportal hepatocytes – responsible for oxidative activities and bile acid secretion
  - Zone 2 – Intermediate area – less metabolic activity
  - Zone 3 – Perivenular hepatocytes – Relatively anaerobic cells, most susceptible to ischemia/hypoxemia, primary site for glycolysis and lipogenesis, biotransformation of drugs/toxins
  - Characteristic site for necrosis in toxic ingestions

Assesment of Liver Function

Pharmacokinetic Considerations in Liver

- Site of production of plasma proteins and drug metabolism
- Hepatic biotransformation:
  - Phase 1 – modification of structure to remove lipophilicity (oxidation/reduction) – P450 enzymes – this ends the action of the drug
  - Phase 2 – conjugation with polar substances – increases water solubility for excretion
  - Phase 1 reactions are the most susceptible to liver disease and age

Hepatic Imaging

- Plain radiographs not helpful (except for pneumobilia)
- Ultrasound is a mainstay – gall bladder, tumors, fat infiltration, ascites
- CT – complementary to US – contrast injection can give a more detailed anatomic picture
- MRI/MRCP – very detailed visualization of biliary tree
- ERCP – visualization and intervention – better than percutaneous approach in IR
- Biopsy – imaging guided, histologic diagnosis to determine nature and extent of injury/disease, contraindicated in coagulopathy

Hepatic Pharmacokinetics (cont'd)

- Hepatic extraction ratio determines the intrinsic metabolic clearance of a drug in the liver
- Drugs with high extraction ratios (lidocaine, metoprolol as examples) are highly dependent on hepatic blood flow for clearance
- Drugs with low extraction ratios (benzos) have clearance that is independent of HBF
- Changes in the free fraction of drugs affect low extraction drugs more than high extraction drugs
- Liver disease affects pharmacokinetics profoundly: shunts, reduction in HBF, hypoalbuminemia, ascites

Hepatic Disease

- Classify to parenchymal disease and cholestatic disease
- Nearly 10% of population in US suffers from some hepatobiliary disease
- Can lose up to 80% of liver parenchyma before seeing a reduction in functional capacity, so there is a great deal of physiologic reserve
- Hepatocytes also have a great deal of regenerative capacity

Viral Hepatitis

- **Hepatitis A** – enteric infection, highly contagious for 21 days, hepatic failure is rare, coinfection with HCV frequently have FHF and high mortality, detected by serum antibody and RNA in stool
- **Hepatitis B** – transmitted by percutaneous inoculation, possible chronic infection, rare to progress to cirrhosis, detected by HbsAg, anti-Hbc (if HbsAg too low), HbeAg (denotes infectivity), immunity confirmed by anti-HbsAg
- **Hepatitis C** – previously transfusion related, transmitted by inoculation (most common blood borne illness in USA), frequently results in chronic disease/cirrhosis/HCC, detected by HCV RNA or anti-HCV
- **Hepatitis D** – RNA strands that coinfect with HBV, HDV coinfection greatly increases chance of FHF and death
- **Hepatitis E** – enteric infection, similar to HAV, restricted in certain geographical
- **Other viruses** – CMV, EBV, HSV – usually opportunistic if disseminated to liver and can be very serious

Cirrhosis

- Affects almost all organ/body systems
- Cardiovascular effects
  - Vasodilation/shunting (dec. SVR) (NO mediated?)
  - Increased CO, maintained BP
  - Increased blood volume but resdistributed to splanchnic bed (appears as hypovolemia)
  - Possible cardiomyopathy
  - Poor response to catecholamines
  - Decreased HBF from reduction in portal flow

Nonpharmacologic Causes of Liver Dysfunction

- Systemic inflammation – acute phase reactants produced in liver,changes in SVR, regional blood flow distribution, tissue oxygen extraction, and metabolism all affect liver function, relative hypovolemia and decreased splanchnic perfusion reduce hepatic oxygen delivery
- Liver is potentially more sensitive to hypoxemia/ischemia than myocardium and brain, ischemic hepatitis may persist for 3-11 days, usually a hx of systemic hypoperfusion, unknown mechanism but likely related to superoxides and free radical formation
- Cardiac disease – congestive heart failure usually from ischemia and poor oxygen delivery, not from congestion
- Surgery – sympathetic activation, RAA activity, and vasopressin release compromise splanchnic circulation and oxygen delivery – exacerbated with laparotomy, laparoscopy still impedes HBF, CPB can aggravate existing liver dysfunction (hypothermia may protect)

Cirrhosis (cont'd)

- Portal hypertension
  - Due to resistance to portal blood flow and increased splanchnic volume
  - Complicated by varix formation – most concerning is esophageal with a potential to bleed and can be life threatening
    - Octreotide and cessation bleeding are the goals – beta blockade, banding, reduce coagulopathy, physical occlusion, TIPS
- Pulmonary Dysfunction
  - Resulting pulmonary pathology – edema, interstitial lung disease, effusions
  - Intrapulmonary shunting common (40%), can be functionally limiting and increases periop risk
  - Hepatopulmonary syndrome is inc A-a gradient + IPVDs
  - Modulation of HPV can help oxygenation (supplemental O2)
  - Portopulmonary HTN very serious – mean PAP >25 with normal PCWP

Fatty/Alcoholic Liver

- NAFLD vs NASH
  - 70% of obese and 75% diabetics have NAFLD
  - Steatosis causes stress to hepatocyte and make more vulnerable to other insults → NASH +/- cirrhosis
- Alcoholic liver disease
  - Steatosis -> hepatitis -> cirrhosis
  - Can be very severe and life threatening
  - 2-3x perioperative morbidity

Cirrhosis (cont'd)

- Ascites and Edema
  - Portal HTN + sodium and water retention
  - Na retention from aldosterone activity (decreased effective plasma vol → inc renin secretion → inc aldosterone)
  - Treated with distal tubule diuretics – spironolactone/amiloride, can also use furosemide but watch for excessive diuresis
  - Refractory ascites often treated with paracentesis and shunt
  - Caution for hypovolemia after large volume taps – usually manifested after 3 hours
- Spontaneous bacterial peritonitis
  - 10-30%, diagnosed with PMN's in ascites fluid, caused by translocation of gut bacteria?
  - May need long term prophyaxis

Cirrhosis (cont'd)

- Renal dysfunction/Hepatorenal syndrome
  - Decreased GFR along with Na retention and water retention
  - Often see dilutional hyponatremia
  - HRS in up to 10% - Dx of exclusion
    - Type 1 – associated with SBP, poor prognosis
    - Type 2 – associated with refractory ascites, usually more moderate and long-standing
    - reduced effective arterial blood volume due to severe splanchnic vasodilation → renal vasocontriction, fluids and vasoconstrictors may actually alleviate, can be very severe
  - ATN – usually after hypotensive/ischemic episodes
  - Cautious diagnosis between prerenal azotemia, HRS, and ATN

Other Hepatic Disease

- HCC
  - Sometimes associated with metabolic liver disease, HCV, ETOH
  - AFP and imaging screening
  - Treat with TACE, resection, OLT
- Pregnancy
  - Acute fatty liver
    - Usually third trimester, defect in fatty acid oxidation, present with liver failure, expedite delivery of fetus
  - HELLP – distingush from AFLP with signs of preeclampsia and hemolysis, less severe course and less incidence of full blown coagulopathy
    - Extreme end involves hepatic rupture or infarction

Cirrhosis (cont'd)

- Coagulation
  - Factors 2, 7, 9, 10, proteins C/S most affected
  - Vitamin K unable to be absorbed due to poor bile production
  - Thrombocytopenia due to splenomegaly and sequestration
    - Usually above 30K
    - Spontaneous bleeding rare
  - Abnormal fibrinogen function the most common finding – mild PT/PTT prolongation)
  - Hyperfibrinolysis due to decreased poor tPA clearance
  - Treatment involves blood component therapy and/or exogenous factor administration

End Stage Liver Disease

- Definition
- MELD
- Treatment – liver transplantation

Cirrhosis (cont'd)

- Hepatic Encephalopathy
  - Multifactorial – more than just ammonia
  - Global depression of CNS function by inhibitory mechanisms (GABAergic?)
  - Potentially from toxic metabolic products entering BBB as well
  - Treat with lactulose/neomycin/OLT

Anesthetic Considerations in Liver Disease

- Preoperative

Anesthetic Considerations in Liver Disease

- Intraoperative

Anesthesia for Liver Resection

- Anesthetic technique
- Access/monitoring
- Blood transfusion
- Acute normovolemic hemodilution
- Analgesic options – epidural?
- To extubate or not to extubate?

Anesthetic Considerations in Liver Disease

- Postoperative

Anesthesia for Liver Resection

- Indications
- Anatomy
- Surgical Considerations
- Vascular control techniques