Hepatic Encephalopathy

Man Piu Wong | Vivek K. Moitra

Risk

- Incidence in pts with hepatic cirrhosis (about 0.1% of the population) is 50–70%. It is frequently subclinical, but can be exacerbated in the postop period by the surgical stress response, dehydration, and postop infection.
- HE is acutely worsened, in about 20% of pts, following surgical portacaval shunts, minimally invasive TIPS, and hepatic resections.

Perioperative Risks

- Precipitation of encephalopathy from benzodiazepines, surgical procedure (portacaval shunt), postop infection, GI hemorrhage, or erosive gastritis
- In pts with severe underlying liver disease, Childs Class B and C, or high MELD score (>15)

Worry About

- Preop respiratory depression from benzodiazepine premedication.
- Hemorrhage from underlying hepatic dysfunction (e.g., decreased coagulation factors, thrombocytopenia).
- Underlying precipitating factor (infection, bleed) may create hemodynamic instability. HE in absence of precipitating factor, or when accompanied by seizure or focal neurologic deficit, should prompt brain imaging to rule out intracerebral bleed.
- Undiagnosed cerebral edema with a risk of cerebral ischemia in fulminant hepatic failure presenting for liver transplantation.

Overview

- A syndrome of alteration in mental status, from impaired concentration to coma, caused by portosystemic shunting, usually in the presence of liver failure. Hyperammonemia from protein breakdown is usually present, and the degree of hyperammonemia generally correlates with the degree of encephalopathy.
- Multifactorial in origin, but altered neurotransmission and elevated levels of endogenous benzodiazepines and opioids appear important contributors. Although not effective in improving outcome, administration of flumazenil and naloxone temporarily improves mental status in about 50% subjects with HE.
- Underlying hepatocellular injury may arise from multiple etiologies, but the most common are chronic alcohol abuse, chronic viral hepatitis, and NASH.
- HE usually reflects advanced hepatic dysfunction and is frequently seen in pts awaiting liver transplantation.

Etiology

- Underlying liver disease with identifiable hyperammonemic precipitating cause in >90% of cases: GI hemorrhage, infection, azotemia, hypoglycemia, electrolyte derangements, diuresis/hypovolemia, constipation, sedatives, especially benzodiazepines
- Elevated levels of endogenous benzodiazepines, γ-aminobutyric acid agonists and opioids
- Direct ammonia neurotoxicity

Usual Treatment

- Identify and treat precipitating cause.
- Reduce plasma ammonia with lactulose: 20 g q6–12 h orally or by NG tube until softening of stool; reduce dose if diarrhea. Alternately, 300 mL lactulose mixed with 700 mL tap water given as retention enema in pts with severe HE that cannot protect their airway.

Certain Antibiotics Can Be Used in Conjunction With Lactulose

- Neomycin (risk of ototoxicity and nephrotoxicity)
- Metronidazole (GI and systemic side effects)
- Rifaximin (combined with lactulose shown to decrease risk of hepatic encephalopathy versus lactulose alone)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Impaired concentration, lethargy, coma	Amnesia/memory deficits Fatigue	Transition of reflexes from hyperactive to hypoactive, and disappearance of asterixis, signify onset of severe HE	Plasma ammonia, CT
CV	Hypotension	Liver failure	Systolic BP 90 may be acceptable in liver failure	BP
RESP	Hyperventilation, hypoxemia	Dyspnea	Ascites, pleural effusions	CXR, ABG, US Abdominal CT
METAB	Hyponatremia, hypokalemia	Correction of hyponatremia or worsening of hypokalemia can further impair mental status	Free water excess exacerbates ascites and anasarca	BMP
HEME	Anemia, coagulopathy	GI bleeding	Pallor, splenomegaly	Hgb, plt count, prothrombin time

Key References: Poh Z, Chang PE: A current review of the diagnostic and treatment strategies of hepatic encephalopathy, *Int J Hepatol* 2012:480309, 2012; Kiamanesh D, Rumley J, Moitra VK: Monitoring and managing hepatic disease in anesthesia, *Br J Anesth* 111(Suppl 1):i50–i61, 2013.

Perioperative Implications

Liver Transplantation

- Recurrent or persistent HE predicts poor survival in cirrhosis and indicates decompensated liver disease which is best treated by liver transplantation.
- When severe, particularly in association with fulminant hepatic failure, HE is frequently associated with cerebral edema. The resulting intracranial Htn may be underestimated by CT scan, and ICP monitoring is indicated to ensure adequate cerebral perfusion pressure periop.
- ICP can be reduced via hyperventilation, hypertonic saline, mannitol, propofol, and elevation of head of bed. Recent evidence of hypothermia has been shown to reduce cerebral edema and intracerebral Htn.

Other Surgeries

- Mental capacity may be impaired to the degree that consent is problematic.
- Pt may be hypovolemic from impaired ability to maintain PO intake, lactulose therapy causing diarrhea, diuretic therapy for associated ascites, or recent GI bleed. Maintenance of hydration is important to prevent acute tubular necrosis the incidence of which is increased in liver failure.
- Placement of TIPS or surgically fashioned portosystemic shunt are performed for refractory esophagogastric variceal bleeding. HE may be precipitated or exacerbated postop, particularly if a significant degree of encephalopathy is present preop, or if the pt is elderly.
- Reversal of benzodiazepine precipitated hepatic encephalopathy can be performed with flumazenil. However, pts with history of alcohol use may tolerate higher doses of benzodiazepines.

Hepatitis, Alcoholic

Anthony K. Woodall | Melville Q. Wyche III | Amir Elhassan | Alan David Kaye

Risk

- In USA, 8.5% of adults met DSM-IV criteria for current alcohol use disorder; 30.3% of adults met DSM-IV criteria for lifetime alcohol use disorder. Approximately 10–15% of alcoholics will develop alcoholic hepatitis and cirrhosis.

Perioperative Risks

- Mortality rate of 60–100% of pts undergoing surgery during acute alcoholic hepatitis.
- Poorer prognosis when accompanied by increased bilirubin, increased Cr, PT >1.5× control, ascites, or encephalopathy.
- >10% of pts develop DTs without prophylaxis.
- Abdominal surgeries are associated with higher risk due to reduced hepatic blood flow.

Worry About

- Anemia and coagulopathy
- Pulmonary shunting leading to arterial hypoxemia
- Altered mental status and/or hepatic encephalopathy
- Cerebral edema and increased ICP with hepatic encephalopathy, which may progress to coma
- Hemodynamic instability secondary to DTs
- Hypoglycemia due to poor gluconeogenesis
- Insulin resistance
- Electrolyte abnormalities
- Renal insufficiency, which means hypotension and nephrotoxic drugs should be avoided
- Citrate toxicity with blood transfusion due to decreased citrate metabolism

Overview

- Most common form of liver disease in USA.
- Usually preceded by period of heavy alcohol consumption.
- An intermediate stage between fatty liver and alcoholic cirrhosis.
- Can vary from mild (with only elevated liver function tests) to severe liver inflammation (prolonged prothrombin time and liver failure).
- Can be chronic (less severe) or acute (more severe).
- Characteristic clinical features include fever, hepatomegaly, jaundice, anorexia, and abdominal bruit over liver (indicated in >50% pts).
- 10–20% mortality risk with each episode of acute alcoholic hepatitis.
- Mortality is 50% within 30 d of onset, with pts having hepatic encephalopathy, derangement in renal function, hyperbilirubinemia, and prolonged PT.

Etiology

- A daily intake of >40 g of alcohol, (e.g., roughly 4 beers or 3.5 oz of 80-proof liquor) in men and >20 g (e.g., 2 beers or approximately 2 oz of 80-proof liquor) in women significantly increases the risk of alcoholic hepatitis.
- Inflammatory process via leukocytic infiltration that leads to hepatocellular necrosis with intracellular deposition of Mallory Bodies (characteristic, not specific).
- Repeated episodes are a precursor to cirrhosis after healing and scar tissue formation.

Treatment

- Abstinence with counseling
- Nutritional support: Diet, multivitamin, and mineral supplementation
- Medications: Pentoxifylline, steroids (which may reduce mortality in pts with severe alcoholic hepatitis or encephalopathy)
- Supportive care including diet adjustment, multivitamin supplementation, lactulose, and neomycin if needed

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	High CO Low SVR Low CO (in advanced disease)	Exercise tolerance	Hyperdynamic cardiac exam	ECG ECHO
RESP	Pulm shunts Restrictive disease Pulm effusions Central hyperventilation	Orthodeoxia Ascites	Effusions on CXR, ascites on abdominal exams	Resp alkalosis on ABG
GI/HEPAT	Disrupted synthetic and metabolic function	Anorexia, N/V, malaise, weight loss, fever	Jaundice, ascites, tender hepatomegaly, splenomegaly	Elevated transaminases (AST/ ALT>2), PT, ALP, bilirubin Decreased albumin
RENAL	Mg^{2+} and PO_4^{2-} wasting Free water retention		Ascites	Serum Mg^{2+} and PO_4^{2-} Hyponatremia
ENDO	Insulin resistance			Glucose
HEME	Anemia and thrombocytopenia GI blood loss Hypersplenism	Bruising/bleeding	Splenomegaly	Hgb/ Hct, plts
CNS	Decreased clearance of amines	Altered mental status	Neurologic exam	NH_3 levels

Key References: Muilenburg DJ, Singh A, Torzilli G, Khatri VP: Surgery in the patient with liver disease, *Anesthesiol Clin* 27(4):721–737, 2009; Steadman RH, Braunfeld M, Park H: Liver and gastrointestinal physiology. In Hemmings HC, Egan TD, editors: *Pharmacology and physiology for anesthesia: foundations and clinical application*, Philadelphia, PA, 2013, Elsevier, pp 475–486.

Perioperative Implications

Preoperative Preparation

- Pt should be assessed via Child-Pugh or MELD score. Elective procedures should be postponed for Child-Pugh score >7 or MELD >8.
- Increased sensitivity to sedative medications (increased cerebral uptake of benzodiazepines).
- Ascites may be treated by diuretics (spironolactone) or percutaneous drainage. Contains <3 g/dL protein and the same concentration as blood for solutes.
- Hypokalemia and hyponatremia should be corrected slowly (over 24–36 h).
- Correct coagulopathy with vitamin K, FFP, and platelets (if needed).

Monitoring

- Consider CVP or PA cath: Following the removal of large amounts of ascitic fluid, IV colloid fluid replacement is often necessary to prevent profound hypotension and renal shutdown.
- Monitor blood glucose closely due to deranged insulin production secondary to liver pathology.
- Arterial cath for hemodynamic lability, frequent blood gas sampling, and large fluid shifts.

Airway

- Rapid sequence intubation: Some pts are at risk for aspiration due to ascites (increased abdominal pressure, and slowed gastric emptying).
- Inadvertent esophageal intubation can cause enough trauma to damage the esophageal varices and cause significant bleeding.
- Beware of airway edema with reduced liver function.

Induction

- Hypoalbuminemia may decrease V_d and therefore increase pharmacologic response to standard drug dosages.
- Water-soluble drugs may have increased V_d, owing to ascites.
- RA is well tolerated (if coagulation status permits).

Maintenance

- Impaired drug metabolism, detoxification, and excretion by the liver can prolong drug half-lives. (Volatile agents, muscle relaxants, analgesics, and sedatives may be affected.)
  - Remifentanil has organ independent metabolism, a benefit for severe liver disease.
  - Fentanyl is a very common opioid choice.
  - Cis/Atracurium are neuromuscular blockers of choice due to organ independent metabolism.
  - Increase initial dose of neuromuscular blockers due to increased volume of distribution, reduce subsequent doses due to decreased metabolism.
  - Decrease dose 50% for morphine, meperidine, barbiturates, and benzodiazepines.
- Desflurane is the most minimally metabolized inhalational agent; however, sevoflurane and isoflurane are also shown to be safe in pts with impaired liver function. Factors known to reduce hepatic blood flow, such as hypotension, excessive sympathetic activation, and high mean airway pressures during controlled ventilation, should be avoided.

Extubation

- Extubate when pt fully awake to ensure highest degree of airway protection.

Adjuvants

- Multivitamins, minerals, and vitamin K 10 mg SQ or IM

Postoperative Period

- Regional pain control is ideal so as to avoid pharmacokinetic disturbances of systemic agents.
- Maintain low threshold for transfer of pt to ICU environment, particularly in unstable pts.
- Vigilant observation for signs of acute hepatic decompensation (jaundice, encephalopathy, and ascites), delirium tremens, and sepsis (with secondary DIC).
- Liver failure is the most common cause of postop death in cirrhotic pts.

Anticipated Problems/Concerns

- Increased risk of postop complications, including acute hepatic failure, sepsis, bleeding, and renal dysfunction
- Need for prolonged airway protection because of altered mental status and pulm dysfunction
- Acute withdrawal from alcohol
- Multiple coagulation abnormalities due to synthetic dysfunction and hypersplenism