Hepatic Encephalopathy

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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

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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