Hepatic Hell: Acute Liver Failure causes and management

Introduction
Acute liver failure: some type of severe liver injury leads to near-immediate failure of the synthetic function of the liver with a high risk of permanent liver infarction and mortality. There are strict criteria and the following MUST be met:

-Encephalopathy

-Impaired synthetic function (INR of ≥1.5) in a patient without preexisting liver disease

-Duration of < 26 weeks (differentiates from chronic)

Someone with preexisting cirrhosis for >26 weeks (due to alcohol, NASH etc) are diagnosed with acute-on-chronic injury. This is not ALF.

The true determinants of prognosis are the causes, which vary greatly depending on the pathology. Viral and drug-induced hepatitis are the most common causes in adults. In the USA, acetaminophen is the most common cause of acute liver failure.

See the table to the right to understand the grading of encephalopathy. Cerebral edema is the most common cause of death in ALF, therefore this drives management decisions.

Presentation
Nonspecific symptoms and signs. Lethargy, anorexia, nausea/vomiting, pruritus, jaundice, abdominal distention, RUQ pain, mental status changes.

Laboratory findings: also nonspecific and depends on time of presentation and cause. Elevated aminotransferase levels, elevated bilirubin, elevated INR (required for diagnosis), thrombocytopenia, hyperammonemia, multiple electrolyte deformities as described below.

GENERAL MANAGEMENT

Setting: Only 40% of patients with acute liver failure recover spontaneously, leaving many needing liver transplantation. Whenever possible, patients with ALF should be managed in an ICU at a facility capable of performing liver transplantation. Transport patients early!

Workup: the obvious liver studies - CMP, PT/PTT/INR, CBC, and ABG. Serial fingerstick glucoses are important because hypoglycemia can be a cause of altered mental status given the liver’s inability to provide stress hyperglycemia.

Patients should be monitored and treated for hypoglycemia, hypokalemia, and hypomagnesemia. Worsening ALF and worsening prognosis is indicated by rising bilirubin & PT/INR.

Hemodynamic management: The goal is to maintain a MAP> 75 mmHg or a CPP>50 to 60 mmHg; initial volume replacement is with normal saline (LR should not be used as the liver will be unable to metabolize the lactate and therefore it will worsen the patient’s acidosis). If the patient is already severely acidotic, one can use ½ -NS with 75 mEq/L Na bicarbonate. There is no right answer here-these patients are usually very sick and any volume resuscitation can be helpful, although one must be cautious due to high risk of volume overload from venous congestion and low oncotic pressure.

If unresponsive to IV fluids, norepinephrine is preferred as the vasopressor of choice. If refractory, Vasopressin can be considered along with stress dose hydrocortisone.

Acute kidney injury is seen in 30-70% of patients. The percentage is higher in those with acetaminophen toxicity and ischemic hepatitis.

Bleeding prevention: Patients with ALF can develop severe coagulopathy. Interestingly, even with an elevated INR, the majority of patients are either hypercoagulable or have normal coagulation. Therefore, prophylactic FFP is not recommended as it can interfere with assessments of liver function and may lead to fluid overload. Correct low platelets and increased PTT only in the setting of bleeding or pre-procedure. The most common site of bleeding is GI.

Infection surveillance/ prevention: studies have shown no benefit for prophylaxis. If there is evidence of infection use piperacillin/tazobactam or a fluoroquinolone. Gram negative and anaerobe coverage is needed.

MANAGEMENT OF COMPLICATIONS

Metabolic abnormalities: initially patients present with alkalosis (mixed respiratory and metabolic abnormality) in early ALF then acidosis as lactic acid accumulates. The most common electrolyte disturbances are hypokalemia, hyponatremia, and hypoglycemia.

Hepatic encephalopathy: ALF can lead to high ammonia, which accumulates in astrocytes causing cytotoxic edema. The table above refers to the grading of encephalopathy. Patients with acute liver failure are not routinely treated with lactulose or rifampin (both used
**Hepatic Hell: Acute Liver Failure causes and management**

Neomycin is nephrotoxic, thus avoid. If the need arises, intubate patient before administering lactulose, especially patients who are unable to maintain their airway protection and there is concern for aspiration.

**Cerebral edema:** uncommon in patients with grade I or II encephalopathy, but it is present in 30% of those with grade III encephalopathy and in approximately 75% of those with grade IV encephalopathy.

**Preventing intracranial pressure elevation:** immediate steps in those with grades III-IV include minimizing patient agitation, elevating the head of the patient's bed, maintaining optimal fluid balance, and lactulose with discussion of intubation.

If concern for increased ICP and Cushing triad, prophylactic administration of 3% hypertonic saline (in grade IV encephalopathy, and patients with ammonia >150 micromol/L should be performed.

**Treatment of ICP:** please refer to our more detailed guide on managing elevated ICP on our website.

**Seizures:** Seizures are common in ALF, especially with worsening encephalopathy and can raise ICP. In patients who require sedation, use sedatives with anti-seizure activity. First line: phenytoin, second line is short activating benzodiazepines. Prophylaxis with an AED is not recommended.

**INTERVENTION FOR SOURCE OF ALF (SEE NEXT PAGE)**

**References**
