Acute Liver Failure

Key Article

Nanchal R, et al. Guidelines for the Management of Adult Acute and Acute-on-Chronic Liver Failure in the ICU: Cardiovascular, Endocrine, Hematologic, Pulmonary, and Renal Considerations. Crit Care Med. 2020; 48:e173-e191.

Case

- 40 yo male without PMHx presents to the ED with a chief complaint of "SOB".
- HPI: 3 days of subjective fevers, chills, myalgia's, arthralgia's, nausea, vomiting, and progressive dyspnea; no known COVID+ contacts; no known sick contacts; no chest pain or chest tightness; some generalized abdominal discomfort without diarrhea; denies anosmia or dysgeusia
- VS: BP 73/43 mm Hg; HR 160 and irregular; RR 40 bpm; SpO2 98% on RA; Temp 100.6 F
- Exam: A/O x 3; muddy sclera; mucous membranes dry; no JVD; tachypnea with accessory muscle use, CTA bilaterally without rales/rhonchi/wheezes; irregularly irregular and tachycardia; abdomen is soft and non-tender without rebound or guarding; extremities unremarkable without edema; neurologic exam is non-focal; skin exam is without areas of erythema or induration
- Within 45 minutes, the Lab calls with two critical values: **pH 6.88** and **Lactate > 17**

Background

- Patients with acute liver failure (ALF) or acute on chronic liver failure (ACLF) have an exceedingly high mortality.
- Early recognition and prompt management of liver failure may improve outcomes.
- The Key Article is intended to be a guide to critical care physicians, emergency medicine physicians, and other acute care providers in caring for critically ill patients with liver failure
- ALF: occurrence of encephalopathy and hepatic synthetic dysfunction within 26 weeks of the first symptoms of liver disease in a patient without evidence of chronic liver disease
- ACLF: acute decompensation of cirrhosis, organ dysfunction, and high short-term mortality

Cardiovascular

- *Fluid Resuscitation*
    - ALF or ACLF is a hyperdynamic state resulting in increased cardiac output and decreased or near-normal BP.

    - Primary mechanism behind hyperdynamic state is peripheral and splanchnic vasodilation
    - No large randomized trials comparing different fluids in patients with ALF
    - Recommend against hydroxyethyl starch and gelatin solutions over crystalloids
    - Suggest using albumin for resuscitation of patients with ALF or ACLF over other fluids, especially when the serum albumin is low (< 3 g/dL)
        - Albumin may also have antioxidant, immunoregulatory, and endothelial regulatory functions
        - Much of the literature, however, is extrapolated from studies on severe sepsis and septic shock
- *Blood Pressure Target*
    - Precise MAP goal in patients with liver failure is uncertain – because it is a hyperdynamic vasodilatory state in which flow may be adequate at lower pressures
    - Suggest using a target MAP of 65 mm Hg with concomitant assessment of perfusion
    - However, this is based on indirect evidence from sepsis literature
- *Monitoring Blood Pressure*
    - Suggest placing an arterial catheter for BP monitoring in ALF
    - Estimation of BP using a cuff likely to be inaccurate
    - Insertion of a radial arterial catheter generally safe in ALF, especially when guided by US
- *Choice of First-Line Vasopressor Agent*
    - Recommend using NE as the first-line vasopressor in patients with ALF or ACLF who remain hypotensive despite IVFs.
    - As discussed, shock states in ALF typically a distributive physiology.
    - Indirect evidence from sepsis suggest that NE should be first-line
    - Epinephrine may cause more splanchnic vasoconstriction and increase mesenteric and hepatic ischemia in setting of ALF. Epinephrine will also increase lactate production and make interpretation of lactate clearance difficult.
- *Vasopressin*
    - Suggest adding low-dose vasopressin to NE in patients with ALF or ACLF who remain hypotensive despite IVFs to increase BP
    - Similar to selection of IVFs and NE, this recommendation is extrapolated from sepsis literature

Hematology

- *Bleeding and Thrombosis Risk*
    - Suggest using viscoelastic testing (TEG/ROTEM) over measuring INR, platelets, and fibrinogen on critically ill patients with ALF or ACLF
    - Individual components often fail to consistently provide an assessment of overall hemostatic function and risk of bleeding
    - INR does not account for deficiencies of the anti-coagulation system, which may result in a hypercoagulable state not captured by INR

    - TEG or ROTEM allows for real time global and functional evaluation of altered activity of the pro- and anticoagulant pathways; also identifies platelet function, hyperfibrinolysis, and premature clot dissolution
- *Hemoglobin Target*
    - Suggest using a transfusion threshold of 7 mg/dL for critically ill patients with ALF
    - Theorized that transfusion may play a role in worsening thrombosis
        - RBC transfusion has been shown to be an independent predictor of mortality post-liver transplant
        - Endogenous epo levels are already elevated in patients with cirrhosis and relate to the degree of portal hypertension
        - Exogenous epo induces thrombosis and platelet activity
- *Bleeding Risk for Invasive Procedures*
    - Recommend TEG or ROTEM over INR, platelet, fibrinogen in patients with ALF undergoing procedures
    - Bleeding rates are low for patients with cirrhosis or ALF undergoing paracentesis (0-3%) and thoracentesis (2%)
    - Bleeding does not correlate with platelet count or INR

Pulmonary

- *Tidal Volumes for Vented Patients*
    - Suggest using a low tidal volume strategy in patients with ALF or ACLF and ARDS
    - No specific studies on ALF patients – extrapolated from studies on general critically ill patients
- *PEEP*
    - Suggest against using high PEEP over low PEEP in patients with ALF or ACLF and ARDS
    - Be mindful of high PEEP given risk of increasing intracranial pressure and reducing venous return
    - Similar to tidal volume recommendation, there are no specific studies on ideal PEEP in patients with ALF or ACLF – extrapolated from studies on general critically ill patients
- *PAH Therapy in Portopulmonary HTN*
    - Portopulmonary HTN is a well-known serious pulmonary vascular complication of portal hypertension
    - Defined as the presence of PAH that evolves because of portal HTN – it is included in Group 1 PH classifications
    - POPH occurs in approximately 4.5-8.5% of liver transplant candidates
    - POPH patients are usually excluded from most RCTs of PAH therapy – thus application of PAH specific therapy in POPH is extrapolated from the broader PAH literature
    - Prostacyclin analogs have shown improvements in POPH hemodynamics
    - Endothelin receptor antagonists has also shown improvements in hemodynamics of POPH patients without significant toxicity
    - Suggest treatment POPH with agents approved for PAH when PAP > 35 mm Hg

- *Hypoxemia in Hepatopulmonary Syndrome*
    - HPS characterized by dilatation of pulmonary precapillary and capillary vessels resulting in hypoxemia early on due to V/Q mismatch, and that later due to shunt physiology
    - Loss of hypoxic vasoconstriction in 30% of cirrhotics leads to loss of pulmonary vascular tone with gravitational changes and development of platypnea and orthodeoxia
    - Severe hypoxemia occurs in about 6-21% of patients with HPS early on (< 24 hrs) after transplant and has a 45% mortality
    - Recommend supportive care with supplemental O2 in the treatment of patients with HPS pending transplant
    - Transplant is the only proven beneficial long-term therapy
- *Hepatic Hydrothorax*
    - 4-6% of patients with cirrhosis develop hepatic hydrothorax
    - General management is aimed at reducing pleural effusion with salt restriction and diuretics
    - In recurrent effusions, best studied treatment is TIPS with complete response in about 56% and partial response in about 18%
    - Traditionally chest tubes were considered a relative contraindication due to fear of infection and leakage of excessive fluids and electrolytes
    - Infection rates range from 0-29%
    - Volume and electrolyte losses have been reported but only in case reports
    - Approximately 50% of patients achieve spontaneous pleurodesis.
    - For those that do not achieve pleurodesis, tube thoracostomy may be considered if there is contraindication to TIPS or as a bridge to liver transplant

Renal

- *Hepatorenal Syndrome*
    - HRS is a distinct form of kidney injury in patients with cirrhosis and ascites
    - Occurs in the absence of structural kidney disease, nephrotoxins, or sepsis
    - Considered a form of pre-renal dysfunction characterized by severe intra-renal vasoconstriction and simultaneous global vasodilation
    - Type I HRS – acute, severe and corresponds to Stage 2 AKI
    - Type II HRS – shows more slowly and less severe degree of renal dysfunction
    - Transplant is considered the best therapy for HRS
    - Vasoconstrictors together with albumin is a frequent intervention
    - Recommend using vasopressors in critically ill patients with ACLF who develop HRS