Management of Acute Liver Failure in the Intensive Care Unit Setting

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KEYWORDS

• Acute liver failure • Hepatic encephalopathy • Acute renal failure
• Intracranial hypertension • Acetaminophen toxicity

KEY POINTS

- Early recognition with serial neurologic examinations is the key to initiating appropriate management of hepatic encephalopathy and cerebral edema.
- Thrombocytopenia is not infrequently seen in acute liver failure (ALF) and is associated with increased incidence of multiorgan failure.
- The development of AKI was associated with increased mortality, with incidence being more common in patients with severe liver dysfunction.
- In patients with refractory hypotension, adrenal insufficiency should be considered.
- Patients with ALF are at high risk for bacterial and fungal infections.

INTRODUCTION

Acute liver failure (ALF) represents one of the most catastrophic conditions encountered in the intensive care unit (ICU). The severity of illness and the rapidity with which the condition progresses to multiorgan failure are alarming and prompt a high index of suspicion to arrive at a diagnosis and provide swift medical care. ALF presents a unique set of complications and management strategies with liver transplantation as the common end point in most cases. This article focuses on the management of ALF in the ICU setting.

Acute liver failure, previously known as fulminant hepatic failure, is defined as development of hepatocellular dysfunction manifesting as coagulopathy and encephalopathy in patients without pre-existing liver disease over a period of 26 weeks. There are over 2500 cases of ALF every year in the United States, with over half of them

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progressing to liver transplantation.[1] Acetaminophen toxicity is by far the most common reason for liver transplantation among ALF patients, followed by other drug-related injuries, viral etiologies, and Wilson disease.[1] The major causes of mortality in ALF are intracranial hypertension (ICH) and infections; however, patients can manifest with varying degrees of hemodynamic derangements and renal dysfunction.

DIAGNOSIS OF ACUTE LIVER FAILURE

A detailed history and physical examination are key to evaluating a patient with ALF to determine the etiology of liver injury. It is important to elucidate the presence of any component of chronic liver disease to identify if this is truly ALF or a representation of acute on chronic liver failure (ACLF).[2] A thorough assessment of lack of social support, medical comorbidities, and history of malignancies should be performed, as these could preclude candidacy for liver transplantation. An initial laboratory evaluation including basic metabolic panel, liver function test, coagulation profile, arterial blood gas (ABG), serum lactate, comprehensive hepatitis panel, and toxicology screen should be obtained. All patients should undergo serial monitoring of liver function tests, coagulation profile, and mental status, given high risk for ICH and coagulopathy. Diagnostic imaging with abdominal ultrasound with Doppler to assess patency of hepatic and portal veins, presence of ascites, and liver size should be obtained. MRI of the abdomen or computed tomography (CT) of the abdomen is recommended for detailed evaluation of liver anatomy and to exclude the presence of chronic liver disease and portal hypertension.[1] Early transfer to the nearest liver transplant center is recommended given the potential for rapid deterioration. As part of the initial evaluation, a constant assessment of the patient's mental status should be performed, as changes signal the development of hepatic encephalopathy. Patients should also be evaluated for intubation, mechanical ventilation, and hemodynamic support at presentation and during the progression of ALF.

INTRACRANIAL HYPERTENSION

Intracranial hypertension (ICH) develops in 20% to 30% of patients with ALF. Hepatic encephalopathy (HE) is considered a precursor to the development of cerebral edema and ICH in these patients. In extreme cases, this can lead to transtentorial herniation, culminating in high mortality rates. The pathophysiology that leads to the development of HE is governed by the interplay between elevated levels, inflammation, and increased cerebral blood flow.[1,3] There is a strong association between elevated ammonia levels and development of ICH, particularly at levels greater than 150 to 200 micromol/L.[1] An acute rise in ammonia levels triggers osmotic shifts, which lead to astrocyte swelling and cerebral edema.

Diagnosis of Hepatic Encephalopathy

Early recognition with serial neurologic examinations is the key to initiating appropriate management of HE and cerebral edema. There are 4 grades of HE, and the grade correlates with development of cerebral edema and prognosis. Grade 1 represents a euphoric state with occasional depression or fluctuation to mild confusion. This state can be identified by an overall slowness in mentation, along with slurred speech. Grade 2 is noted to be an accentuation of grade 1 primarily dominated by drowsiness, inappropriate behavior, with an ability to maintain sphincter control. The hallmark of grade 3 is prolonged periods of sleeping with the ability to be aroused along with incoherent speech and marked confusion. Finally, grade 4 is a state where the patient is unarousable with minimal response to painful stimuli. Identification of the original