Modern Management of Acute Liver Failure

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KEYWORDS

• Liver transplant • Acute liver failure • MELD

KEY POINTS

- Acute liver failure causes a systemic response leading to multiorgan failure that requires supportive care in the critical care setting.
- *N*-Acetylcysteine is beneficial for acetaminophen-induced acute liver failure and may provide a survival benefit in nonacetaminophen causes when administered before the onset of advanced encephalopathy.
- Progressive encephalopathy and intracranial hypertension continue to be the most important factors to prognosticate survival and must be avoided or reduced as much as possible.
- Many prognostic tools are available, but the decision to pursue transplantation should not be based on a single tool, but rather with a multifactorial approach.

INTRODUCTION

Acute liver failure (ALF) is a rare disease, but when it occurs, it can be life-threatening. The most widely accepted definition of ALF is an abnormal International Normalized Ratio (INR) of greater than or equal to 1.5 and any degree of encephalopathy in a patient without preexisting underlying chronic liver disease.[1] Based on the American Association for the Study of Liver Diseases guidelines, the timeframe between the onset of acute symptoms should be within 26 weeks to be considered acute rather than chronic liver failure.[2] Some exceptions to the definition of ALF are patients with Wilson disease, acute presentation of autoimmune hepatitis (AIH) or Budd-Chiari syndrome, which can all present with ALF even if there is some degree of underlying chronic liver disease. These patients are treated as having ALF rather than acute-on-chronic liver failure.[2]

Although there are various guidelines to help clinicians with the management of ALF, there can be wide variation in clinical practice.[3] This is partly due to a lack of

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randomized, controlled trials providing firm data on particular management strategies owing to the rarity of the disease. As critical care medicine and access to emergency liver transplantation have improved over the years, it becomes increasingly important to understand how to improve survival in patients presenting with ALF. In this article, we discuss the current management strategies for ALF.

DISCUSSION

Etiology of Acute Liver Failure

The etiology of ALF plays into the decision-making process and treatment of ALF. Depending on the etiology of ALF, patients may or may not be candidates for liver transplantation.[1,4] The epidemiologic etiologies of ALF vary depending on the geographic region, with viral hepatitis being the most common causes in the developing world, whereas drug-induced liver injury, specifically acetaminophen toxicity, is the most common etiology in the United States.[2,4] Multiple medications have been associated with ALF and a thorough history of any medication use as well as herbal or supplement use must be assessed at the time of admission[2] (**Box 1**).

Certain conditions preclude emergency listing for transplant, and include malignant infiltration of the liver, usually from lymphoma, extensive metastases, or acute ischemic injury and hypoxic hepatitis from cardiovascular or respiratory system disorders.[1] In patients presenting with Budd-Chiari syndrome, malignancy should be investigated before listing for liver transplantation; however, frequently Budd-Chiari syndrome may be related to an underlying myeloproliferative disorder and this is not necessarily a contraindication to liver transplant.[5] Relative contraindications for emergency liver transplantation include those systemic diseases that can cause secondary liver failure, including hemophagocytic lymphohistiocytosis or infectious processes such as malaria, dengue, and rickettsial disease, or certain toxin ingestions causing multiorgan failure.[1,6,7]

ALF has been classified in 3 well-known systems: the O'Grady, Bernuau, and Japanese systems.[8–10] These systems can help to identify potential causes of ALF given the timing of injury, but these systems may not be particularly helpful, because the different varieties of ALF, namely, hyperacute, acute, or subacute, are not typically used for prognostication.[1]

DIAGNOSTIC STUDIES

Initial diagnostic testing for all patients involves blood testing for specific etiologies of ALF and blood work to assess the severity of the condition. Initial evaluation typically includes:

Hepatitis A immunoglobulin (Ig)M
Hepatitis B core IgM
Hepatitis B surface antigen
Hepatitis C antibody
Hepatitis C virus RNA
Herpes simplex virus IgM
Human immunodeficiency virus antibody
Antinuclear antibody
Anti–smooth muscle antibody
IgG levels
Lipase/amylase (for complications)
Toxicology screen