

ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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Alcoholic Liver Disease



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G&H What is alcoholic liver disease, and how prevalent is it in the United States?

LB Alcohol abuse is the third leading preventable cause of death in the United States, according to the Centers for Disease Control and Prevention. Alcoholic liver disease is one of many conditions associated with alcohol misuse. It has a broad spectrum, ranging from mild fatty changes in the liver to frank cirrhosis of the liver. Nearly all individuals who consume a significant amount of alcohol (ie, >40 grams a day) will develop early fatty changes that can be seen on liver biopsy, and approximately 10% to 20% will eventually go on to develop cirrhosis.

In addition, there is another distinct form of alcoholic liver disease, acute alcoholic hepatitis, which is a lethal and feared complication of alcohol abuse. This condition occurs in approximately 30% to 45% of alcoholics at some point in their lives. This is a dangerous disease in which the 28-day mortality in severe cases can be as high as 50%.

G&H Have there been any recent trends in the epidemiology of alcoholic liver disease?

LB In the United States, the prevalence of alcoholic liver disease is essentially flat, with perhaps a very slow downward trend in the past 5 years or so. In the general population, alcohol has been observed to play a role approximately half of the time in hospital discharges related to cirrhosis, so it is estimated that approximately 50% of cirrhosis cases are alcohol-related.

I work in the Veterans Affairs (VA) health care system, where the incidence, or rate of new cases, of alcohol-

related liver disease has been starting to trend downward since approximately 2010, and the overall prevalence (ie, the total number of cases per 100,000 in the general population) has essentially been stable. In the VA health care system, alcohol accounts for approximately 30% of cirrhosis cases, and there is another 30% of patients who have both alcoholic liver disease and another liver disease, such as viral hepatitis. Therefore, in the VA health care system, alcohol is a factor in approximately 60% of all cases of cirrhosis. Other data suggest that this is similar in the general US population as well.

G&H What other consequences and complications are associated with alcoholic liver disease?

LB Alcohol abuse is very costly and causes significant morbidity and mortality. All of the health consequences of alcohol, not just those limited to the liver, were estimated to account for 11% of the total US health care cost in 2006. The annual inpatient cost for alcohol-related cirrhosis, not including outpatient treatment, was approximately \$850 million in 2014, according to the National Institute on Alcohol Abuse and Alcoholism. Up to 50% of severe cases of acute alcoholic hepatitis will lead to death, even with medical support.

G&H Are there any ways to counteract these consequences of alcoholic liver disease?

LB Of course, the best way to counteract alcoholic liver disease is prevention. Unfortunately, for US patients who already engage in problematic alcohol use, treatments are

very often limited in terms of access and efficacy. Once cirrhosis or acute alcoholic hepatitis develops, quitting drinking becomes a matter of life and death.

G&H Could you expand on the risk of mortality in these patients?

LB Alcoholic liver disease is the second most common cause of disease in patients who are listed for liver transplant, but listed patients represent a highly selected group, given that patients with active substance use disorders are generally ineligible for transplant listing. In terms of mortality rates, an estimated 18,000 people in the United States died of alcoholic liver disease in 2013, and the death rate is highest in younger and middle-aged individuals. However, these numbers are likely underestimates because alcohol is a cofactor in other liver diseases and therefore may not be accurately counted as a cause of death. For example, in people who have viral hepatitis and alcoholic liver disease, alcohol is often not listed as one of the main causes of death.

G&H Should patients with alcoholic liver disease be screened for other conditions?

LB The American Association for the Study of Liver Diseases recommends that all patients with cirrhosis, including those with alcoholic cirrhosis, be screened regularly for hepatocellular carcinoma. Patients with alcoholic cirrhosis should also receive routine screening for gastroesophageal varices.

In addition, all individuals who are known or suspected to misuse alcohol should undergo additional screening for mental health and psychosocial concerns. This would include asking about comorbid conditions such as nonalcohol substance use, mental illness, and housing insecurity. Management of these comorbidities is very complex and requires multidisciplinary support from other services, such as primary care, mental health, and social work.

G&H What symptoms are associated with this condition? Are any patients asymptomatic?

LB Presentations of patients with alcoholic liver disease can vary. Alcoholic liver disease is frequently asymptomatic in its early stages, which is why health care providers should be vigilant and should screen patients for alcohol use as part of routine practice.

Patients with acute alcoholic hepatitis are often extremely ill, and the condition can manifest as liver failure. Clinically, the classic presentation for acute alcoholic hepatitis is a patient with a history of alcohol abuse who

presents with a fever, enlarged liver, and jaundice. Often, the patient also has leukocytosis and moderately elevated transaminase levels.

Finally, there is a subset of patients who have alcohol-related cirrhosis. These patients can be asymptomatic in the early stages, but when they develop decompensated liver disease, they become highly symptomatic.

G&H How is alcoholic liver disease usually diagnosed?

LB Usually, alcoholic liver disease can be diagnosed based on patient history and laboratory test results, especially if the patient has examination findings that suggest chronic liver disease. Sometimes, a liver biopsy is performed if the diagnosis is not clear or if there are multiple disease etiologies suspected. Liver biopsy is still the gold standard for diagnosis. However, because liver biopsy is so invasive and carries a risk of complications, clinical practice is moving toward noninvasive methods of ascertaining liver fibrosis in lieu of liver biopsy.

G&H Other than alcohol abuse, are there any risk factors for alcoholic liver disease?

LB With research on this issue starting to enter the literature, we are developing a better understanding of all of the risk factors for alcoholic liver disease beyond just the amount and duration of alcohol intake. For example, alcoholic liver disease appears to be more likely to occur in women, younger people, and those with poor nutritional status. There are also multiple genetic factors that we are only starting to understand related to how the body breaks down ethanol and how it handles inflammation.

There is an emerging new body of research on the relationship between the gut microbiome, the liver, and alcoholic liver disease. It turns out, interestingly, that alcohol disrupts the mucosal barrier of the gut, which leads inflammatory bacterial products called lipopolysaccharides to enter the blood supply. This causes liver inflammation to accelerate and, if the process spirals out of control, it produces the clinical syndrome of alcoholic hepatitis.

G&H How are these patients treated? Is cessation of alcoholic intake sufficient?

LB Once someone develops acute alcoholic hepatitis, a number of interventions have traditionally been used. An exciting recent trial on this subject was STOPAH (Steroids or Pentoxifylline for Alcoholic Hepatitis), which was a randomized trial of 2 commonly used drugs for alcoholic hepatitis, pentoxifylline and prednisolone. The trial found that neither of these drugs has a sustained benefit

on mortality after 28 days, and only prednisolone reduces mortality before 28 days. Thus, the researchers concluded that pentoxifylline should no longer be used for treatment of acute alcoholic hepatitis.

My personal opinion is that after 28 days, survival really depends on the patient quitting drinking. There is no drug that will beat alcohol abstinence in terms of the long-term impact on patient prognosis. Even so, approximately one-third of patients with alcoholic cirrhosis who quit drinking will be dead in 5 years. Thus, even with alcohol cessation, there is still a significant risk of mortality.

Dr Beste has no relevant conflicts of interest to disclose.

Suggested Reading

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