ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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Current Management of Patients With Alcohol-Associated Hepatitis

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G&H How has alcohol use changed since the COVID-19 pandemic?

BL Heavy alcohol use had been declining before the COVID-19 pandemic. The pandemic saw a significant rise in heavy alcohol use, particularly among women and ethnic minorities. Substance use, whether involving alcohol or cigarettes, is known to increase in times of crisis as people try to cope with stress. Alcohol-associated hepatitis and alcohol-associated liver disease in general increased significantly during the COVID-19 pandemic as well.

G&H What are the implications of the new nomenclature for metabolic dysfunction-associated steatotic liver disease with increased alcohol consumption?

BL Metabolic dysfunction-associated steatotic liver disease with increased alcohol consumption (MetALD) is a new term for patients with cardiometabolic risk factors who have high alcohol consumption (140 g/week for women and 210 g/week for men) but lower than the threshold for alcohol-associated liver disease (350 g/week for women and 420 g/week for men). This new nomenclature is important because it acknowledges that separating metabolic dysfunction-associated steatotic liver disease (previously referred to as nonalcoholic fatty liver disease) from alcohol-associated liver disease does not reflect what is seen in the real world; many people both use alcohol and have metabolic risk factors. My colleagues and I have published that the prevalence of MetALD is greater than that of alcohol-associated liver disease based on the new nomenclature definitions. We have also previously published that heavy alcohol use had been declining before the COVID-19 pandemic even though there has been a surge in alcohol-associated liver disease deaths since 2009. Thus, despite declining rates of heavy alcohol use, the rate of metabolic syndrome had been increasing and the interaction of heavy alcohol use with metabolic risk factors causing liver disease had increased.

> We found that recompensation is very rare, occurring in less than 10% of patients at 6 months.

Our hypothesis in putting all of these findings together is that even if rates of heavy alcohol use are declining, if the population is more sensitized to liver disease (meaning they have higher rates of obesity or diabetes and metabolic syndrome), patients are at higher risk for liver disease. The new terminology draws attention to the fact that both alcohol use and metabolic risk factors need to be addressed to treat liver disease.

G&H How can prognosis be best determined in patients with alcohol-associated hepatitis?

BL Many scoring systems have been devised to try to prognosticate short- and longer-term mortality in

patients with alcohol-associated hepatitis. Thus far, it appears that the most accurate and validated tool is the joint-effect model from an international study by Louvet and colleagues that combined both Model for End-Stage Liver Disease (MELD) score and day 7 Lille score. Based on a nomogram of these 2 scores, providers are able to predict 2- and 6-month mortality with high accuracy. The strongest risk factor of long-term mortality is alcohol relapse, so it is important to address alcohol use disorder to achieve favorable long-term outcomes.

G&H Currently, how else should patients with alcohol-associated hepatitis be managed?

BL Alcohol-associated hepatitis is a disease with high mortality, morbidity, and burden but no effective long-term treatments that are approved by the US Food and Drug Administration (FDA), so it also has high unmet need. That being said, corticosteroids and N-acetylcysteine have been shown in meta-analyses to reduce short-term (28-day) mortality, although not long-term mortality. Liver transplant has been demonstrated to be lifesaving, but it is not available to the vast majority of patients with alcohol-associated hepatitis because of organ scarcity.

G&H In terms of corticosteroid initiation, is there an optimal therapeutic window?

BL Patients should first be ruled out for any contraindications, including any active infection. I do not start corticosteroids until, at the earliest, day 3 of hospitalization because I wait 48 hours to rule out infection.

G&H Which patients with alcohol-associated hepatitis are able to recompensate?

BL The idea of recompensation is very interesting. Of patients with alcohol-associated hepatitis who are decompensated either with ascites, variceal bleeding, or hepatic encephalopathy, who will not only survive but also recompensate from their liver disease? Not much data are currently available on this issue, but my colleagues and I have looked at patients in the American Consortium for Early Liver Transplantation for Alcohol-Associated Liver Disease (ACCELERATE) cohort who were declined for early liver transplant. We found that recompensation is very rare, occurring in less than 10% of patients at 6 months. A separate single-center study by Musto and colleagues found that the strongest predictors of recompensation were young age (less than 44 years) and lower MELD score (less than 34). However, more data are needed. Because the event rate has been low, good prediction models for recompensation are not available. This is an important issue, though, to try to predict which patients will recover and do not need a liver transplant.

G&H How should patients with alcohol-associated hepatitis be selected and evaluated for early liver transplant?

BL In general, when I look at a patient with alcohol-associated hepatitis, I consider their candidacy for early liver transplant (ie, with less than 6 months of abstinence) if they meet both clinical criteria and psychosocial criteria. In terms of clinical criteria, I look for a patient who is not likely to recover and does not have enough time to survive to participate in alcohol rehabilitation with a transplant that is not early (as opposed to a transplant traditionally performed following 6 months of alcohol abstinence). For such evaluation, I use the MELD and Lille scores. The psychosocial criteria are very nuanced and constitute an area of very active research. In general, I look for a patient whose alcohol use disorder seems that it would be manageable posttransplant. This is based on a comprehensive psychosocial evaluation typically by an experienced transplant social worker and an addiction specialist. Risk factors that have been found to be important in terms of predicting posttransplant relapse and difficulty in managing alcohol use disorder include failed rehabilitation attempts, very heavy drinking before liver transplant, and young age. I also look at factors such as insight and motivation, as well as history of alcohol-related legal issues. Also considered are protective factors. For example, the degree of social support has been found to be a very strong protective factor and is always thoroughly assessed during liver transplant evaluation.

G&H Could you discuss recent research on the outcomes associated with liver transplant for alcohol-associated hepatitis?

BL My colleagues and I have published a number of studies trying to inform selection and management of patients undergoing early liver transplant in the ACCELERATE cohort across the United States. Our most recent data show that most patients who undergo careful selection are able to remain abstinent posttransplant or have only what are called slips of alcohol and then are able to regain abstinence and do not cause graft injury. We have found that approximately 70% to 80% of liver transplant recipients fall into this category. We have also found that survival is excellent in that 5-year survival is comparable with what we would consider benchmarks for successful liver transplant in terms of survival.

In addition, we have found that alcohol relapse occurs in a small but sizable population and that it is the

strongest risk factor for posttransplant death. Therefore, areas of focus should be how to identify these patients before liver transplant and what interventions are most effective to prevent and treat alcohol relapse in liver transplant recipients. The goal is to try to optimize both selection and outcomes for patients being considered for early liver transplant.

Long-term management of alcohol use disorder is key to optimizing outcomes after liver transplant.

G&H What is the role of multidisciplinary care in the management of these liver transplant recipients?

BL We are finding that although liver transplant is able to cure liver failure, it does not cure alcohol use disorder. Alcohol use disorder is a disease that is chronic, relapsing, and remitting. Long-term management of alcohol use disorder is key to optimizing outcomes after liver transplant. Integration of addiction resources in this transplant population is important. Centers should maximize the resources they are able to offer for addiction and alcohol use disorder to liver transplant recipients to produce the best outcomes for their patients. This ideally involves having addiction specialists as well as trained substance use specialists experienced in managing both substance use disorders and transplant, in addition to having resources accessible for patients, whether this be group therapy, counseling, cognitive behavioral therapy, and pharmacotherapy to prevent and treat alcohol relapse (eg, acamprosate). Integration of these resources and specialties within the transplant program is where the field is headed, and hopefully improved outcomes will be seen because of these efforts.

G&H What gaps remain regarding alcohol-associated hepatitis?

BL There are still many gaps. The reality is that alcohol-associated hepatitis is such a common disease that hepatologists see it on a weekly, if not daily, basis in the hospital. However, good treatments that are accessible to the majority of patients are not yet available. Liver transplant is lifesaving, but most patients cannot access it. There are still no FDA-approved medications. The main research gaps are treatments that are accessible, inexpensive, and cost-effective and that also improve long-term survival. Knowledge gaps include how to expand and optimize access to transplant and also how to optimize outcomes after transplant.

G&H What stereotypes and misconceptions exist in this area?

BL There are many stereotypes as well as stigma related to alcohol-associated liver disease and alcohol-associated hepatitis. The reality is that heavy drinking is common and, in fact, normalized in society. Many patients with alcohol-associated liver disease might not necessarily meet the criteria for alcohol use disorder. The idea of reducing harmful patterns of drinking is very important.

A common misconception is that alcohol use disorder is a personal choice or behavior, which, again, relates to stigma. There needs to be an understanding that alcohol use disorder is a disease, and there are medical treatments for it. Providers, namely hepatologists, need to become more comfortable with evidence-based treatments for alcohol use disorder to effect change for this population. Alcohol-associated liver disease accounts for more than 50% of cirrhosis-related deaths. To be able to treat the patient community, hepatologists need to become comfortable treating alcohol use.

Disclosures

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Suggested Reading

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