ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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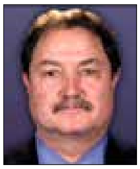
Update on Liver Transplantation in Patients With Alcoholic Hepatitis



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G&H How has alcoholic hepatitis traditionally been treated?

CO Alcoholic hepatitis has traditionally been treated with thiamine, folic acid, and multivitamins and by increasing the patient's nutritional status with energy-dense foods. In addition, a social worker and addiction specialist would speak with the patient to try to help prevent relapse to alcohol. If the patient had acute alcoholic hepatitis and a Discriminant Function score of over 32, he or she was placed on prednisone. The disadvantage of this approach was that, although there was an opportunity for patients to improve, if they did not do so within 30 days, there was a fairly high mortality rate. After patients were discharged from the hospital, classically patients were expected to test negative on outpatient spot alcohol blood tests and maintain 6 months of sobriety to show that they were not going to return to harmful drinking before they could be assessed for a liver transplant. This was known as the 6-month rule, and liver transplantation was considered to be controversial in patients with alcoholic hepatitis and, thus, was not performed often for this indication at first.

However, liver transplantation is now being performed more often for the treatment of alcoholic hepatitis. Alcoholic liver disease, which includes alcoholic hepatitis, is currently one of the leading indications for liver transplantation. Many transplant programs, including the one where I work, have altered their approach to alcoholic hepatitis based upon changes to the transplant criteria that were made by the Ohio Solid Organ Transplant Consortium (OSOTC) several years ago. The OSOTC exception criteria allow patients to be evaluated on a case-by-case basis rather than applying the standard 6-month abstinence rule.

G&H How are patients currently being screened and assessed before undergoing liver transplantation for alcoholic hepatitis?

CO In general, my colleagues and I advise all of our patients to start alcohol abstinence from the time of their first appointment, and this should be reinforced by all staff dealing with patients at all appointments to enact consistent messaging. We administer substance abuse screening and have patients sign a release-of-results form, in which they need to acknowledge that they must abstain from alcohol as well as other substances such as nicotine, narcotics, and amphetamines. The second part of the form strongly discourages consumption of all forms of marijuana. In the past, if a patient tested positive for tetrahydrocannabinol or marijuana, he or she would be removed from the liver transplant waiting list. Given changing state regulations, we just note the positive test for marijuana. Although we try to counsel patients to avoid marijuana in general, if they use it instead of alcohol, at least it keeps them away from alcohol. We screen for substance abuse with and without notification. If patients fail to comply with screening, that is considered to be a positive test and could result in dismissal from the transplant list.

In addition, we perform psychosocial assessment via risk factor scoring systems. The Stanford Integrated Psychosocial Assessment for Transplant (SIPAT) is a scoring system that stratifies individuals into high-, moderate-, or low-risk groups for negative outcomes after transplantation. The OSOTC risk score is similar but shorter. We use both scoring systems together to decide candidacy for a transplant at the selection meeting. The SIPAT is usually scored by the social worker since it is significantly longer to use. I find the OSOTC risk score much easier to use and therefore use it on initial screening in the patient's room.

We also perform toxicology testing using the new phosphatidylethanol (PEth) test for alcohol, which is a blood test that shows whether an individual has consumed a significant amount of alcohol in the preceding 30 days. Previously, spot tests for alcohol were only able to determine whether alcohol was consumed the preceding night. A PEth test is not positive if the patient just had 1 drink last night; the patient has to drink a large amount of alcohol consistently to produce a positive test result.

Since the 6-month rule has not been shown to be statistically significant and does not correlate with whether or not a patient relapses, my colleagues and I look at the patient's history of drinking and drug use within 1 year of evaluation, inpatient charts, toxicology results, and the amount of alcohol the patient drinks. Then we recommend a 12-week course for outpatients with psychotherapy and an adherence letter from the provider or a recovery group. Inpatients who are too sick to actively participate in a 12-week recovery program can be examined for a series of factors to determine whether they are at low risk of relapse. If eligible, these patients can be transplanted on that admission. Factors for low risk of relapse are more than 1 month of confirmed abstinence, a signed contract and commitment to begin a rehabilitation program if the patient's health permits, and continued active participation in a posttransplant program.

G&H What were the main recommendations from the recent Dallas Consensus?

CO The Dallas Consensus Conference on Liver Transplantation and Alcohol Associated Hepatitis was recently convened to establish criteria for determining liver transplant candidacy for patients with alcoholic hepatitis, and a meeting report was published in *Liver Transplantation*. If a patient is being transplanted for acute alcoholic hepatitis, he or she still has to fulfill the criteria for transplantation. The patient cannot have any other uncontrolled morbidities. Most transplant facilities calculate the patient's Discriminant Function score, Model for End-Stage Liver Disease (MELD) score, or Lille score, and if the score is in a certain range, the patient is treated with prednisone or prednisolone. Treatment response is an improvement in the Lille score, the MELD score, or the Discriminant Function score or a decrease in the level of bilirubin 7 days after starting therapy, which is usually prednisone 40 or 60 mg per day. If an improvement in the scoring system occurs in the first week, treatment is continued for 4 weeks. If there is no decrease, the patient is considered to be a prednisone nonresponder, which triggers the process of examining the patient's candidacy for liver transplantation. Prednisone nonresponders have a relatively high 30-day mortality.

When examining candidacy for transplantation, it is important to look for patients with a low risk of relapse, in particular patients who accept their diagnosis and are willing to follow up with an addiction specialist. The main factors that predict relapse are starting to drink very early in life and drinking consistently, as well as having more than 10 drinks per day at the time of transplant consideration. Having multiple failed rehabilitation program attempts and having a history of legal problems or of driving under the influence can prevent patients from being transplanted on their first admission. To be a candidate for liver transplantation, the patient has to clearly show that he or she understands his or her diagnosis and is committed to doing whatever it takes to stay clear of repeat alcohol abuse. A history of untreated mental illness can also prevent candidacy. Candidates should have a history of adherence to treatment. If a patient is noncompliant to all follow-up recommendations from a doctor, the patient will not be compliant after transplantation. Social support is also important to help keep the patient abstinent and to bring the patient back to the hospital after transplantation for meetings and medical follow-up.

However, if a patient's MELD score is over 22, the OSOTC model is usually followed. If the patient is not abstinent for 6 months or is too ill to actively participate in a recovery program, he or she is stratified by the risk of recidivism. A low risk of recidivism is associated with 1 to 3 substance relapse factors, a medium risk with 4 to 5 factors, and a high risk with 6 or more factors. Low-risk patients can be transplanted on that admission, medium-risk patients need 3 months of outpatient-confirmed abstinence, and high-risk patients are followed until there is no longer a concern for relapse; the 6-month rule does not apply.

G&H Currently, approximately how often do patients experience alcohol relapse following liver transplantation?

CO This question can be broken up into 2 parts. The first is how often patients return to drinking alcohol, and the second is how often this drinking is an active problem.

In most programs, approximately 20% of patients return to drinking alcohol after the first year. However, the rate of patients whose drinking interferes with their life again is lower; for example, at my institution, the rate is likely approximately 6% to 8%.

G&H How effective are alcohol abstinence programs in patients with alcoholic hepatitis?

CO If patients want to get better, these programs are fairly effective. If there was an acute life event that triggered drinking too much alcohol and the patient has a low or even medium risk of recidivism, these programs are very effective. However, the programs are not very effective for patients who have a high risk of recidivism and have frequent episodes of relapse. Patients in the high-risk group tend not to undergo transplantation at any time, either immediately or later on.

G&H How are the current liver transplant outcomes for patients with alcoholic hepatitis?

CO At my institution, patients who were transplanted for alcoholic hepatitis last year had a 94% chance of surviving at 1 year, which was a little better than the rate overall in the United States according to the United Network for Organ Sharing (93%). The expected probability of return to any alcohol at my institution is approximately 20%, whereas overall in the United States, it is 25% at 1 year, approximately 30% at 2 years, and 35% at 3 years. However, of the patients who return to alcohol at 1 year, only approximately one-third are problem drinkers (approximately 8%). Problem drinkers make up approximately 6% to 8% at my institution.

G&H Is liver transplantation still considered to be somewhat controversial in patients with alcoholic hepatitis?

CO As long as transplant centers follow guidelines and have systems in place with social workers and addiction specialists to prevent patients from returning to active drinking again, I do not think that liver transplantation is controversial anymore for alcoholic hepatitis. If patients with alcoholic hepatitis acknowledge their drinking problem, are willing to do what it takes to avoid relapse, and meet the criteria for transplantation, they should be able to undergo the procedure. However, the public does not tolerate patients who receive a transplant just so they can return to active drinking. Alcoholic abuse affects not just patients themselves and their families, but other people around them (eg, if the patients perform poorly at work or injure or kill other people in an automobile accident). Just because a liver is replaced does not mean that the underlying problem has been solved. Therefore, it is important that transplant centers have very clearly structured programs and that it is possible to look at those programs and make sure that the results are what is expected.

G&H What are the next steps in research in this area?

CO It would be helpful to have a medication that can decrease the desire to return to drinking and/or prevent the patient from drinking. Although there has been a series of medications tested for these purposes, they do not actually prevent drinking. Some patients decrease the amount of alcohol they drink, but the medications do not entirely stop drinking.

Not all alcoholic abuse patients are alike, so it would also be useful to have a marker that could identify the gene associated with the need to drink alcohol. Having such a genetic marker would help doctors determine which patients are more likely to relapse.

Dr O'Brien has no relevant conflicts of interest to disclose.

Suggested Reading

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