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Treatment Updates in Alcoholic Hepatitis & Acute Kidney Injury in Cirrhosis

Dr. Buch:
Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch. Joining us to provide an update on alcoholic hepatitis and acute kidney injury in cirrhosis is Dr. Paul Kwo, Professor of Medicine and Director of Hepatology at Stanford University.

Dr. Kwo, welcome to the program.

Dr. Kwo:
Dr. Buch, thanks so much for inviting me to be here.

Dr. Buch:
So, Dr. Kwo, let's dive right in. How do you assess the severity of alcoholic hepatitis?

Dr. Kwo:
When approaching someone with clinical diagnosis of alcoholic hepatitis, the most important thing is to remember that this is still for us a clinical diagnosis, so you're evaluating somebody who has a history of alcohol use disorder with excess consumption of alcohol, typically an onset of jaundice within the last couple of months with elevated liver tests, and typically the AST and the ALT are both elevated about 1.5 times the upper limit of normal, rarely above 200, and if any of these values, the transaminases, are over 400, you need to be thinking of another diagnosis. And it's accompanied with elevated bilirubin, typically above 3 mg/dL.

And so, when trying to assess the severity, the most common assessment has been with what we call the Maddrey's Discriminant Function Score, and this utilizes 2 of our biochemical tests, the prothrombin time and the bilirubin, and we consider severe alcoholic hepatitis in those who have a Maddrey's score of above the score of 32. And these are the individuals who can benefit from a short course of corticosteroid use to try and reduce morbidity and mortality.

There are other ways to assess the severity as well; there's a Glasgow Alcoholic Hepatitis Score that adds the creatinine, the age, and the white count, and if you add these to a discriminant function, it probably does lead to better selection of patients who are going to benefit from alcoholic hepatitis. We utilize the score for severe alcoholic hepatitis that allows us to stratify for transplant, and that's called the MELD score, and in general, those who are above 21 have a poorer prognosis. And we have actually modified it. We now use a MELD sodium score, which if that one is above 28 also is associated with a poor prognosis.

The good news is we do have tools that are quite well-validated to help us stratify those who are going to have the most deleterious outcomes.

Dr. Buch:
And what are the steps in treating alcoholic hepatitis?

Dr. Kwo:

So treatment of alcoholic hepatitis is actually evolving. The de facto standard of care that we have utilized for years was the prednisone or prednisolone for 28 days, and you can utilize the Maddrey's Discriminant Function Score above the score of 32, and these individuals will benefit from a short-term course of corticosteroids with reduced 90-day mortality. Now corticosteroids in somebody who has a systemic inflammatory response has to be used with great care because alcoholic hepatitis, particularly severe alcoholic hepatitis, is a severely immunocompromised state, and these individuals are prone to infections, GI bleeding, and other complications, but with the improvement in care that we now give those with alcoholic hepatitis, we're able to give corticosteroid therapy now more broadly than we have been historically.

We certainly do have other options and you should not exclude these as well. Tn addition to prednisone, you should address the nutritional state. And then other different therapies are introduced. Some people have used N-acetylcysteine. There was a TNF scavenger pentoxifylline that has been used and of course good nutrition.

The final thing about treatment is that we do have reasonable futility rules now with the so-called Lille score that we can use that allows us to cease steroids early on if they're not going to respond to steroids, and you can calculate this with the creatinine-age bilirubin and the liver test or albumin and the other liver tests, and if the score is greater than 0.45, these are individuals who will not respond to steroids, and you can safely get the patients who have alcoholic hepatitis off. That's very important because you don't want to be treating somebody with a corticosteroid who may have high risk for infection and other complications.

Dr. Buch:
So let's switch gears to another topic which I think is extremely important for our audience members. Can you share the new definitions for acute kidney injury in patients with cirrhosis?

Dr. Kwo:
So what you're referring to are the hepatorenal syndrome and subtypes. And we used to define hepatorenal syndrome as type 1 or type 2 where type 1 was this rapidly progressive renal failure with a creatinine being greater than 2.5 or the creatinine clearance being less than 20 mL per minute, and these individuals have a very high mortality rate, with type 2 hepatorenal syndrome being a more slowly progressive disease with an elevated creatinine and was typically associated with refractory ascites. Those have historically been the definitions that we have applied to our patients, but we now have adapted the KDIGO criteria, and we have adopted a new definition. Rather than hepatorenal syndrome, we talk about acute kidney injury, or AKI, and we stage this, and so the definition of acute kidney injury in cirrhosis now is an increase in serum creatinine of greater than 0.3 mg/dL within 48 hours or an increase in serum that is up over 50% from the baseline of presumed within the prior 7 days. And the reason we do this now is because this empiric cutoff of greater than 1.5 for type 2 that was used historically or greater than 2.5 for type 1 was actually interfering with more rapid intervention for these individuals with acute kidney injury.

There are also now definitions for the old type 2 hepatorenal syndrome, which now include HRS non-AKI of which they have subtypes HRS-AKD and HRS-CKD. That means hepatorenal syndrome acute kidney disease, which means less than 3 months duration of an estimated GFR less than 60 mL per minute, and the HRS-CKD is, again, the same estimated GFR less than 60 mL per minute but greater than 3 months. And, of course, both of these are in the absence of other structural causes.

It will take time for everybody to be comfortable utilizing these in our practices, but again, with greater and broader adaptation of these definitions, it's also going to allow us to identify and more rapidly intervene to correct the injuries that we see in our patients with end-stage liver disease.

Dr. Buch:
For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Paul Kwo about alcoholic hepatitis and acute kidney injury in cirrhosis.

So people have been waiting for this answer. Dr. Kwo, what is the stepwise approach to treating acute kidney injury in cirrhotic patients?

Dr. Kwo:
So, the history is very important, and you want to find out if there has been an exposure to nephrotoxic drugs. You want to look

rigorously at their recent diuretic use and whether or not there's the potential for volume depletion, which if present, is something that can be addressed rather rapidly with albumin infusion, You also want to look and see what the underlying liver disease is because with any AKI in the setting of cirrhosis, that usually improves if you can improve liver function as well. You look for the common precipitating factors, and you also assess immediately for infection. So somebody who has an AKI could have an infection, such as spontaneous bacterial peritonitis, bacteremia, or urinary tract infection.

In addition to pan culturing these individuals, you should also then withdraw your diuretics. And many of our cirrhotic patients are on nonselective beta blockers, and then, of course, removal of harmful drugs, such as nonsteroidals, should be initiated or undertaken. Once those are removed, then you should see if it resolved, and if it does not, then you can start giving albumin. And hopefully, these individuals who have had their deleterious medicines withdrawn and infection treated and volume expansion with albumin, hopefully, they are going to respond. If they don't and there's no other competing etiology, such as an acute tubular necrosis or a post-renal obstruction, then these are individuals who would then meet the criteria for hepatorenal syndrome and c you should initiate vasoconstrictors and albumin.

Dr. Buch:
Thank you so much. This was certainly a great discussion on the consequences of alcohol-induced liver injury. And I want to thank Dr. Paul Kwo for sharing his insights. Dr. Kwo, it was a pleasure having you on the program today.

Dr. Kwo:
I appreciate the opportunity to come on and hope to hear from you again soon. Thank you.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GIInsights where you can Be Part of the Knowledge. Thanks for listening, and see you next time.