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Hepatic Encephalopathy: Unmet Therapeutic Needs

Announcer:

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Dr. Flamm:

This is CE on ReachMD, and I'm Dr. Steven Flamm from Rush University in Chicago. And today I'm with Dr. Robert Brown from Weill Cornell in New York.

Bob, what are the current unmet needs for treatment of hepatic encephalopathy?

Dr. Brown:

Steve, that's a great question, because we definitely have more than one unmet need in the treatment of hepatic encephalopathy. We recognize that hepatic encephalopathy is one of the most serious complications of cirrhosis and portal hypertension. It's associated with increased mortality. It's an independent indication for the need for transplantation. And not only does it affect our patients' mortality, it has a severe impact on their quality of life. And as we've highlighted in earlier episodes, even minimal HE affects their quality of life.

So the first thing that we would love to have would be some type of primary prophylaxis that would delay the onset of the first HE episode. The way we have beta-blockers to prevent bleeding from esophageal varices, it would be great if someone who is identified as having high risk for developing HE, that we could put them on a therapy that would delay the onset. It would certainly improve their quality of life and probably would have an impact on their survival.

And then the second real unmet medical need is a good treatment for minimal HE. So for many patients who have minimal HE, we know it impacts their quality of life. It impacts their likelihood of having auto accidents and falls. And so if we had an effective, well-tolerated therapy that would improve minimal HE, prevent minimal HE from going to overt HE, that would be great.

We don't know whether lactulose works in this situation, and it likely has too many side effects for patients to take it. Rifaximin would be a great potential treatment for minimal HE, but we lack the data that we need to have it be an FDA-approved option.

And then finally, for many patients, they don't tolerate lactulose as well. And still, even with lactulose plus rifaximin, we have patients who develop breakthrough. So we need more treatments so that 100% of our patients with either minimal HE can get a treatment that will prevent progression, and all of our patients with HE can get effective, well-tolerated therapy that will minimize their risk of having hospitalizations and overt episodes.

What do you think?

Dr. Flamm:

You're absolutely right, Bob. There are a lot of unmet medical needs in this field. When rifaximin came on the market 15 years ago or so, it really was an advance, because it noticeably decreased the risk of having recurrence of encephalopathy. But you are right; lactulose is very poorly tolerated.

One quick question. Because people tolerate lactulose poorly and many think it works as a so-called laxative, what are the data on using other laxatives in its place?

Dr. Brown:

Well, lactulose has a lot of effects. One, it changes the microbiome. It acidifies the colon, and we don't know if the laxative effect is the major issue. We know in patients with dense HE, that simple purgatives, like using polyethylene glycol, will improve HE. But as a chronic therapy, we're not as certain as to what the effect is. And unfortunately, the effects of lactulose are linked to the side effects, because they're linked to the production of methane and gas that leads to gastric distention. So what we really need is an alternative to lactulose that's better tolerated.

Dr. Flamm:

Yes, we do. So every step toward addressing unmet medical needs counts, Bob, and this was one of them. Thanks so much, and we'll see you next time.

Announcer:

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