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Treating Patients With T2D and MASLD: Is the Tide Changing?

Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Alkhouri:

This is CME on ReachMD, and I'm Dr. Naim Alkhouri, the Chief Medical Officer and the Director of the Steatotic Liver Program at Arizona Liver Health in Phoenix, Arizona.

Obesity is associated with an increased risk of major adverse cardiac events, and we know that patients with MASLD and MASH die from cardiovascular disease, actually more than liver disease. So decreasing MACE and cardiovascular disease burden is a high priority in patients with MASLD and MASH. The approach to managing obesity include a lifestyle intervention, unfortunately, with limited success. Typically, patients lose 3 to 5% of their total body weight. We have antiobesity medications, and we have now second generation medications that can lead to weight loss in the realm of 15 to 20% total body weight. And then we also have bariatric surgery and endobariatric procedures, where patients can lose up to 30% of their total body weight with the Roux-en-Y gastric bypass, lifestyle interventions and older antiobesity drugs as I mentioned they have limited success with managing obesity and no clear benefit in reducing cardiovascular, events.

Bariatric surgery, on the other hand, has been shown to lead to significant weight reduction, but more importantly, to lower cardiometabolic risk and reduce risk of MASH. So this is very important to keep in mind.

Now, the newer antiobesity drugs, are very effective to induce weight loss, but now we have a recent data that even in nondiabetic patients there's significant reduction in cardiovascular disease burden. The best study we have is called the SELECT trial, where a very large cohort of patients was treated with semaglutide 2.4 mg weekly compared to placebo, and showed very clearly that semaglutide was superior to placebo and reducing the incidence of death from cardiovascular causes and reducing MIs and nonfatal stroke.

We have a few medications to choose from when it comes to second generation antiobesity medications. Semaglutide is a GLP-1 agonist. We have a dual agonist, called tirzepatide for GLP-1 and GIP. Both of these medications are FDA approved for the management of obesity and type 2 diabetes, and they're undergoing clinical trials for MASLD and MASH. We also have some promising new dual agonists for GLP-1 and glucagons such as survodutide, efinopegdutide, and pemvidutide. And we also have triple agonists for GLP-1, GIP, and glucagon such as retatrutide. So a very promising field, and obesity pipeline is deep, and we hope to have more options for our patients.

Now in terms of treating obesity, specifically in the context of patients with MASLD and MASH we have data showing that you know GLP-1 receptor agonists not only target the liver disease, but they target the underlying metabolic and inflammatory pathways in MASH. And we have data showing that in patients with MASLD and MASH, GLP-1 receptor agonists can help improve glycemic control, biochemical, markers of liver injuries such as ALT and AST also liver histology in terms of achieving MASH resolution and importantly

for our patients, also improving health-related quality of life and what we call patient-reported outcomes. The only caveat in the phase 2b trial with semaglutide, that there was no improvement in liver fibrosis on histology, although there was less progression to more advanced disease.

So the current recommendations for managing obesity in patients with MASLD and MASH is to be aggressive with antiobesity medications and use the newer drug especially semaglutide at 2.4 mg per week. You can also consider using tirzepatide, for the obesity indication. And by doing this, you're going to tackle the metabolic causes of MASLD and MASH, and hopefully lead to improvement in disease severity. However, more longitudinal data are needed to see if there will be effect on fibrosis.

So my takeaway message is that as providers that take care of patients with MASLD and MASH, we need to be very familiar with all the tools we have to manage obesity, especially antiobesity medications. These medications can be prescribed by gastroenterologists and hepatologists in addition to PCPs and endocrinologists.

Announcer:

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