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Key Therapeutic Insights on Semaglutide in Adolescent Obesity

Dr. Buse:

For adults with obesity, once-daily semaglutide may be an effective treatment option. But can the same be said for our adolescent patients?

Welcome to *Diabetes Discourse* on ReachMD. I'm Dr. John Buse. And joining us to share clinical data on semaglutide for the treatment of adolescents with obesity is Dr. Silva Arslanian. Dr. Arslanian is a professor of Pediatrics and Clinical and Translational Science. She's the Director of the Pediatric Clinical and Translational Research Center and the Scientific Director at the Center for Pediatric Research in Obesity and Metabolism at the University of Pittsburgh.

Dr. Arslanian, thanks so much for speaking with me today.

Dr. Arslanian:

Thank you for inviting me, Dr. Buse. It's a pleasure to participate in this podcast.

Dr. Buse:

Obesity in adolescents has risen rapidly over the last 50 years. With that in mind, Silva, how have we managed pediatric obesity in the past, and how successful have we been?

Dr. Arslanian:

So, typically, when we didn't have anti-obesity medications in adolescents, we used to focus on family-centered cognitive behavior and lifestyle intervention with recommendations for healthy eating habits. What do I mean by healthy eating habits? Portion size control is critical. We used to recommend low-fat, low-sugar foods, avoid calorically dense, nutritionally empty foods, such as potato chips, nachos and sweet treats, avoid sweetened beverages, avoid fast food because they are calorically very dense, increase fresh vegetables and fruit intake and high-fiber food, avoid frequent snacking. So this is what we considered and we still consider healthy nutritional choices, of course, in addition to increasing physical activity. It doesn't mean go to the gym and sweat and get short of breath, but increase your daily physical activity. Instead of taking the elevator, take the stairs. Instead of parking close to the entrance to the mall, park far away and walk a little bit. However, it is very difficult to do all of this because we live in an obesogenic environment.

Dr. Buse:

Well, that's a perfect segue way. Let's dive into some of your research. Can you give us background on your study recently published in *The New England Journal* on once-weekly semaglutide in adolescents with obesity?

Dr. Arslanian:

Sure. So this was a multinational study which included 37 participating centers. It was a double-blind, parallel, randomized study, meaning that, you know, none of the participants, the investigators, nobody had control over what the participant ends up receiving. It included adolescents 12 to less than 18 years of age with a BMI equal or above the 95th percentile, which is consistent with the CDC definition of adolescent obesity for sex and age, or someone who has overweight BMI in the 85th percentile or higher with an obesity-associated complication. There was only one person with that in the whole study. And then the participants, 201 of them, were randomized to either receive semaglutide with an escalating dose up to 2.4 mg weekly subcutaneously, or placebo for 68 weeks together with lifestyle intervention. And the randomization was 2:1, meaning more participants were assigned to semaglutide versus half of them to placebo. And what the study showed was that at 68 weeks, there was an initial run-in period for 12 weeks where the participants had to do lifestyle intervention. If at the end of that period their BMI was still within the acceptable obese or overweight range, then they were randomized. And at 68 weeks, what we noticed that participants who were adolescents who were randomized to

semaglutide, their BMI decreased by 16.1 percent, whereby the ones who were randomized to placebo, their BMI increased by 0.6 percent. This is almost similar to undergoing bariatric or metabolic surgery. In addition, 73 percent of adolescents who received semaglutide achieved 5 or more percent weight loss versus 18 percent of the placebo. So, many more adolescents achieved more than 5 percent weight loss. And if you want to extend it a little bit, 37 percent of semaglutide recipients had 20 percent or more weight loss versus 3 percent in the placebo. So, if you want to translate this to somebody who is 5'5" tall and weighs 240 pounds, the average reduction in BMI was equivalent to shedding around 40 pounds. So, not only BMI and weight improved tremendously, but cardiometabolic risk factors improved too. What do I mean by cardiometabolic risk factors? Those adolescents receiving semaglutide, their waist circumference decreased, their glycohemoglobin decreased, their lipids decreased except for the high-density lipoprotein cholesterol, and their ALT, which is a liver enzyme, improved. And I think this is the first time any weight loss medication in adolescents that we see improvement in cardiometabolic risk factors.

Dr. Buse:

That's amazing. For those just tuning in, you're listening to *Diabetes Discourse* on ReachMD. I'm Dr. John Buse, and today I'm speaking with Dr. Silva Arslanian about the efficacy of once-weekly semaglutide in adolescents with obesity.

So Silva, diving deeper into your findings, can you tell us about the safety and tolerability of semaglutide in adolescents with obesity? You know, my view of it was it was really pretty remarkable.

Dr. Arslanian:

You are right, John. The most frequent side effects were GI side effects. Around 62 percent of semaglutide recipients had the GI side effects versus 42 percent. And most of the GI side effects were nausea, vomiting, abdominal pain. And when we looked at serious adverse events, they were similar in the 2 groups, 11 percent and 9 percent, so nothing important. I think it's very important to mention that there were no episodes of pancreatitis because with semaglutide being a GLP-1 receptor agonist, people worry about pancreatitis, or participants who have had history of pancreatitis should not be given those medications. So there were no episodes of pancreatitis, but there were five participants in the semaglutide group which adds up to four percent who had cholelithiasis. Again, we know that obesity is associated with gallbladder disease, so whether it's the obesity association of cholelithiasis or semaglutide remains to be teased out.

Dr. Buse:

Absolutely. You know, to me, the most striking thing is there really wasn't a difference in the discontinuation rate between semaglutide and placebo related to adverse events. It was 5 percent versus 4 percent. You know, in the adult trials, particularly in diabetes, there are more withdrawals, so that really suggested, you know, these kids were all in on taking this medication I guess because they were seeing the benefits.

Dr. Arslanian:

You're absolutely right, John, because 90 percent of those adolescents completed the trial, and that's amazing in any patient-oriented clinical trial.

Dr. Buse:

Do you think this study is going to change the approach to care for adolescent patients with obesity from what you described at the beginning of this podcast?

Dr. Arslanian:

Well, you know, I think we have to stress here that obesity, or an individual having excess weight or having the burden of obesity, is not a matter of looks or appearance, it's a matter of health. Once people start thinking about obesity, whether in adults or pediatrics, as a health issue, then I think slowly the mindset will change into using anti-obesity medications, but it's going to take a while. And I say this partly from a personal experience because when I offer to my teenage patients that you do have an option of daily injections for liraglutide, which was approved in 2019, or c now we can say that you have the option of weekly because semaglutide was approved by the FDA December 23, some of my patients declined it. They say, "No, I will continue trying lifestyle change," even though they have been with me for a year or more and it hasn't worked. So I think we have to be patient and work together with the patients and their families until they are convinced that this is something that will help them and will improve the situation.

Dr. Buse:

Wonderful. As we finish up our discussion for today, any final thoughts from you, Silva?

Dr. Arslanian:

I said, John, several years ago I used to say we need some pharmacotherapy for adolescent obesity or youth obesity because lifestyle change is not working. Now, I'm sure you've seen this in adults. These anti-obesity medications, once they are started, because in this

trial at 68 weeks, the study medications were stopped, and participants continued without any semaglutide or placebo for another seven weeks. There is weight rebound. So now my dream is, and I know it will come true several years from now, pharmaceutical companies will find a way to minimize the weight rebound. Because a patient may decide to take a break from daily injections or weekly injections for financial reasons, insurance reasons, whatsoever, so I'm wondering, and maybe I'm being futuristic, that the day will come that it will be like flu shots. You take a break for three months, then you get a booster for a month or something like that. But I know within my heart that there will be a solution for the weight rebound.

Dr. Buse:

Well, thank you. With those thoughts in mind, I'd like to really thank my guest, Dr. Silva Arslanian, for sharing key data on semaglutide in adolescents with obesity.

Silva, it was a pleasure speaking with you today.

Dr. Arslanian:

Thank you.

Dr. Buse:

For ReachMD, I'm Dr. John Buse. To access this episode and others from our series, visit ReachMD.com/DiabetesDiscourse where you can be Part of the Knowledge. Thanks for listening.