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Discussing a T2D Medication That Could Reduce Insulin Needs in T1D

Dr. Cheeley:
Semaglutide belongs to a class of medications known as GLP-1 receptor agonists and have been approved for type 2 diabetes and obesity. However, new research suggests that semaglutide could also benefit patients with type 1 diabetes.

Welcome to *Diabetes Discourse* on ReachMD. I'm Dr. Mary Katherine Cheeley, and joining us for a discussion on type 1 diabetes and obesity is Dr. David Selzer. Dr. Selzer is a Clinical Instructor of Medicine at NYU Grossman School of Medicine and leads the medical weight loss program at NYU Langone Medical Associates in the Florida division.

Dr. Selzer, thanks for speaking with me today.

Dr. Selzer:
Thank you for having me on. It's an honor and a privilege.

Dr. Cheeley:
All right, let's jump in because I am so excited about this topic. To start us off, what do we currently know about obesity rates among patients with type 1 diabetes?

Dr. Selzer:
So type 2 diabetes, it's dramatically high, meaning most of the patients who develop type 2 diabetes, not all, initially develop a sense of insulin resistance, which is correlated with obesity, so the more obese a person is the higher their insulin needs are. Then over time, as you're getting a receptor hit over and over again, which is the insulin, the insulin becomes resistant. And as you develop more insulin resistance because you have more and more of it, you need more and more of it, so all of a sudden, it doesn't go as well as you would like, and therefore, people become insulin-deficient, and they need more insulin, and they need more treatment. Type 1 diabetes is a totally different perspective. Type 1 diabetes is an autoimmune disease, and when there is that autoimmune disease process, all of a sudden, the pancreas stops working because there's antibodies against the pancreas, and we can measure that. We look at what we call GAD65 to get an idea of how aggressive the person's type 1 diabetes is.

So that is amazing, but that's also theoretical, meaning not every type 1 diabetic does not have any level of insulin reserve in their pancreatic function. So what happens is that even in the classical picture of the type 1 diabetes—someone develops a type 1 diabetes—they go into what we call ketoacidosis. They get very sick very quickly. All of a sudden, they have no level of insulin administration, and they go into what we call ketoacidosis, and they have multiple problems. The reality of the matter is there's some level of gray area there, and we see that there's some level of gray area, and as we can treat and be more aggressive in that gray area, we can help the patients.

Dr. Cheeley:
So for patients who have type 1 diabetes who are obese, what are the risks for those patients?

Dr. Selzer:
I mean, they're sort of having a double whammy in a sense, meaning they're going to develop insulin resistance to some extent, and their body is not able to produce any level of insulin, so they need higher and higher levels of insulin. With that noted, our job as physicians is to treat them and try to find that right method. There have been more and more pumps that come out that are getting smarter and smarter, especially with artificial intelligence. It used to be that you could give a pump, but the pump wouldn't talk to the glucometer readers. We're doing a better job of having the Dexcoms and FreeStyle Libres connect with our insulin pumps in order so the two parties connect, and we know how much insulin to give based on the amount of glucoses in the body.

Dr. Cheeley:
So in the patients that you see in your medical weight loss program, of those that have diabetes, what do you think is the recipe for success in reducing obesity in those patients?

Dr. Selzer:
I'm a big member of the Obesity Medicine Association, and I firmly believe in what they have to say. We should look at four different approaches to help patients, and medical therapy. That's number one. Number two is nutrition therapy, number three is physical therapy, and number four is emotional therapy.

So first off, we're talking about different medications, so either we're talking about the GLP-1's, which is our glucagon-like peptide-1 medications, and also, we can just throw in our dual insulinotropic polypeptide medications. Those are the tirzepatides of the world. Those can help people with weight loss. We shouldn't forget our SGLT2's, like our Jardiance and our Farxigas, and also, old-fashioned metformin does help people lose weight. And when you use that as an adjunct to your GLP or your dual GLP/GIP medications, those can help the patient synergistically with weight loss. So that's your number one approach.

Then in our office, we have a nutritionist, and she helps people come up with specific nutrition plans for their lifestyle. She also helps with patients who have chronic kidney disease, and that meshes. We have a social worker, and she helps people with the emotional aspects of overeating. It's more than that, meaning a lot of our patients come from food scarcity—or even generations of that has been linked into their minds that there's just less food available—and now that their food is there, they have to grab at it, and it takes an enormous amount of teaching that you don't have to go that route. It's very hard for people to change how they grew up and how they were as time went on, so I think that's a very important part.

And then we have two amazing physical therapists. If you tell a 60-, 70-, 80-year-old patient, "Let me tell you what you have to do, you have to exercise more." They're like, "Do you know how much pain and discomfort I'm in? Doc, let me tell you." So what I say to them is "Okay, we're going to have you work with a physical therapist. We're going to come up with a plan." So we try to do like a full-pronged approach in order to help the people.

Dr. Cheeley:
I love that. I love as a pharmacist, utilizing one med to hit multiple disease states, the disease state of obesity, as well as the disease state of diabetes that in this instance these patients have. On that backbone of nutrition therapy, I think exercise, like you said, is so vital to these patients because they need to be moving more. I think there's still so much that we're learning in obesity medicine about the emotional and psychological aspect of how we treat these patients.

For those of you just tuning in, you're listening to *Diabetes Discourse* on ReachMD. I'm Dr. Mary Katherine Cheeley, and I'm speaking with Dr. David Selzer about obesity in patients who also have type 1 diabetes.

So let's turn our attention back specifically to semaglutide. Can you give us just some background on this med? And then what is it intended to be used for in the obesity space?

Dr. Selzer:
So semaglutide is one of many glucagon-like peptide receptor agonists, and they are medications that help lower the amount of glucose in the body, but most importantly is that they slow the removal of food for patients. There is some neurological aspect where it decreases the desire also, but at its core, it chemically constricts the stomach and decreases appetite, so in a lot of ways, we are treating patients by cutting their stomach and making them less hungry.

There's a study that came out from University of Buffalo that happened in early September that shows that patients who were treated with semaglutide right after they had an episode of ketoacidosis. The first step that we start seeing type 1 diabetes did significantly well, and they were able to get off their insulin. It was a retrospective study that looked at patients from 2020 through 2022. There were 10 patients between the ages of 21 and 39 years who had initiated the semaglutide treatment within three months after their diagnosis of type 1 diabetes. At the time, four of the 10 had presented initially with diabetic ketoacidosis. The others had just classical polyuria, which means that they urinated often; polydipsia, they were drinking a lot, and weight loss. Nine of them had the classical GAD, glutamic acid decarboxylase, and one had actually a slightly different autoantibody. It was against islet antigens. At the time their A1c was 11.7, which is extremely high. Our target goes around 6.5 to seven, depending on what you read, with very low fasting C-peptide levels, which means that they had very low levels of their own insulin.

Semaglutide, which is the molecule in Ozempic, was started actually at weekly doses of .125 milligrams, which is actually half of what we start a typical patient on. And as they sort of titrated them up, their prandial insulin levels were adjusted down, meaning the amount of insulin that they needed were going down, and the semaglutide dose was increased to 0.5. All these patients, eventually, their hemoglobin A1c fell to 5.9, and their fasting C-peptide levels went up, so they got their insulin levels back. They got their A1c's under control.

And I just want to have our listeners take a moment and realize how low of a dose of semaglutide we actually were giving them. When we give patients Wegovy, we do a treatment dose of up to 2.4 milligrams. The 0.5 milligram dose that these patients did well on in early type 1 diabetes only went up 0.5 milligrams, so if they were even more aggressive in the treatment, who knows what it could be. And I think it's such an important aspect of understanding that number one the differences between type 1 and type 2 diabetes, and also realize that we're just quote unquote "scratching the surface" of what these molecules can do for our diabetic patients and how they can help us in the future.

Dr. Cheeley:
In your patients that have type 1 diabetes that you're using semaglutide in, do you preemptively or overtime decrease their prandial insulin like you saw in the study?

Dr. Selzer:
Of course. Our goal is get these patients off insulin. I always tell patients that the worst medication they could be on is insulin because it leads to a cycle of weight gain because people don't really clearly grasp this concept, so I think we should take a step back and speak about it.

When we say that somebody's glucose is very high, what we're really saying is that they're starving because they have a lot of glucose inside their blood, but it's not inside their cells, so they're not talking to each other, the different parts of the body; so even though you got tons of sugar cooking up, which is why you get tons of infection when your A1c is not controlled, they're not actually using it.

So in this scenario what we want to do is we want to control the A1c, but on the other hand, when you give insulin and you lower the patient's glucose, all of a sudden they become hypoglycemic. Their glucose is low. So what do they do? They eat. Then what happens? Their sugar goes up. And do you know what they do? They need more insulin, and then they eat, and they go through the cycle. It may not be over four hours. It may be over a couple weeks. But all of a sudden, that leads to weight gain and all the difficulties that happen. So I try to push my patients with all my might "Get off the insulin." "Get off the insulin." "Okay, you don't need it." "Unless you are a definitive type 1, try your best to stay away from the insulin."

Dr. Cheeley:
This has been an amazing discussion, specifically talking about type 1 diabetes, obesity, and the impact of GLP-1 receptor agonists for this patient population. I would love to thank my guest, Dr. David Selzer, for being here and sharing your insights. It has been a true pleasure.

Dr. Selzer:
It's an honor and a privilege to be on. Thank you so much.

Dr. Cheeley:
For ReachMD, I'm Dr. Mary Katherine Cheeley. To access this and other episodes from our series, visit *Diabetes Discourse* on Reachmd.com where you can Be Part of the Knowledge. Thanks for listening.