

## **Episode 195: GLP-1: Can It Help Headache and Migraine?**

### **Lindsay Weitzel, PhD:**

Hello and welcome to HeadWise, the videocast and podcast of the National Headache Foundation. I'm Dr. Lindsay Weitzel. I'm the founder of Migraine Nation and I have a history of chronic and daily migraine that began at the age of four. I'm super excited to be here today with a repeat guest and headache medicine specialist, Dr. Fred Cohen. Hello, Dr. Cohen, how are you today?

### **Fred Cohen, MD:**

Hi. Well. Thank you for having me again.

### **Lindsay Weitzel, PhD:**

Thanks for being here. Dr. Cohen is an Assistant Professor at the Icahn School of Medicine at Mount Sinai. He is also section chair of the Primary Care Special Interest Section within the American Headache Society. And he is also a Board Member of the National Headache Foundation. We're very excited to have him. He always has awesome things and very interesting things to tell us.

We have a new and interesting topic today, something we've never discussed before. We plan to discuss the group of medications known as GLP-1 agonists. Many people are being prescribed these medications for type 2 diabetes or for weight loss. And we're going to discuss why and how they might be relevant to our migraine and headache community. Many people that are prescribed them likely also have migraine.

So we're just going to chat about them a little bit. Dr. Cohen, for our guests who might not know who you are, why don't you go ahead and tell us just a little bit about yourself?

### **Fred Cohen, MD:**

So just like yourself, I have suffered from migraines since as long as I can remember. And it was when I was in residency that I found the headache specialist and that really changed my life around. So my background is in Internal Medicine and also a fellowship in Headache Medicine, and I'm now a headache specialist in New York City. I'm very passionate about what I do, for the change I have to give to my patients as well.

### **Lindsay Weitzel, PhD:**

Okay. So let's talk about what GLP-1 agonists are, what they do, what they're prescribed for. Because this is likely the first time we've dedicated an episode of HeadWise to discuss a medication that is not for headache or for migraine. These are actually approved to treat type 2 diabetes and weight loss. Many people are taking them for these reasons but may also have migraine or another type of chronic or severe headache. And that is why we kind of want to chat about it.

So let's begin by listing some of the trade names of these medicines so that everyone knows what we're talking about, and give the background of just what they are.

**Fred Cohen, MD:**

Sure. So common ones that you might have heard of are Trulicity, Victoza, and Saxenda. And I don't know why that's hard for me to say. And the one that's getting a lot of press is the generic is semaglutide, is the generic name, but that's what Ozempic, Wegovy, Rybelsus, I think it's how you pronounce that one. And then a more recent one also is tirzepatide, which is Zepbound and Mounjaro.

So what these GLP-1 drugs are, GLP stands for a glucagon-like peptide. And the way I'll explain is they were designed for type 2 diabetes. And let's sort of think what diabetes is. This drug deals with how insulin works and how other hormones in that cycle work. So the drugs increase insulin secretion. So what does insulin do?

Insulin brings down our blood sugar when we eat. It suppresses glucagon, which think of glucagon as the opposite of insulin. Insulin brings blood sugar down. Let's say your body needs more energy and glucagon raises blood sugar up. The other effects that GLP-1s have is they slow gastric emptying, meaning that your stomach, let's say doesn't empty as quickly. And that helps with post-meal blood sugar spikes and promotes a feeling of fullness. And then also it promotes the feeling of appetite suppression. And that is where they think the weight loss effects come from.

**Lindsay Weitzel, PhD:**

We previously recorded an episode with Dr. Amelia Scott Barrett about the relationship between migraine and obesity, or migraine, and BMI. Let's back up a bit and discuss this relationship. Because while migraine and chronic headache patients come in all shapes and sizes, there is data to show that obesity can make a person's migraine disease worse. So can we just discuss that really quick?

**Fred Cohen, MD:**

So it's various population studies, studies that are aimed to see how much is migraine affect people in the country, their burden, their impact, etc.. Those studies have found that obesity was a common risk factor for progressive episodic migraine. So having eight or less monthly migraine days to progress into chronic migraine, which is more than that. So it was found these things are a risk factor for that.

And the reason behind that is obesity can cause several things in sort of the cycles in the body. And one of those is it can interact with inflammation. Obesity is associated with being in a chronic state of inflammation. And the reason why is adipose tissue, which is the fancy way to say fat cells, they release these chemical markers like cytokines as well as C-reactive protein. And these are things that cause inflammation.

And headaches, not just migraine. Well, migraine, like I said, that's been linked. What are headaches and migraine on a basic level if you want to really just say one sentence. They are conditions of neuroinflammation. So when I speak to patients, because I get asked all the time why am I having migraine, there's several reasons. There's not usually one thing. It's things that deal with inflammation. I talk about sleep. I talk about diet, I talk about their stressors. They're all related. Obesity is one of them. It's not the only cause. I want to make that clear that migraine is not a problem from obesity. It's just that obesity can compound on it.

So what I tell my patients is by having a BMI of this much can lead to worsening of your headache. But it's not the root cause.

**Lindsay Weitzel, PhD:**

We have had people before who they say to us that, oh, I went to my headache specialist because I had migraine, and I had this feeling that they were telling me it's my fault because I'm overweight. And that's really not at all what we're saying here. We have to build rock walls against our migraine, and we need a lot of rocks or a lot of tools to keep the migraine away. And one of the rocks can be our controlling weight. So this is just one of the things.

**Fred Cohen, MD:**

Migraine is not always oh, it's only prescription medication for the migraine. Again, it's evaluating other lifestyle components as well.

**Lindsay Weitzel, PhD:**

Okay. So my question is, because I think this is something if you kind of flip this question around, this is something people always want to hear. Do we know or has it been found that a person's migraine burden can actually decrease if they lose weight, if they are overweight?

**Fred Cohen, MD:**

So while there hasn't been I would say a direct test that, but we've seen again through these population studies that with reducing obesity there is improvement in migraine burden. I can't say oh specifically that. But in patients who in addition to proper migraine treatment, I'm not just saying losing weight alone, but in addition to adequate migraine therapy and losing weight, yes, there's been a decrease in severity.

I'll say, just this week I had a patient who I have various migraine regimen for. I'm giving her prescription meds for her migraine. But she also got bariatric surgery, not a GLP-1, and she's done fantastic weight loss. And she has had a great improvement in her migraine burden. Now I'm not saying all that was losing weight. No, I do think it was a portion of it.

**Lindsay Weitzel, PhD:**

Now this is probably a good time to point out that people do not prescribe these types of medicines for head pain or for the purpose of improving headache or migraine. Do they?

**Fred Cohen, MD:**

No. Again, these GLP-1s are not FDA approved for treating migraine. Again, I bring it up in the sense that this is a component. And of course, obesity can lead to other serious health complications such as coronary heart disease, risk of stroke. So it's more of a overall health picture.

**Lindsay Weitzel, PhD:**

Okay. There was something that I think we wanted to address. And it's another type of headache. Severe headache actually that is not as well known as migraine at all. It's called IHH or idiopathic

intracranial hypertension. It's known to be more prevalent in people who are overweight. It's actually underdiagnosed. Often it's misdiagnosed as migraine. And I'm curious to know if this is something that could be helped if people lose weight, or maybe if the prevalence of IIH decreases when people go on certain medications like this, etc.

**Fred Cohen, MD:**

So I guess I quickly explain what IIH is. Think of our brains as fish in a fishbowl, and the water is something called cerebral spinal fluid. So our brain is surrounded by fluid and we have systems in our body that keep that pressure at a certain area.

What happens when the pressure gets too high. That's what idiopathic intracranial hypertension is. The pressure is too high. And headache is a very common symptom of that, typically a positional headache. And the issue with that is if it goes untreated, it can lead to several complications, including permanent vision loss. So anyone that comes into my clinic for a new visit, I always do a few tests to make sure we're not dealing with this.

There are three major risk factors to developing IIH, and we're not exactly sure why these are. But again, population studies show these are things that can lead to that. And it's commonly seen in women with of childbearing age who also have obesity. And it can happen outside. I've diagnosed people underweight with IIH. It's just that's a common population.

And we think that obesity interferes with our bodies, our brain's ability to regulate that pressure. So to go to your question can GLP-1 agonists be used to treat that. That is again GLP-1 agonists are used to treat the weight issue. And then the thought because this is improving it, the thought would be if obesity comes down then the prevalence of IIH would come down.

That's not been proven. But in theory it sounds like it should have an impact on that.

**Lindsay Weitzel, PhD:**

Here is where things get really interesting, because most people probably don't know this, but it's popping up all over the internet and I think people are going to be noticing it. And so I want to make sure we address it. There is a small slight indication in the scientific literature that GLP-1 agonists could be beneficial in pain and central sensitization pathways like migraine, independent of weight loss.

In other words, perhaps this is effective in pain pathways and you and I have chatted about this a little bit. It's only a little bit of literature, but let's address it because people are probably going to start seeing it popping up on the internet, etc.

**Fred Cohen, MD:**

So there's been a lot of interesting studies and results coming from the GLP-1 class. Again this is designed for type 2 diabetes, then we found to be effective on weight loss. And then there is other areas in medicine popping up that it's being effective. And one of the areas that popped up was using it actually in substance abuse, that it was found to sort of improve with that, specifically opioid abuse.

The issue when you take a lot of opioid medication is it leads to your body being in this chronic, hypersensitive situation of pain. And they found those patients that that comes down. And that's what led to further studies that show that the use of drugs in the GLP-1 receptor can deal with receptors that we see involved with the central sensitization phenomenon with chronic migraine.

Now, this hasn't been proven. This is more of a exploration of a novel theory. But so far data shows that that's actually an interesting side effect. Now will they make a GLP-1 like drug, like a newer generation that hones in on that more? That's possible. I don't design drugs, not my expertise. But again this is how medicines get further developed, that it's, oh so side effects are not always a bad side effect.

It's like oh, that's a neat side effect. How can we enhance that more. So it wouldn't stun me in five, ten years that a newer generation of drug targets that side effect. And the story I always like to say is remember, off topic, but remember Viagra? It wasn't designed for erectile dysfunction. It was designed for a lung issue. And then it turns out, oh, it actually helps with this issue. And that happens in drug discovery. So maybe we'll see down the road that a newer generation of this class of drug is actually able to treat symptoms of chronic pain.

**Lindsay Weitzel, PhD:**

One of the questions that will probably come up, people watching this, is where do they go to get this? Do headache specialists prescribe this at this time? Is it mostly primary care doctors that prescribe it?

**Fred Cohen, MD:**

So originally it was an endocrinologist that would prescribe it. And now we're seeing more primary care doctors do it. Some headache specialists do this again. Like with any drug it comes to how comfortable and knowledgeable the prescriber is. For instance, if you have a medical license, I can prescribe whatever, but I'm only going to prescribe things that I'm comfortable prescribing.

You might find that it's not within a headache toolbox. So your headache specialist might not be familiar enough to prescribe it. But with that said, your primary care might be or if this is something you like to explore, they might be able to refer you to someone such as an endocrinologist who is comfortable, knowledgeable to explain and prescribe it to you.

**Lindsay Weitzel, PhD:**

And as with any medications, I can sort of see where this one might have a possibility for abuse. What sorts of abuse possibilities do you see with this medication?

**Fred Cohen, MD:**

Of course any drug, anything could be abused. People think weight loss, suppressing diet is good. It's useful, but it's not always the solution or answer. Underweight is actually more dangerous than overweight. This goes to when I used to be a primary care provider and a patient would say why can I take more insulin? I want my blood sugar lower. And I say well, high blood sugar hurts you slowly. Low blood sugar could be lethal, could kill you. And as with this, this isn't the kind of drug, like yeah it's like a multivitamin, everyone take GLP-1s. No, there is a time and a place for it, and it should only be given with a discussion with your prescriber that they also agreed to meet this.

Otherwise. Yes. Again being underweight leads to a whole plethora of medical issues. It could have gastrointestinal side effects. Like I know there could be issues with those who have a history of certain thyroid cancers. Like there are reasons not to give this.

**Lindsay Weitzel, PhD:**

Is there anything else you'd like to add on this topic of GLP-1 agonists and people possibly taking it who happen to have migraine or other headache disorders?

**Fred Cohen, MD:**

I would like to end it on sort of, again, this is the approach of treating migraine and headaches. And this is why I love what I do. It's not just of one sort of if you're able to take one pill and everything's great, that's fantastic. Everyone's different. Every headache is unique because I get asked questions about, oh, I took this migraine diet my friend did, but it didn't help me. Or I took this pill and it didn't help me.

Everyone's headache is unique, and this is why it's a discussion with you and your headache provider. And it may be that I'm not saying, oh, treating your obesity is going to be treating your headache. No, but it may benefit your headache condition by treating the obesity. I'm not coming out of saying, oh, this is the one true treatment to do it. No, but if you suffer from frequent headaches as well as from obesity, it's definitely worthy of a discussion with your provider.

**Lindsay Weitzel, PhD:**

That's great. That's a great way to put it. And thank you so much for being here today and discussing this interesting new topic that we've never really discussed. And thank you everyone for joining us. Please join us for our next episode of HeadWise. Have a great day.