

Episode 44: Ozempic and GLP-1 Weight Loss Drugs - Benefits, Overdose, and Counterfeits

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Transcript

Hi everyone, welcome back to the Tox Lab. I'm Rebecca. I'm Rob. This week we're gonna be looking at GLP-1 agonists, specifically semaglutide, which is more often called by its brand names, Azempic and Wigovi. And these have been seeing a lot of press recently for their almost miraculous weight loss abilities.

And they've been being pushed by celebrity influencers and there's been a huge rush on people trying to get hold of them, global shortages. Before we dive too hard into that, I thought we could maybe have a look at some older weight loss drugs that have come and gone over the years. I thought we could have a little quiz, Rebecca. Oh, okay.

So I'm gonna name some weight loss drugs and I want you to tell me if you have heard of them and for a bonus point, what went wrong with them? Okay, let's do this. So first of all, amphetamine. Heard of it.

And what went wrong with it? Too addictive? Basically, yeah, basically. It was quite effective as a weight loss agent, but people became dependent on it.

And also it did have some cardiac effects and things like that. All right, let's do some harder ones. Fen, Fen, heard of that? No.

So that is a fenfluramine-phenamine combo. So a combination of a serotonergic and a stimulant drug. That was big in the 1990s. What went wrong with it?

You've never heard of it. You can't tell me. No idea. Led to some serious heart valve disease, weirdly, and pulmonary hypertension.

So that was pulled from the shelves. Have you come across rainbow pills? No, but they sound fun. Well, so rainbow pills is a big catch-all term that captures really any combinations that were pushed.

They were big really in the 60s, the 70s, and maybe a bit later. And they were a mix of pretty much anything. Amphetamines, diuretics, laxatives. All right, two more.

Allistat, heard of that one? Yes, that's pancreatic lipase inhibitors. Oh, well done. Yes, that's correct.

What went wrong with that one? That one, I'm not sure. Well, it's a trick question, because it is still used, still sees some use in medical weight management. Does have a fairly unpleasant side effects in the form of greasy stools.

And finally, thyroid hormone. I'd hope so, given you're a biochemist. This was, and probably still is a bit used at super physiological doses to promote weight loss. And sometimes it's not refined thyroid hormones.

Sometimes it's desiccated pig thyroid. And again, that can lead to all sorts of thyrotoxic effects. So that brings us on now to the next big thing in weight loss, which is GLP-1 agonists. As I say, we're going to specifically be looking at semaglutide, which is sold under a couple of different brand names.

But other GLP-1 agonists are available as well now, aren't they? Before we dive into today's episode, if you want to stay up to date with our content, you can find us on Instagram at @the_tox_lab. We also have a LinkedIn page, which we're fairly active on. So go check us out over there.

And for those of you who don't use social media, but want to get in touch with episode suggestions or comments about our episodes, you can email us at thetoxlab@gmail.com. This episode was suggested to us by one of our listeners. So thank you for getting in touch and suggesting this. So as we've mentioned, GLP-1 agonists are gaining popularity.

In a survey of 1,000 randomly selected Americans, 17% of them reported using Asemptic for weight loss. And Asemptic or semaglutide, which is non-brand name, works to increase insulin release and decrease glucagon in a glucose-dependent manner. So GLP-1, glucagon-like peptide, is one of the gut hormones. Gut hormone cascades are incredibly complicated.

So I don't really understand all of the details, but GLP-1 is secreted by part of the gut in response to food entering the stomach, and it modulates insulin release. GLP-1 agonists are drugs that stimulate that receptor, and drugs like semaglutide are modified versions that are resistant to degradation. Endogenous GLP-1 has got a very short half-life, minutes. GLP-1 agonists like semaglutide last for days.

And this has really two effects. Firstly, it modulates insulin release and makes people more insulin sensitive. And secondly, it has effects on the stomach and the hypothalamus. You get reduced gastric motility and slower stomach emptying, and also increased fullness at the level of the brain.

Ultimately, this means people eat less and lose weight. So GLP-1 agonists have been prescribed to manage type 2 diabetes for many, many years, and have also been prescribed for weight loss in obese patients who have one weight-related condition, such as hypertension or raised blood pressure. In some studies, certain GLP-1 agonists are showing positive cardiovascular effects, so liraglutide, albiglutide have shown significant reductions in the risk of a major adverse cardiovascular event.

And it's thought this works because GLP-1 receptors are also expressed on cardiomyocytes and vascular endothelial cells, and they promote myocardial glucose uptake and utilization, decrease oxidative stress, and inhibit cardiomyocyte apoptosis, which are all cardioprotective effects and prevent adverse cardiac remodeling. Activation of GLP-1 receptors also induces vasodilation, which can reduce blood pressure as well. So not only do they treat diabetes, which is a big risk factor for cardiovascular disease, they lead to weight loss, which is another big risk factor for cardiovascular disease.

And independent of all this, they seem to actually actively reduce cardiovascular disease in other ways too. Yeah. This sounds like a miracle, right? It does, yeah.

Too good to be true? Possibly. So there are some adverse effects, aren't there? Although generally these drugs are incredibly well tolerated and they have shown in safety studies to actually drastically improve cardiovascular events and things like that, there are some side effects.

Mostly they're mild. We do see GI symptoms, nausea, vomiting, reduced gastric motility. There have been reports of pancreatitis, haven't there? When they occur, and these are quite severe, although I think they are relatively rare compared to the number of people taking these drugs.

There's also now reports of optic neuropathy or diabetic retinopathy being worsened. And we think this is to do with effectively poorly controlled diabetes being fixed too quickly. So there's osmotic shifts within the eye. And there has been some other rarer occurrences.

So there have been reports that semaglutide increases sorts of depression and suicide. And the European Medicines Agency is currently reviewing this. They've received about 150 reports. So are

looking into this effect further.

Be interesting to see the outcome of this. It might be really hard data to unpick because it's possible there's some social confounding factors in there as well. Yeah. So all in all, a really effective drug, relatively safe in terms of normal therapeutic use when prescribed.

What happens if somebody takes too much, Rebecca? So just a heads up on this next case, if you are talking about suicides, this is something you don't want to be listening to, feel free to skip ahead or listen to another episode. So this case involves a 39 year old female with bipolar disorder, PTSD, borderline personality disorder and autism who was brought to the emergency department after an intentional osmopic overdose. She admitted that this was a suicide attempt and had made previous attempts through intentional injections of her mum's insulin and ear piercing cleaning solution.

As a result of this attempt, she was admitted to an inpatient psychiatric facility. In terms of prescribed meds, she was on the Rosadona 80 milligrams a day, peroxetine at 40 milligrams a day and was prescribed osmpic for the past two years and had lost approximately a hundred pounds. So 45 kilos thereabouts ballpark. And she also admitted to using cannabis daily.

The normal protocol was to inject one milligram of osmpic once a week into her abdomen, but on this occasion, she's injected three four milligram vials of osmpic, so approximately 12 milligrams. She felt fatigued and lightheaded soon after injecting and developed mild nausea. Upon arrival to the emergency department, her vital signs were unremarkable. She had mildly elevated white cell count and cannabis was detected in the urine.

They did measure her glucose, which was found at a concentration of four millimoles per liter. And on serial point of care measurements, this fluctuated between 4.3 millimoles per liter and 5.1 millimoles per liter. So there was no hypoglycemia present at all. And she experienced no complications as a result of this attempt.

So there's not a lot of case studies out there as they're looking at semaglutide overdose. But this one case really demonstrated that a massive overdose actually didn't have any real adverse effects whatsoever beyond a bit of nausea. The risk with diabetic drug overdose often is hypoglycemia. When you think of some but not all drugs that can cause that, insulin being the big one, obviously insulin overdose can be very dangerous.

Sulfonylureas can lead to hypoglycemia. GLP-1 agonists don't seem to. And we think this is because the effect on glucose or rather the effect on insulin is glucose dependent. So although you sensitize the pancreas and it releases more insulin, it only releases that insulin in response to a spike in glucose.

So on their own, they're actually relatively safe drugs. So now we want to transition and look at what is perhaps the darker side of these miraculous weight loss drugs. And that actually isn't the drugs themselves, but rather counterfeit products that have been appearing on the market. So the Medicines and Healthcare products Regulatory Agency, or the MHRA, in the UK seized approximately 369 fake Ozempic pens between January 2023 and October 2023.

The World Health Organization has also identified fake Ozempic in the regulated supply chain in Brazil, the UK and the US. And there are reports of fake Ozempic in, I think, 40 other countries. In June 2023, Novo Nordisk, who are a manufacturer of Ozempic, reported counterfeit Ozempic pens reportedly bought at a retail pharmacy in the US actually contained insulin rather than their GLP-1 agonist. So these concerns have been echoed around the world, haven't there?

There seems to be a number of cases where counterfeit Ozempic has been seized and some of them did contain insulin. As we've described, Ozempic, semaglutide, is relatively safe. You inject yourself

with insulin, particularly if you use too much, and that could lead to hypoglycaemia, coma or ultimately death relatively fast.

And so the bigger risk here seems to be actually these counterfeit pens. So as we mentioned at the beginning, Ozempic and other GLP-1 agonists have been endorsed by a number of different celebrities. Recently in the news this week, Serena Williams had been signed as the face of Ro, which is a telehealth company prescribing GLP-1 agonists. And celebrity endorsements are always a bit of a worry, especially with things like GLP-1 agonists and the counterfeit pens that are on the market, because people are going to try to emulate the celebrities they're seeing and go out and try and buy some Ozempic and aren't always going to get actual Ozempic.

It's a worry, isn't it? So we've got this drug that is incredibly good at doing what it's supposed to do. We've got a global surge in demand, particularly marketed, influenced by celebrities driving this demand on top of the fact that even if you didn't have celebrities selling it, probably sells itself, right? A miracle weight loss drug that actually works.

And as a result, people are turning to cheaper alternatives. Go onto a website, somebody's selling you Ozempic at half the price. Why not? What's the worst that could happen, you think?

Maybe it doesn't work. Well, it turns out if there's insulin in it, actually the worst could be a lot worse than that. It is a real concern. I was trying to work out why there's insulin in there, because if you're gonna make a counterfeit, you just use saline, right?

And I think there's a few theories floating around. The first is that actually it's repurposed insulin pens rebranded to look like Ozempic because the delivery mechanism is essentially the same as what insulin-dependent diabetics use to inject their insulin. And the second is this idea that if you do inject yourself with a little bit of insulin, you'll feel it. And so people can maybe inject it and feel like the counterfeit drug is working.

I feel like counterfeit medications is an emerging theme on this podcast. It does seem to be. We've definitely talked a bit about counterfeit benzodiazepines and now we're moving into the world of counterfeit weight loss medications. I'm sure I saw an article in a newspaper the other week about how there's been this huge rise in all sorts of counterfeit medications.

And it is a concern. People struggle to access healthcare sometimes and therefore turn to the internet to treat themselves and don't always know that what they're buying isn't actually the regulated thing that they think they're buying. So what do you think, Rebecca? Do you think people without diabetes should be being prescribed it given that there is a global shortage and it was a diabetic drug and now diabetics are struggling to get hold of it?

I think it should be prioritized as much as it can be for management of diabetes because that's what it's used for. It does have like benefits for people who are obese with other health complications who can't lose weight traditionally. I think we do need to jump in a little bit here and say, we acknowledge that weight loss is hard, right? Like, yes, there's this celebrity culture driving behind it, but as someone who I've been on my own weight loss journey for my whole life, it is not an easy thing to do.

And therefore access to a drug that has these almost miraculous properties. I can see why there's such demand. So is this as much a craze really about health or is it just another cultural thinness trend dressed up as healthcare? Oh, it is worrying.

Like, diet culture has been around for forever and it does worry me that like the surge of influencers who were never really that overweight using Ozempic and dropping pounds like that and lots of people are gonna look at that and go, oh, that's what I should be looking like with every trend. I've definitely

come across people who are on it and I look at them and I think, do you need to be on it? But then perhaps I didn't know what they were like before they were on it. So it's quite hard to comment.

And actually we haven't talked about this, but there is often rebound weight gain when people come off it. It's not a drug easy to come off of and maintain that weight loss. So people are often on it for maintenance rather than just the initial weight loss. So final question then, is semaglutide and other GLP-1 agonists, are these drugs genuinely safer than those previous weight loss drugs we were chatting about at the start?

Or are we just in a honeymoon phase? And we're actually gonna see lots of long-term complications. That is a good point. At the moment they seem to have a relatively decent safety profile and those quite beneficial like cardio protective effects but as with any drugs that's not been around for that long, who knows what the long-term consequences of being on it are, are only the consequences of coming off it.

Yeah, I mean, so they're not new drugs. GLP-1 agonists have been around for a long time treating diabetes. But in this population of? Exactly.

For purely weight loss rather than for diabetes management? I think that's fair. I think it is always a case of watch this space. I'm really interested to see what the EU Medicines Agency make of the psychiatric association.

It'll be interesting to see what happens when that data concludes. And I'm also interested to see more data on the counterfeit Zempic actually making it into the academic literature because currently we've got alerts and people have reported the presence of insulin. I don't know how that has translated to genuine cases of hypoglycemia and potentially even fatality. Is this trace amounts of insulin because they've repurposed an injector or is this therapeutic amounts of insulin that carries with it significant risk?

I don't think we've got that data yet. And so I think for me, I'm interested to see that when that comes out for sure. Okay, so in conclusion, semaglutide, Zempic, Wigovie, other GLP-1 agonist drugs are here. They're effective, relatively safe even in overdose but there is a worrying trend of global demand leading to people seeking out counterfeit products and some of these counterfeit products potentially not only not doing what they say they're gonna do on the tin but potentially being harmful.

And so I think it really is a case of watch this space, see what happens with the long-term effects of GLP-1 agonists but also let's keep our eye on those counterfeits. I hope you've enjoyed listening to us this week. Do, if you've enjoyed listening, give us a like, give us a follow, give us a rating on Spotify. That'll be amazing.

Hope you all have an amazing week and we'll see you next time, bye.