CASE REPORT

Semaglutide-induced Erectile Dysfunction: A Case Report on Glucagon-like-peptide1 (GLP-1) Agonist Medication

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ABSTRACT

This case report examines the potential relationship between Semaglutide use and worsening erectile dysfunction (ED) in a 55-year-old male engineer with a history of diabetes, hypertension, and dyslipidemia. Despite initial improvements in metabolic health following treatment with Glucophage, Amlodipine, and Simvastatin, the patient continued to experience persistent ED. After switching to a regimen including Ozempic (Semaglutide), he reported a significant decline in libido and difficulties maintaining erections, suggesting that the medication may have exacerbated his erectile issues. Notably, his sexual desire improved after discontinuing Semaglutide. This case highlights the potential sexual side effects of GLP-1 receptor agonists and emphasizes the need for healthcare providers to monitor sexual health in patients undergoing treatment using GLP-1 agonists for metabolic syndrome (MetS). Future research should focus on larger studies to better understand the impact of Semaglutide on sexual health outcomes.
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INTRODUCTION

Semaglutide (sold as Ozempic) is a medication that mimics the GLP-1 hormone. Though its primary purpose is managing type 2 diabetes, it is now frequently prescribed to help non-diabetic patients lose weight. It operates as a GLP-1 receptor agonist, influencing appetite regulation and the brain's reward system. By mimicking the effects of the natural hormone GLP-1, Semaglutide stimulates insulin secretion in response to elevated blood glucose levels while simultaneously inhibiting glucagon release, which helps stabilize blood sugar levels. Importantly, it also slows gastric emptying, promoting a prolonged sensation of fullness and reducing the urge to eat (1).

There are many potential side effects of Semaglutide, which were gastrointestinal. These symptoms are generally mild and time limited. While gastrointestinal issues are well-documented, there is emerging evidence suggesting that this medication may also be linked to sexual dysfunction, particularly erectile dysfunction (ED) and decreased libido (2). Some studies have shown that non-diabetic men using Semaglutide for weight loss may experience an increased risk of developing ED. We will describe a case where a patient on Semaglutide experienced worsening erectile dysfunction alongside significant improvements in metabolic parameters, highlighting the complex relationship between diabetes management and sexual health.

CASE REPORT

A 55-year-old male with a Body Mass Index (BMI) of 34 presented with a ten-year history of persistent erectile dysfunction (ED) and metabolic syndrome, including diabetes mellitus, hypertension and dyslipidemia. At

baseline, his glycated haemoglobin (HbA1c) was 9.8%, blood pressure was 145/90 mmHg, and total cholesterol was 6.8 mmol/L. Initial management with metformin (1700 mg/day), amlodipine (5 mg), and simvastatin (20 mg) improved his blood parameters and systemic symptoms, yet ED persisted. Oral phosphodiesterase type 5 inhibitors (PDE-5i), specifically sildenafil (100 mg) and tadalafil (20 mg), yielded only mild-to-moderate success.

In late 2023, following a rise in HbA1c to 7.9%, his regimen was intensified to include a combination of dapagliflozin and metformin (Xigduo XR), atorvastatin (10 mg), allopurinol (300 mg) for gout, and subcutaneous semaglutide (Ozempic), titrated from 0.25 mg to 1.0 mg weekly. While this successfully reduced his HbA1c to 6.1% and BMI to 28, it coincided with a precipitous decline in sexual health. Within three months of starting semaglutide, the patient reported a marked loss of libido and intractable ED that became refractory to PDE-5i.
This worsening sexual dysfunction triggered significant marital strain and symptoms of major depressive disorder, including anhedonia and insomnia. However, the patient declined psychological intervention. He observed a direct temporal link between semaglutide use and the total suppression of sexual desire. Upon the recommendation of his spouse, he discontinued semaglutide. Following cessation, he experienced a notable recovery in libido and a return to baseline ED severity, once again achieving penetrative intercourse with the aid of sildenafil (See Table I for the chronological progression of treatment and symptoms). This case suggests a potential correlation between semaglutide and exacerbated sexual dysfunction despite significant improvements in metabolic parameters.

DISCUSSION

This case illustrates the complex relationship between metabolic syndrome, medication use, and erectile dysfunction (ED). Initially, the patient experienced persistent ED before starting Semaglutide, which indicates that his erectile issues may not solely stem from this medication. However, after transitioning to Semaglutide, he reported a noticeable decline in libido and difficulties sustaining erections, suggesting that the medication might have exacerbated his existing condition. This observation is further supported by the temporary improvement in his sexual desire after discontinuing Semaglutide. While the patient was concurrently prescribed atorvastatin and allopurinol, the onset of his refractory erectile dysfunction and loss of libido followed a distinct temporal pattern specifically aligned with the titration of Semaglutide, rather than the initiation of these other agents.

Ozempic (Semaglutide), a GLP-1 receptor agonist for managing type 2 diabetes, may contribute to erectile dysfunction (ED) through various hormonal and neurological mechanisms. Hormonal changes are significant, as GLP-1 agonists can affect testosterone levels, which are vital for sexual function and libido. A study by Able et al. (2022) found that non-diabetic, obese men on Semaglutide had a 4.5-fold increased risk of developing ED compared to those not on the medication, along with a 1.9-fold increased risk of testosterone deficiency (2). Potential explanations include interactions with Leydig cells, which express GLP-1 receptors and influence testosterone secretion (3). Semaglutide may indirectly influence dopaminergic pathways through its effects on appetite regulation and reward mechanisms. As a GLP-1 receptor agonist, Semaglutide primarily acts on the hypothalamus to modulate hunger and satiety signals, thereby altering food intake and energy expenditure. The GLP-1 analogues may influence the reward value linked to food and other substances, implying a possible interaction with dopaminergic signalling that affects motivation and reward (4). Furthermore, researchers proposed a "serotonergic mechanism" where GLP-1 drugs increase activity at the 5-HT2C receptor (the same receptor linked to SSRI-induced sexual dysfunction) (5). This may dampen the brain's reward response to sex, much like it dampens the reward for food.

Recognizing and addressing ED in patients using Semaglutide is crucial. The complexity of this association could also be viewed in the intricacy of the relationship between the inhibitory effects of the dopamine-oxytocin-nitric oxide neural pathway, the oxidative process of the vascular system, causing vasculopathy in this patient leading to poor blood flow to the pelvis, poor self-esteem due to poor self-image secondary to obesity, and side-effects of medications like the statin (Fig.1).

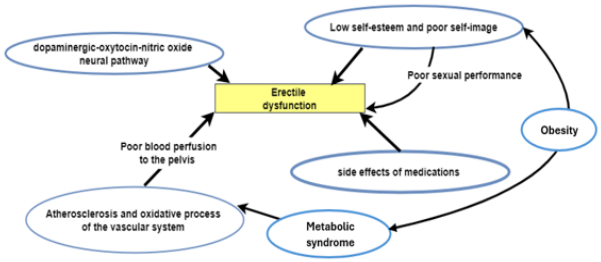

Fig.1 Factors that contribute to erectile dysfunction (ED). Ozempic or Semaglutide acts on the dopaminergic system of the brain. Other relevant factors may interact to be associated with an ED.

This case report suggests that healthcare providers should be aware of potential sexual side effects when prescribing GLP-1 receptor agonists like Semaglutide. Despite the insights gained from this case, limitations exist within this area of research. Establishing causality in single-patient cases can be challenging due to confounding factors such as pre-existing conditions or concurrent medications that may also contribute to ED. Therefore, future research should focus on larger cohorts

or controlled studies that systematically evaluate the relationship between GLP-1 receptor agonists and sexual health outcomes. In summary, while GLP-1 agonists are effective for diabetes and obesity, their potential impact on sexual health needs further investigation. This will help healthcare providers make informed decisions and improve patient care.

CONCLUSION

While Semaglutide effectively improved glycemic control and weight loss, its potential impact on sexual health underscores the importance of monitoring and addressing quality-of-life concerns. Clinicians should maintain open communication about possible side effects and reassess treatment regimens to balance benefits with patient well-being. Multidisciplinary care is essential, and further studies are needed to clarify the mechanisms linking GLP-1 receptor agonists with sexual dysfunction and to guide evidence-based management strategies.

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