GLP-1 Agonists Can Affect Mood: A Case of Worsened Depression on Ozempic (Semaglutide)

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ABSTRACT

Glucagon-like peptide-1 (GLP-1) receptor agonists have garnered significant attention in diabetes management, and they act by mimicking the effects of GLP-1, a hormone that regulates insulin secretion and appetite. While these medications have become increasingly popular, their impact on mood and other psychiatric manifestations remains uncertain because of inconsistent data. It has been shown to affect brain regions involved in emotional regulation. This case report underscores the adverse mood changes possibly linked to semaglutide and the need for further study in this area.

KEYWORDS: GLP-1 agonists, semaglutide, mood

Glucagon-like peptide-1 (GLP-1) receptor agonists are a class of medications used to treat Type 2 diabetes by mimicking the effects of GLP-1, a hormone that promotes insulin secretion and reduces appetite. Over the past few years, GLP-1 receptor agonists have emerged as a promising treatment option for individuals with Type 2 diabetes, and they are now being widely used. However, there are limited and variable data on the effects of GLP-1 receptor agonists on mood. GLP-1 has been found to influence brain regions involved in regulating emotions. An experimental study in rodents showed that GLP-1 agonists induced anxiety immediately after the commencement of treatment. This anxiety subsided with chronic treatment and was replaced by positive effects on mood, manifested by reduced depression-like behavior.[1]

Results from a randomized, controlled trial of liraglutide showed a slight numerical imbalance in suicidal ideation reports in the liraglutide group. No differences were noted in suicidal ideation/behavior or depression between liraglutide and other treatments, based on prospective questionnaires.[2]

Ozempic (semaglutide) is a GLP-1 receptor agonist that is commonly prescribed for the management of Type 2 diabetes. While the medication has been shown to be effective in improving glycemic control and promoting weight loss, there have been reports of negative mood changes associated with its use. On July 11, 2023, the European Medicines Agency (EMA) posted a statement that their safety committee was reviewing data on the risk of suicidal thoughts and thoughts of self-harm with GLP-1 receptor agonists, including Ozempic (semaglutide), Saxenda (liraglutide), and Wegovy (semaglutide).[3]

CASE PRESENTATION

We present the case of a 54-year-old female patient with a history of hypertension, hyperlipidemia, and depression. She had been managing Type 2 diabetes for the past 15 years. Despite taking maximal doses of metformin, her glycemic control was suboptimal, with a hemoglobin A1C (HbA1c) of 9.2 percent. She presented to our clinic for a routine follow-up, and after discussing treatment options with her, we initiated semaglutide 0.5mg once weekly as an adjunct to her current medication regimen. Initially, the patient tolerated the medication well, and her blood glucose levels improved, with an HbA1c reduction to 8.5 percent after four weeks of treatment.

After four weeks of treatment with semaglutide, the patient reported feeling more irritable and anxious than usual. She also experienced difficulty sleeping and a loss of interest in activities she previously enjoyed. These symptoms persisted over the next two weeks and began to interfere with her daily life. We suspected that her negative mood changes were consistent with major depressive syndrome. She did report a past history of one depressive episode about five years ago and stopped antidepressants after one year of treatment. Given her worsening depressive

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symptoms, which temporally correlated with starting on semaglutide, we decided to discontinue semaglutide and switch her to a different medication. Over the next several weeks, the patient's mood symptoms improved, and she reported feeling more like herself again. It is unknown if the patient's depressive symptoms were secondary to pre-existing susceptibility, given her previous history of depression, or triggered by primary effects on mood by semaglutide. This needs to be explored further in studies.

DISCUSSION

The emergence of depressive symptoms with semaglutide use in this case is puzzling and necessitates further inquiry. Given the prior history of depression, the possibility of a predisposing vulnerability cannot be dismissed or excluded. However, the timeline of the emergence of depressive symptoms following the initiation of semaglutide therapy raises concerns about the potential role of the medication in precipitating or exacerbating mood disturbances. A comprehensive investigation through longitudinal studies encompassing rigorous assessment of psychiatric history and medication response profiles will help inform clinical decision-making and optimize patient care.

CONCLUSION

This case highlights the potential negative mood changes associated with semaglutide in patients with Type 2 diabetes and a history of depression. While semaglutide can be effective in improving glycemic control, healthcare providers should be aware of the potential risk of negative mood changes and monitor patients closely for any changes in mood or behavior during treatment. Additionally, referral to a mental health specialist might be warranted for further evaluation and treatment of mood disorders.

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