Patient Safety in the Era of Compounded Obesity Therapy: A Case Report of An Unintentional Semaglutide Overdose

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Abstract

Semaglutide is a glucagon-like peptide-1 receptor agonist (GLP-1RA) used for obesity management, but due to barriers such as supply shortages, lack of insurance coverage, and high medication cost, patients may have a difficult time obtaining it. Because of this, patients are turning to on-line weight-loss clinics to obtain a compounded semaglutide salt form, bypassing regulatory efforts of the FDA to confirm efficacy and safety. Very few cases are available in the literature to guide management of GLP-1RA toxicity. We report a case from the emergency department where a woman presents after injecting too much compounded semaglutide she obtained from an online source. Though no hypoglycemia or gastrointestinal effects occurred during her observation period, health care providers must be prepared to intervene to help patients avoid overdoses and patient harm, and advocate for patients to have access to safe and effective medications.

Background

Semaglutide is a glucagon-like peptide-1 receptor agonist (GLP-1RA) initially developed to manage type 2 diabetes at subcutaneous doses of 0.25-1.0 mg once weekly. GLP-1RAs aid with glycemic control by enhancing incretin hormone effects like glucose-dependent insulin secretion, inhibition of glucagon secretion, and notably, increased satiety and slowed gastric emptying leading to appetite suppression. Consequently, trials found significant weight loss among diabetes patients as well as in those with overweight/obesity without diabetes. This led to a higher dose semaglutide (1.7-2.4 mg) product specifically indicated for overweight/obesity and expanded the diabetes dose to 2.0 mg. Adverse effects are primarily gastrointestinal and include nausea, diarrhea, decreased appetite, vomiting, constipation, dyspepsia, and abdominal pain. Warnings include pancreatitis, gallbladder disease, and use with certain thyroid cancers[1].

Extreme costs, insurance coverage barriers, and medication shortages have made these drugs difficult to obtain[2]. Despite these limitations, the soaring obesity crisis has desperate patients turning to on-line weight-loss clinics to obtain them at lower costs[3]. Semaglutide is dispensed by pharmacies in a pen injection device from the manufacturer and is dosed in milligrams[1]. The on-line "compounded" versions come as vials of semaglutide salt forms used for research, marked 5 mg/mL, and are injected using an insulin syringe dosed in units[4]. These alternatives can confuse patients leading to improper dosing and administration, as in the following case. This case was submitted to the institutional review board for ethics review which was waived.

Case

A 51-year-old woman with state Medicaid prescription coverage presented to the emergency department concerned she had injected too much semaglutide. Her past medical history included obesity, type 2 diabetes, hypertension, and hyperlipidemia. She presented on the day of her first dose of semaglutide, and she was concerned she took 3 weeks of medication all at once. She explained she was confused by the instructions provided and this led to her error in dosing. Her medication was dispensed in a vial and her understanding was that she was supposed to take 50 units but instead injected 150 units. Her previous GLP-1RA, dulaglutide, was discontinued to initiate semaglutide. On physical exam, the patient appeared euvolemic with moist mucous

membranes, was well-appearing, not distressed, not toxic, and denied any adverse effects. Her vital signs and laboratory tests were stable aside from an elevated blood pressure of 161/58 mmHg and a fingerstick glucose of 166 mg/dL. The state's poison control center was contacted and recommended supportive care, observation for 8-12 hours, frequent glucose monitoring, and symptom observation for nausea, vomiting, and diarrhea. After further investigation, it was determined the patient had taken 2.16 mg of semaglutide, a dose at the upper end of the titration range but much higher than the initiation dose. Blood glucoses were drawn every two hours and were 161, 105, 100, 106, and 116 mg/dL, consistent with her outpatient A1c of 6.3% approximately one month prior. She continued to deny any adverse gastrointestinal symptoms or hypoglycemia and was discharged the next day with instructions to follow up with her primary care physician. From that visit, documentation states they were unable to determine where the patient obtained semaglutide, as this medication was not prescribed by her primary care physician. Due to the confusing dosage form, the unintentional error made, and the determination that state Medicaid would not cover semaglutide at the time, the physician and patient decided to discontinue the compounded semaglutide and restart dulaglutide.

Discussion

The United States Food and Drug Administration states that semaglutide salt forms are not proven safe and effective and should not be used, but this practice is rampant and affecting many patients[4]. In addition to unconfirmed efficacy, patient safety suffers when unclear directions are given for unfamiliar and unregulated compounded products dosed and administered differently than the original agents, potentially increasing the risk of adverse effects.

Though information is lacking regarding how to manage toxicity from GLP-1RAs, patients should be monitored for gastrointestinal distress, acute pancreatitis, worsening gastroparesis, and hypoglycemia[5,6]. Fortunately, the patient described above had been previously taking dulaglutide when she started semaglutide, which may have contributed to her tolerance of the elevated dose. However, caution was appropriate based on the patient's concern, initially unknown dose, and poison center's recommendation. Notably, patients in a similar case series have experienced a range of mild to serious gastrointestinal events after unintentionally taking higher doses of their GLP-1RA due to similar reasons of unclear dosing instructions[7].

Conclusion

With GLP-1RA-related calls to poison centers increasing as much as 1500%, many future cases of unintentional overdoses are likely to occur as patients try to find affordable and accessible semaglutide[3]. We advocate for patients to have access to safe and effective medications to avoid confusion and subsequent errors such as this. Until this is addressed, health care providers must be prepared to intervene to avoid overdoses and patient harm. This case of an unintentional overdose of semaglutide may heighten clinicians' awareness of these risks.

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