International Journal of Pharmacy and Pharmaceutical Sciences

Print ISSN: 2656-0097 | Online ISSN: 0975-1491 Vol 16, Issue 6, 2024

Review Article

EXPLORING THE UNINTENDED CONSEQUENCES OF MISUSE OF WEGOVY AND OZEMPIC IN WEIGHT MANAGEMENT: A COMPREHENSIVE REVIEW

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Received: 14 Feb 2024, Revised and Accepted: 06 Apr 2024

ABSTRACT

In recent years, Glucagon-Like Peptide-1 (GLP-1) receptor agonists have emerged as promising options for weight management, offering not only glycemic control benefits but also significant reductions in body weight. Among these agents, Wegovy (semaglutide) and Ozempic (semaglutide) have gained attention for their efficacy in promoting weight loss, even in individuals without diabetes. However, the off-label use of these medications for weight management raises several questions and concerns regarding their safety, efficacy, and long-term effects. This comprehensive review aims to explore the complexities of GLP-1 agonists in weight management, focusing on their mechanism of action, clinical evidence, safety profile, dosing considerations, potential interactions, and future directions.

Keywords: GLP-1 receptor agonists, Obesity pharmacotherapy, Weight management, Metabolic health, Adverse events, Patient-centered care

DOI: https://dx.doi.org/10.22159/ijpps.2024v16i6.50611 Journal homepage: https://innovareacademics.in/journals/index.php/ijpps

INTRODUCTION

The global epidemic of overweight and obesity poses significant public health challenges, necessitating novel sustainable solutions. Traditional lifestyle interventions often produce modest and temporary weight loss, while bariatric surgery, despite its efficacy, comes with inherent risks and accessibility issues. In this landscape, pharmacological strategies have gained traction as potentially viable options for long-term weight management. GLP-1(Glucagon-Like Peptide-1) receptor agonists, initially developed as glucose-lowering medications for type 2 diabetes, have serendipitously demonstrated robust effects on body weight reduction. Their multiplicity of effects targeting key regulation points of energy intake and expenditure makes them alluring candidates for weight management.

However, as these injectable agents have become more extensively used for cosmetic and medically unsupervised weight loss purposes, important questions have arisen regarding their safety, efficacy, and ethicality in these off-label application settings. While Wegovy (semaglutide) has now received Food and Drug Administration (FDA) approval specifically for chronic weight management in obese patients, its chemical twin Ozempic (semaglutide) has not. Additionally, their use at doses higher than clinically studied for further amplification of weight loss remains highly questionable. As the hype around dramatic body transformations attributed to these medications permeates social media, their unintended long-term consequences, optimal patient selection criteria, and sustainability of effects remain unclear. Therefore, a deeper look into the risks versus benefits of using GLP-1 agonists off-label is warranted to guide clinical practice and policy decisions around their appropriate use for weight management moving forward [1-5].

In recent years, the exploration of pharmacotherapeutic interventions for weight management has intensified, with a particular focus on GLP-1 receptor agonists. These agents, notably Wegovy (semaglutide) and Ozempic (semaglutide), have garnered significant attention due to their efficacy in promoting weight loss, even among individuals without diabetes. However, the off-label utilization of these medications for weight management purposes has raised numerous questions and concerns regarding their safety, efficacy, and long-term consequences. The primary objective of this comprehensive review is to delve into the complexities surrounding GLP-1 agonists in weight management. This exploration encompasses various facets, including their mechanism of action, clinical evidence supporting their efficacy, safety profiles, dosing considerations, potential interactions, and future research directions.

To conduct this review, a systematic search was undertaken utilizing pertinent sources, including but not limited to PubMed, Embase, and relevant medical databases. Key search terms included GLP-1 receptor agonists, obesity pharmacotherapy, weight management, metabolic health, adverse events, and patient-centered care. The search was not restricted by publication date, encompassing literature from inception to the present. Furthermore, specific criteria were employed to select relevant studies and data for inclusion in this review. Emphasis was placed on studies investigating the use of GLP-1 agonists, particularly Wegovy and Ozempic, for weight management purposes. Studies exploring the safety and efficacy of these medications, as well as those examining their impact on metabolic health and patient-centered outcomes, were prioritized.

Through this meticulous examination, this review seeks to provide insights into the unintended consequences of the misuse of Wegovy and Ozempic in weight management, thereby contributing to a better understanding of the risks and benefits associated with these pharmacotherapeutic interventions.

GLP-1 Signaling: physiology and pharmacology

GLP-1 belongs to the class of incretin hormones released from intestinal L cells in response to nutrient ingestion. By stimulating GLP-1 receptors present on pancreatic beta cells, GLP-1 triggers insulin secretion in a glucose-dependent manner, thereby serving as a key mediator of postprandial glycemic regulation. Additionally, activation of central and peripheral GLP-1 receptors exerts myriad other effects that collectively reduce food intake, increase satiety, and promote weight loss. These diverse actions make pharmacological targeting of GLP-1 signaling an attractive prospect for managing obesity and type 2 diabetes simultaneously.

Several GLP-1 receptor agonists have now been developed as injectable medications for type 2 diabetes treatment. These agents mimic endogenous GLP-1's effects but circumvent its rapid degradation by the enzyme dipeptidyl peptidase 4 (DPP-4), thereby prolonging its actions. Two such GLP-1 agonists, Ozempic (semaglutide) and Wegovy (semaglutide) have received particular attention due to their additional obesity-lowering benefits observed

consistently across their clinical development programs. Both contain the same active compound, semaglutide, but are approved for different indications based on the clinical trials conducted-Ozempic for chronic diabetes management in adults and Wegovy for weight management in obese or overweight persons with comorbidities [6, 7].

Mechanism of action

GLP-1 receptor agonists mimic the action of endogenous GLP-1, a hormone secreted by the gut in response to food intake. By activating GLP-1 receptors in the brain and peripheral tissues, these agents exert multiple effects that contribute to weight loss, including decreased appetite, delayed gastric emptying, increased satiety, and reduced food intake. Additionally, GLP-1 agonists may influence energy expenditure, fat metabolism, and body composition, further enhancing their weight-reducing effects [8, 9].

General information

Different brands of semaglutide should not be used simultaneously. It's crucial to recognize that blood sugar levels can be influenced by various factors such as stress, illness, surgery, exercise, alcohol consumption, or irregular meals. Low blood sugar (hypoglycemia) symptoms include feeling empty, dizzy, irritable, or shaky. To promptly address hypoglycemia, consuming fast-acting carbohydrates like candy, crackers, raisins, fruit juice, or non-diet soda is recommended. In severe cases, a glucagon injection may be necessary, and the doctor should be informed of frequent symptoms of high blood sugar (hyperglycemia), such as increased thirst or urination. Patients should consult their doctor before altering their medication or treatment schedule. Treatment may involve a combination of medication, diet, exercise, weight control, medical tests, and specialized medical care. During prolonged illness, dehydration should be prevented, and medical advice sought if experiencing vomiting, diarrhea, or decreased appetite. It's essential to never share injection pens, as doing so can transmit infections or diseases.

Ozempic (semaglutide) is not recommended as the primary treatment for diabetes. Its safety and efficacy in patients with a history of pancreatitis have not been established. Additionally, Ozempic is not intended for use in individuals with type 1 diabetes or diabetic ketoacidosis. Its safety in children under 18 y of age has not been determined. Dosing adjustments may be necessary due to changes in various factors such as physical activity, weight, stress levels, illness, diet, or concomitant medication use [10, 11].

Warnings

Patients should promptly notify their doctor if they experience signs of a thyroid nodule, such as swelling or a lump in the neck, difficulty swallowing, a hoarse voice, or shortness of breath. Studies in rodents have shown that semaglutide and similar drugs may cause thyroid nodules, including thyroid cancer. The potential risk of thyroid nodules or Medullary Thyroid Carcinoma (MTC) in humans is not fully understood. Semaglutide should be avoided in patients with Multiple Endocrine Neoplasia type 2 (MEN 2) or a family history of MTC. Symptoms of a serious allergic reaction should be reported immediately to the doctor, including swelling of the face, lips, or throat, difficulty breathing or swallowing, severe rash or itching, dizziness, or lightheadedness. Additionally, caution is advised for patients with a history of stomach or intestinal disorders, pancreatitis, eye problems associated with diabetes, depression, suicidal thoughts, or other mental health issues.

A potential risk of thyroid C-cell tumors, including MTC, has been observed in animal studies with semaglutide. While the human relevance of these findings is uncertain, patients with MEN 2 or a personal or family history of MTC should avoid Ozempic. Patients should be counseled about the symptoms of thyroid tumors and monitored accordingly. Other warnings include the risk of pancreatitis, acute kidney injury, and hypersensitivity reactions. Ozempic pens should never be shared between patients to prevent the transmission of blood-borne pathogens [12].

Dosage

The dosage of semaglutide should be initiated at a low dose and gradually increased to minimize gastrointestinal side effects. The recommended dose escalation schedule for patients aged 12 and above involves increasing the dose over several weeks until reaching the maintenance dose of 2.4 mg injected subcutaneously once a week. If patients cannot tolerate the maintenance dose, a temporary reduction to 1.7 mg once a week may be considered, with careful monitoring and subsequent dose adjustments.

The recommended dosage initiation for Ozempic is a 0.25 mg subcutaneous injection once weekly for 4 w. This dosage is primarily for treatment initiation and may not effectively control blood sugar levels. After 4 w, the dosage is increased to 0.5 mg once weekly. Further dosage adjustments may be made based on the patient's glycemic control needs, with a maximum recommended dosage of 2 mg once weekly. Ozempic should be administered at the same time every week, and if a dose is missed, it should be taken within 5 d of the scheduled dose. Injection sites should be rotated, and the medication should be visually inspected before use.

Ozempic is available as a clear, colorless solution containing 2 mg/1.5 ml (1.34 mg/ml) of semaglutide. It is supplied in pre-filled, disposable, single-patient-use pens delivering either 0.25 mg or 0.5 mg per injection for treatment initiation or maintenance treatment, respectively. Additionally, a pre-filled pen delivering 1 mg per injection for maintenance treatment is available.

The active ingredient in Ozempic is semaglutide. Other components include disodium phosphate dihydrate (as a buffer), propylene glycol (an isotonic agent), phenol (a preservative), water (as the injection vehicle), and hydrochloric acid or sodium bicarbonate (to adjust acidity).

This comprehensive information on Ozempic's considerations, warnings, dosing, and ingredients should be integrated into the manuscript for a thorough understanding of its use in diabetes management [13, 14].

Clinical evidence

Clinical trials evaluating the efficacy of GLP-1 agonists in weight management have demonstrated consistent and significant reductions in body weight across various patient populations. Studies investigating Wegovy and Ozempic have reported average weight losses ranging from 10% to 15% of initial body weight, surpassing the results observed with traditional weight loss interventions. Moreover, improvements in cardiometabolic risk factors, such as blood pressure, lipid levels, and glycemic control, have been observed alongside weight loss, highlighting the potential for comprehensive metabolic benefits [15, 16].

Safety profile

While generally well-tolerated, GLP-1 agonists are associated with specific safety considerations that warrant careful monitoring and patient education. Common adverse effects include gastrointestinal symptoms, such as nausea, vomiting, diarrhea, and constipation, which tend to diminish over time with continued therapy. However, more serious adverse events, including pancreatitis, thyroid abnormalities, and allergic reactions, have been reported, necessitating vigilance and appropriate risk assessment before initiating treatment [17].

Serious side effects

Complications of Diabetic Eye Disease (Retinopathy): Patients should inform their doctor if they experience any changes in vision during treatment [18].

Inflamed Pancreas (Acute Pancreatitis): Symptoms include severe abdominal and back pain that persists. Immediate medical attention is necessary [19].

Some common side effects of Ozempic include nausea and diarrhea, which often improve over time. Other common side effects may include vomiting, low blood sugar (hypoglycemia), indigestion, gastritis, reflux, stomach pain, bloating, constipation, burping, gallstones, dizziness, tiredness, weight loss, decreased appetite, flatulence, and increased pancreatic enzymes. Low blood sugar can occur, especially when Ozempic is used with other antidiabetic

medicines, and may manifest with symptoms like sweating, pale skin, headache, rapid heartbeat, nausea, hunger, changes in vision, weakness, nervousness, confusion, difficulty concentrating, or shaking. It's important to follow the doctor's guidance on managing low blood sugar, and they may adjust the dose of other antidiabetic medicines accordingly. Uncommon side effects may include altered taste perception, rapid pulse, injection site reactions (such as bruising, pain, irritation, itching, or rash), allergic reactions (like rash, itching, or hives), and delayed gastric emptying. Before combining Ozempic with other medications, it's essential to consult with a doctor or pharmacist to avoid potential drug interactions [20-23].

Safety profile

Semaglutide, the active ingredient in Ozempic, has not been associated with hepatotoxicity based on published reports. However, like all medications, Ozempic can cause side effects, although not everyone experiences them. Serious side effects include diabetic eye complications (retinopathy), inflamed pancreas (acute pancreatitis), and severe allergic reactions (anaphylactic reactions, angioedema), which require immediate medical attention. Common side effects may include headache, nausea, vomiting, diarrhea, constipation, stomach pain, dizziness, fatigue, weight loss, decreased appetite, flatulence, increased pancreatic enzymes, and low blood sugar (hypoglycemia) when used in patients with type 2 diabetes. Uncommon side effects such as hypotension, dizziness upon standing, and rapid heartbeat may also occur [24].

Shelf life and storage

The shelf life of Wegovy (semaglutide) is 2 y, and it can be stored unrefrigerated for up to 28 d at temperatures not exceeding 30 °C. However, the pen should be discarded if left out of the refrigerator for more than 28 d. It should be stored in its original packaging to protect it from light.

Storage conditions for ozempic

Before Opening: Store in a refrigerator (2 °C–8 °C), avoiding freezing and keeping away from the cooling element.

During Use: The pen can be stored for up to 8 w at temperatures below 30 °C or in a refrigerator (2 °C–8 °C), protected from light with the cap on. Do not freeze. Do not use if the solution is not clear and colorless.

Disposal: Do not dispose of medications via wastewater or household waste. Consult a pharmacist for proper disposal methods to protect the environment [25, 26].

Dosing considerations

The dosing of GLP-1 agonists is critical to achieving optimal therapeutic outcomes while minimizing adverse effects. Both Wegovy and Ozempic are administered once weekly via subcutaneous injections, with dose escalation protocols designed to enhance tolerability and adherence. Starting with low doses and gradually titrating up over several weeks allows patients to adjust to the medication and mitigate gastrointestinal side effects. However, individualization of therapy based on patient characteristics, preferences, and response to treatment is essential to optimize efficacy and safety [27].

Potential interactions

GLP-1 agonists may interact with other medications, affecting their absorption, metabolism, or pharmacodynamic effects. Close monitoring and dose adjustments may be necessary when coadministering GLP-1 agonists with drugs that influence gastrointestinal motility, renal function, or glucose metabolism. Additionally, caution should be exercised when combining GLP-1 agonists with other agents known to affect pancreatic or thyroid function, as the risk of adverse events may be increased [28].

Interaction with other medications

Semaglutide may delay gastric emptying and affect the absorption of orally administered medications. It should be used cautiously with medications that undergo rapid gastrointestinal absorption. When co-administered with paracetamol, semaglutide may reduce the rate of gastric emptying but does not significantly affect overall paracetamol exposure. Semaglutide does not appear to affect the effectiveness of oral contraceptives, atorvastatin, digoxin, metformin, or warfarin. However, frequent monitoring of the International Normalized Ratio (INR) is recommended when initiating semaglutide treatment in patients on warfarin or other coumarin derivatives [29].

Ozempic may interact with medications that can increase heart rate. Patients should consult their doctor or pharmacist before taking any other medication with Ozempic, especially drugs used to treat hypertension, heart failure, Human Immunodeficiency Virus (HIV) infection, attention deficit-hyperactivity disorder, or those that suppress appetite or cause weight loss [30].

Future directions

The evolving landscape of obesity pharmacotherapy continues to advance with the development of novel agents targeting various pathways involved in energy homeostasis and body weight regulation. While GLP-1 agonists represent a significant advancement in this field, ongoing research aims to elucidate their long-term safety, durability of weight loss effects, and potential role in combination therapies. Additionally, efforts to address barriers to access, affordability, and adherence are essential to maximize the impact of GLP-1 agonists on population health [30].

CONCLUSION

In conclusion, GLP-1 receptor agonists, such as Wegovy and Ozempic, offer promising opportunities for weight management, demonstrating substantial efficacy and favorable metabolic effects. However, their off-label use for weight loss necessitates careful consideration of individual patient characteristics, potential risks, and alternative treatment options. Clinicians play a pivotal role in guiding patient-centered decisions, providing comprehensive education, and monitoring for adverse events to ensure the safe and effective use of GLP-1 agonists in the pursuit of sustainable weight loss and improved metabolic health. This underscores the importance of ongoing research, healthcare policy initiatives, and interdisciplinary collaboration to address the multifaceted challenges associated with obesity management.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

Ms. Madhura Satish Chothave: data analysis, manuscript drafting and editing, Conceptualization, study design, critical revisions, major contribution to manuscript writing.

Mr. Sarthak Kute: Literature Review, Conceptualization, study design, critical revisions, major contribution to manuscript writing.

Ms. Vaishnavi Kale: Data collection, analysis, interpretation.

Mrs. Anupama Kapadnis: Supervision, guidance, critical revisions, final approval.

Ms. Prajakta Rote: Data interpretation, manuscript editing.

CONFLICTS OF INTERESTS

Declared none

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