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SEMAGLUTIDE- REVOLUTIONARY DRUG IN OBESITY MANAGEMENT

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ABSTRACT

Semaglutide is one of the most widely used glucagon-like peptide-1 receptor agonists, initially approved for the treatment of type 2 diabetes and now increasingly utilized for obesity treatment. Its efficacy in weight reduction has led to a surge in popularity; however, concerns regarding its safety profile and potential side effects have emerged. This review aims to analyze the mechanism of action, therapeutic efficacy, and potential risks associated with semaglutide use.

KEYWORDS

Semaglutide, GLP-1 Agonist, Obesity, Weight Loss, TDM2

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1. Introduction

1.1 General information

Obesity is a chronic disease and global public health challenge [3-5]. The worldwide obesity prevalence, defined by body mass index (BMI) ≥30 kg m^{-2}, has nearly tripled since 1975. [13] BMI is a good surveillance measure for population changes over time, given its strong correlation with body fat amount on a population level, but it may not accurately indicate the amount or location of body fat at the individual level. [13,14] In fact, the World Health Organization defines clinical obesity as 'abnormal or excessive fat accumulation that may impair health. Obesity can lead to insulin resistance, hypertension, and dyslipidemia. [6] It is also associated with complications such as: type 2 diabetes, cardiovascular disease, and nonalcoholic fatty liver disease [4] and reduces life expectancy. More recently, obesity has been linked to increased numbers of hospitalizations, the need for mechanical ventilation, and death in persons with COVID-19. [12] Multiple weight loss interventions have been developed during the past decades. They include lifestyle and behavioral interventions (eg, diet and exercise), antiobesity medications, endoscopic interventions, and surgical procedures. AOMs are an effective treatment for weight loss, aiming to improve quality of life and control weight-related comorbidities. One of the most popular is GLP-1 receptor agonist called semaglutide, also known as famous Ozempic.

What is it exactly? Semaglutide is a glucagon-like peptide-1 receptor agonist that has been clinically approved for treatment of type 2 diabetes mellitus and now has emerged as promising pharmacological treatment for obese patients. [1]

1.2 Mechanism of action

Glucagon-like peptide-1 receptor agonists are a well-established class of glucose-lowering agents that induce glucose-mediated stimulation of insulin secretion, reduce glucagon release, reduce hepatic glucose output, delay gastric emptying, increase satiety, and improve cardiovascular risk factors. [8-11] GLP-1RAs provide effective control of glycemia with a low risk of hypoglycemia, while reducing body weight, blood pressure, and in some cases, cardiovascular events.

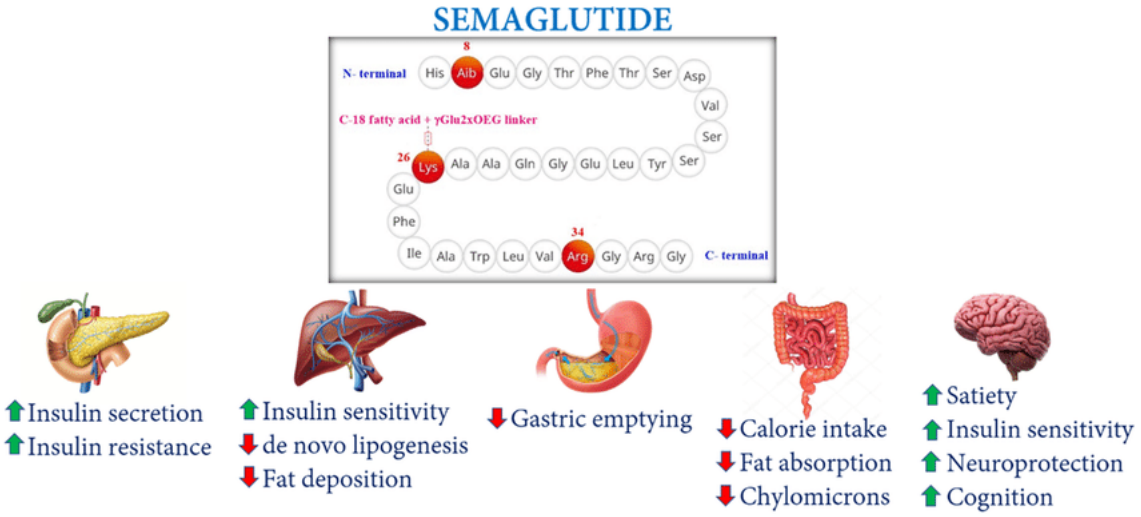

Fig. 1. *Mechanism of semaglutide for management of obesity, NASH, and neurodegenerative diseases. [7]*

1.3 Administration of semaglutide

Semaglutide can be administrated in different ways. The most common is subcutaneous injections. Semaglutide in the form of an injectable solution is most commonly administered once a week. Common injection sites include the abdomen, thigh, or upper arm. It's important to rotate injection sites to reduce the risk of skin irritation. It is typically supplied in pre-filled pens, either disposable or reusable. Semaglutide also comes in tablet form, which must be taken daily. The pill is taken in the morning, on an empty stomach, with a small amount of water (no more than 120 ml). After taking the tablet, you should avoid eating, drinking other liquids, or taking any other medications for at least 30 minutes to ensure proper absorption.

2. Methodology

This article is a medical literature review based on publications on PubMed, Google Scholar, Frontiers and Science Direct from 2015-2025. The selection process included both original research articles and review papers discussing the mechanism of action, effectiveness, safety profile, and potential side effects of semaglutide. Special emphasis was placed on clinical studies—both randomized controlled trials and observational studies—as well as the recommendations of scientific associations involved in obesity and diabetes management.

Publications unavailable in full text or lacking specific clinical data were excluded in the initial screening. In the next step, the focus was placed on the most recent and frequently cited sources to ensure the relevance and reliability of the information presented. Ethical and societal perspectives on the increasing off-label use of GLP-1 receptor agonists were also considered.

The collected data were categorized into key thematic areas: semaglutide's effectiveness, adverse effects, and ethical concerns related to its use. The final selection of sources was based on methodological quality, clinical significance, and relevance to the objectives of the review.

3. Review of results

3.1 Effectiveness of semaglutide

Semaglutide has demonstrated significant effectiveness in clinical studies for both type 2 diabetes management and weight reduction in individuals with obesity or overweight. [11,12,13] Semaglutide lowers blood glucose levels by stimulating insulin secretion in response to meals and suppressing glucagon release. Clinical trials have shown that semaglutide effectively reduces HbA1c levels, often achieving reductions of 1.5–2.0% or more, depending on the dose. [12] Many patients reach the target HbA1c of less than 7% while using semaglutide, making it a highly effective option for improving long-term glucose control. [1,2,10,11] In obesity and overweight studies, semaglutide has led to substantial weight loss compared to placebo. Participants taking semaglutide often experience weight reductions averaging 10–15% of their initial body weight or more when combined with lifestyle interventions such as balanced diet or increased physical activity. This makes semaglutide one of the most effective pharmacological options for weight management that is currently available among patients.[12,13, 15] Semaglutide has also shown cardiovascular benefits in people with type 2 diabetes, reducing the risk of major adverse cardiovascular events such as heart attack, stroke, or cardiovascular death. Its demonstrated cardiovascular safety profile makes it a preferred choice for individuals with type 2 diabetes who are at high cardiovascular risk. [1,2,6]

3.2 Side effects of semaglutide

Semaglutide, like any medication, can cause side effects. According to clinical trials and reviewed medical literature, these include:

gastrointestinal effects: nausea which is the most frequently reported side effect, especially during the initial weeks of therapy. Vomiting and Diarrhea can also occur, often coinciding with dose escalation. Some individuals experience slowed bowel movements and mild to moderate abdominal discomfort. [12,15]

hypoglycemia (when combined with certain other medications): semaglutide alone does not typically cause hypoglycemia. However, when used with sulfonylureas or insulin, there's a higher risk of low blood sugar levels. Patients may experience symptoms such as dizziness, sweating, and confusion if their blood glucose drops too low. [12]

weight loss-related effects: while weight loss is generally a desired outcome, rapid weight reduction may lead to side effects such as fatigue, hair thinning, or gallbladder-related issues (e.g., gallstones). These issues can occur due to metabolic shifts associated with significant weight loss.[12]

The term **"Ozempic face"** has gained increasing popularity as an informal description of a potential side effect associated with rapid weight loss. It refers to the noticeable facial volume loss and skin laxity that may occur in individuals undergoing treatment with semaglutide (Ozempic). This condition is caused by a reduction in subcutaneous fat in the facial region, leading to loss of volume, the appearance of wrinkles, sunken cheeks, and diminished jawline definition, resulting in a prematurely aged facial appearance.

cardiovascular considerations: some patients have reported increased heart rate, though this has not been definitively linked to negative cardiovascular outcomes. Nonetheless, clinicians often monitor heart rate as a precaution. [12,16]

potential risk of pancreatitis and thyroid concerns: there have been rare reports of acute pancreatitis in patients using GLP-1 receptor agonists like semaglutide. Animal studies have indicated a potential link to thyroid tumors, including MTC, but these findings have not been confirmed in human studies. As a precaution, semaglutide is not recommended for patients with a personal or family history of MTC or MEN 2). [17]

To sum up, the most common side effects of semaglutide are gastrointestinal, particularly nausea and diarrhea, which often improve with time or dose adjustments. More serious side effects are rare but can include pancreatitis or gallbladder issues. It is important for patients to discuss any unusual symptoms with their healthcare provider and to have regular follow-ups to monitor their response to treatment. [12,15,16,17]

3.3 Ethical problems

Public reception of semaglutide has also been mixed. On the one hand, there has been a surge of popularity of semaglutide, primarily for its efficacy as a weight loss drug. At the same time, however, those who take it for weight loss are often shamed for taking ‘the easy way out’. Some commentators are concerned that the surge in popularity of semaglutide will leave those who need it most for therapeutic purposes worse off. [18]

4. Conclusions

Semaglutide has become a standout therapeutic option for managing both type 2 diabetes and obesity, demonstrating exceptional results in improving blood sugar control, promoting weight reduction, and decreasing cardiovascular risks. Its efficacy has spurred widespread use, though certain drawbacks remain. Gastrointestinal disturbances, the most frequently observed side effects, can often be controlled and typically lessen as treatment continues. However, the risk of more severe complications, such as inflammation of the pancreas or gallbladder-related conditions, calls for careful oversight by healthcare professionals. Ethical considerations about equitable access and public perception further underscore the need to ensure that semaglutide remains available to individuals with the greatest medical need. As the popularity of this medication continues to grow, medical providers and policy leaders must carefully weigh the advantages against any potential hazards, striving to use semaglutide responsibly for the benefit of patients who can achieve the most meaningful health outcomes.

5. List of abbreviations

GLP-1- glucagon-like peptide-1
TDM2- type 2 diabetes
GLP-1Ras- glucagon-like peptide-1 receptor agonists
HbA1c- glycated hemoglobin
AOMs- antiobesity medications
BMI- body mass index
MTC- medullary thyroid carcinoma
MEN2- multiple endocrine neoplasia syndrome type 2

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