Article type: Editorial

Issue URL: https://www.alliedacademies.org/food-technology-and-preservation/

The future of obesity treatment: GLP-1 receptor agonists in non-diabetic populations.

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Received: *01-Mar-2025, Manuscript No. AADY-25-166636;* ***Editor assigned:*** *03-Mar-2025, PreQC No. AADY-25-166636(PQ);* ***Reviewed:*** *16-Mar-2025, QC No. AADY-25-166636;* ***Revised:*** *22-Mar-2025, Manuscript No. AADY-25-166636(R);* ***Published:*** *25-Mar-2024,DOI:10.35841/aady-9.1.245*

Introduction

Obesity has emerged as a major global health challenge, affecting over 650 million adults worldwide and contributing significantly to morbidity and mortality. Beyond its well-known link to type 2 diabetes, obesity increases the risk of cardiovascular disease, certain cancers, and a host of metabolic complications. Despite widespread recognition of the problem, effective long-term treatment options for obesity remain limited. However, recent advances in pharmacotherapy, particularly the development of glucagon-like peptide-1 (GLP-1) receptor agonists, offer promising new avenues for managing obesity even in individuals without diabetes [1].

GLP-1 is an incretin hormone secreted by intestinal cells in response to food intake. It exerts multiple physiological effects including enhancing insulin secretion, inhibiting glucagon release, slowing gastric emptying, and promoting satiety. GLP-1 receptor agonists (GLP-1 RAs) are synthetic analogues designed to mimic these effects, initially developed and widely used to treat type 2 diabetes by improving glycemic control [2].

Interestingly, one of the observed benefits of GLP-1 RAs in diabetic patients was significant weight loss, which sparked interest in their potential use as anti-obesity agents. This has led to clinical trials and eventual regulatory approval of specific GLP-1 RAs for obesity treatment in non-diabetic populations.

Several GLP-1 RAs have been studied for weight management in non-diabetic individuals, notably liraglutide and semaglutide. Both have demonstrated substantial efficacy in reducing body weight compared to placebo.

Administered as a daily injection, liraglutide has been shown to induce an average weight loss of 5-8% of initial body weight over 1 year in non-diabetic obese adults. It works by reducing appetite and calorie intake through central nervous system pathways. A more recent addition, semaglutide is administered weekly and has shown even greater weight reduction—up to 15% or more in some trials. Semaglutide's superior efficacy and convenient dosing schedule have positioned it as a leading option in obesity pharmacotherapy [3].

These agents not only promote weight loss but also improve metabolic markers such as blood pressure, lipid profiles, and inflammatory markers, which are critical in reducing obesity-related complications.GLP-1 RAs reduce weight primarily through appetite suppression by acting on hypothalamic centers that regulate hunger and satiety. They slow gastric emptying, prolonging the sensation of fullness after meals. Additionally, they may influence reward pathways related to food intake, reducing cravings for high-calorie foods.

Importantly, these effects are achieved without the severe side effects associated with older weight loss medications, such as cardiovascular risks or central nervous system toxicity. Most common side effects with GLP-1 RAs are

gastrointestinal—nausea, vomiting, and diarrhea—typically transient and manageable. The approval and integration of GLP-1 RAs into obesity management protocols mark a paradigm shift. Here are some ways they are shaping the future: Traditionally, obesity treatments included lifestyle modification, bariatric surgery, and limited pharmacological options. GLP-1 RAs provide a safe and effective alternative for patients who do not qualify for surgery or have not succeeded with lifestyle changes alone [4].

Ongoing research aims to identify patient subgroups that respond best to GLP-1 RAs, enabling more tailored therapies. Genetic, behavioral, and metabolic markers may guide treatment selection and optimize outcomes. Researchers are exploring combining GLP-1 RAs with other agents such as GIP (glucose-dependent insulinotropic polypeptide) agonists, or other hormonal modulators to enhance weight loss and metabolic benefits.

As these drugs are used more widely, longitudinal studies will clarify their long-term impact on obesity-related morbidity and mortality, adherence patterns, and cost-effectiveness.Increasing awareness and reducing stigma associated with obesity as a chronic disease is crucial. Access to GLP-1 RAs can be limited by cost and insurance coverage, challenges that need addressing to ensure equitable care [5].

Conclusion

GLP-1 receptor agonists represent a groundbreaking advancement in the pharmacological treatment of obesity, offering hope for millions struggling with excess weight who do not have diabetes. Their demonstrated efficacy in inducing meaningful weight loss, coupled with a favorable safety profile, positions them as a cornerstone in future obesity management. As research continues, these therapies may be integrated with personalized approaches and combination regimens to further improve outcomes. Overcoming barriers related to cost, access, and long-term management will be essential to fully harness their potential and mitigate the global obesity epidemic.

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Citation: Tripati S. The future of obesity treatment: GLP-1 receptor agonists in non-diabetic populations. J Diabetol. 2025;9(1):245