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NEXT-GENERATION GLP-1 PHARMACOTHERAPY: ADVANCES IN OBESITY TREATMENT WITH CONSIDERATIONS FOR PHYSICAL PERFORMANCE AND POPULATION HEALTH

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ABSTRACT

Introduction and aim of the study: Obesity is a global health issue increasing risks for various diseases and straining healthcare systems. Traditional treatments often prove ineffective, spurring interest in new therapies. GLP-1 receptor agonists have emerged as promising options for treating obesity, gaining attention for their benefits on physical performance and body composition. The aim of this study is to review current knowledge on the mechanisms of action, clinical efficacy, and safety of GLP-1 receptor agonists in obesity treatment, including their implications for public health and potential relevance in physically active populations.
Review methods: A literature review was conducted using databases such as PubMed and Google Scholar. The search included keywords like: Obesity; Glucagon-Like Peptide 1; Public Health; Sports Performance; Energy Metabolism.
Current state of knowledge: GLP-1 receptor agonists can reduce body weight by 10–21% while decreasing risks of metabolic complications, such as type 2 diabetes and cardiovascular issues. Besides their primary effects, they also regulate appetite, enhance fat oxidation, and improve energy efficiency, attracting interest from physically active individuals looking to optimize body composition. Their action mechanisms include delayed gastric emptying, increased satiety, and enhanced insulin sensitivity.
Summary: The use of GLP-1 receptor agonists marks significant progress in obesity treatment with vital public health benefits. However, their off-label use among athletes raises ethical and safety concerns, especially regarding potential lean body mass loss affecting performance.

KEYWORDS

Obesity, Glucagon-Like Peptide 1, Public Health, Sports Performance, Energy Metabolism

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Introduction

Obesity is one of the most serious health challenges of the 21st century, affecting over 650 million people worldwide [1]. This condition significantly increases the risk of developing serious health problems such as type 2 diabetes, cardiovascular diseases, non-alcoholic fatty liver disease, and certain cancers, all of which may result in severe complications and a lower quality of life [2]. In spite of the numerous efforts that have been made to encourage and implement lifestyle changes aimed at promoting healthier living, a significant number of individuals continue to struggle and ultimately fail to attain sustainable weight loss, which has consequently led to an intensified search for alternative and more effective treatment options that can offer real solutions to this growing problem. In recent years, a class of medications known as GLP-1 receptor agonists - specifically, semaglutide, liraglutide, and dulaglutide - originally developed for and utilized in the treatment of type 2 diabetes, have unexpectedly gained renewed importance and recognition as groundbreaking pharmaceutical options in the realm of obesity management, showcasing their potential to make a significant impact in addressing this debilitating health issue [3].

Materials and Methods

The literature review was conducted based on scientific articles retrieved from PubMed, Google Scholar, Scopus, and Web of Science databases. The following search terms were used:”Glucagon-Like Peptide-1 Receptor Agonists, ”“obesity/therapy, ”“semaglutide, ”“liraglutide, ”“public health, ”“appetite regulation, ”“obesity epidemiology, ” and”tirzepatide, ” both individually and in various combinations. Only articles published in English were included. The analysis focused on studies examining the effects of GLP-1 receptor agonists on obesity treatment, appetite regulation, and the epidemiological and public health aspects of obesity. Studies not directly related to the review topic, those lacking detailed methodological descriptions, and articles raising concerns about the reliability of their findings were excluded.

Mechanism of Action of GLP-1 Receptor Agonists

Obesity is a disorder of energy homeostasis in which gut hormones - particularly glucagon-like peptide-1 (GLP-1) - play a crucial role. Endogenous GLP-1 is secreted by L-cells located in the distal small intestine and colon in response to food intake. It acts through specific GLP-1 receptors (GLP-1R), which are distributed throughout the body, with the highest concentrations found in the pancreas, central nervous system, and gastrointestinal tract [4]. In the pancreas, GLP-1 exerts a particularly important effect on the β-cells of the islets of Langerhans, where this hormone stimulates insulin secretion in a strictly glucose-dependent manner. This mechanism of action encompasses the activation of a Gs protein-coupled signaling pathway, which subsequently leads to an elevation in levels of cyclic AMP, followed by the activation of protein kinase A, and this entire cascade of biochemical events ultimately culminates in a marked enhancement of insulin release from pancreatic cells [5]. At the same time, GLP-1 suppresses glucagon release from α-cells both directly and indirectly by promoting the secretion of insulin and somatostatin, which results in a substantial decrease in hepatic glucose production [6]. Within the central nervous system, GLP-1 has particularly pronounced effects in the hypothalamus, where it regulates the activity of two essential groups of neurons in the arcuate nucleus - it activates neurons that produce proopiomelanocortin (POMC) while inhibiting neurons that release neuropeptide Y (NPY) and agouti-related peptide (AgRP). This intricate regulation leads to an average decrease in food consumption by 25–30% and a marked enhancement in satiety [7]. Additionally, GLP-1 acts on brain regions associated with reward, particularly the nucleus accumbens, where it reduces cravings for high-calorie foods and diminishes the hedonic component of food intake [8]. One particularly significant effect that GLP-1 receptor agonists possess is the ability to slow down the process of gastric emptying, which consequently leads to extended feelings of fullness, also known as satiety, while simultaneously resulting in a decrease in blood sugar levels following a meal, referred to as postprandial glycemia. This specific mechanism operates through the intricate influence on both the vagal nerve pathway and the direct impact it has on the smooth muscles that constitute the gastrointestinal tract [9]. GLP-1 receptor agonists, including liraglutide and semaglutide, have been designed to replicate the effects of endogenous GLP-1 while simultaneously prolonging their half-life. Liraglutide incorporates a fatty acid moiety that attaches to albumin, in contrast to semaglutide, which boasts additional amino acid alterations and an elongated chemical linker. These enhancements facilitate less frequent administration while sustaining effective therapeutic levels [10]. The most recent iterations of these medications, such as tirzepatide, provide extra advantages through a dual-action mechanism that engages not just GLP-1 receptors but also those for glucose-dependent insulinotropic polypeptide (GIP). This intricate mechanism produces a synergistic effect characterized by not only increased weight loss but also enhanced insulin sensitivity and other metabolic indicators [11]. Crucially, GLP-1 agonists demonstrate modulatory impacts on the inflammatory processes linked to obesity, including lowering inflammatory marker levels, diminishing pro-inflammatory cytokine synthesis, and enhancing endothelial function by mitigating oxidative stress and boosting nitric oxide availability. These mechanisms elucidate their positive effects on the metabolic complications associated with obesity [12].

Contemporary Approaches to Obesity Treatment Using GLP-1 Agonists

At present, GLP-1 receptor agonists are employed in managing both type 2 diabetes and obesity. Liraglutide, administered at a dosage of 3.0 mg/day, became the first medication from this class to receive FDA approval in 2014 for obesity treatment, showing a body weight decrease of roughly 8% when compared to a placebo [13]. A significant advancement in the field of weight management and obesity treatment was achieved with the introduction of semaglutide, which is administered at a weekly dosage of 2.4 mg, and this innovative medication, as demonstrated in a particular clinical study, resulted in participants experiencing an impressive average weight reduction of 14.9% following a comprehensive 68 weeks of consistent therapeutic intervention, while it is noteworthy that an astonishing 86% of the individuals involved in the study successfully attained a weight loss of at least 5% of their initial body weight as measured from baseline [14]. Even greater hopes are now intricately linked with the promising medication known as tirzepatide, which, in the context of the SURMOUNT-1 clinical trial, demonstrated the remarkable ability to induce a substantial reduction in body weight amounting to an impressive 20.9% when administered at a dosage of 15 mg per week, thus drawing ever closer to matching the level of effectiveness typically observed with bariatric surgery procedures [15]. It is important to emphasize that the benefits of treatment extend far beyond mere weight loss. Research shows that therapy with GLP-1 agonists leads to significant improvements in glycemic control (with an average HbA1c reduction of 1.0 to 1.8%), decreases in blood pressure (with systolic pressure reduced by 3 to 7 mmHg), and improvements in lipid profiles (with triglycerides decreasing by 10 to 20%) [16].

The Evolution of Therapeutic Strategies in Obesity Treatment Over Recent Years

In recent years, the strategy for treating obesity has experienced a remarkable evolution. While traditional methods like diet and exercise remain essential, they are increasingly supplemented by innovative pharmacological treatments. Progress in science and technology now enables more efficient and tailored therapies that not only facilitate weight loss but also enhance the overall well-being of patients. The traditional approach, mainly focused on lifestyle modification, has proven insufficient for most patients, who experienced the yo-yo effect and difficulties maintaining weight loss [17]. In this context, the emergence of potent antidiabetic medications that also facilitate weight loss has opened up novel therapeutic avenues. Previously utilized drugs, including orlistat and lorcaserin, were noted for their moderate effectiveness (weight reduction of 3-7%) alongside considerable adverse effects [18]. A significant advancement occurred with the introduction of medications originally designed for diabetes management, such as GLP-1 agonists, which have demonstrated a markedly enhanced efficacy in weight loss. At present, we are observing a rapid evolution of innovative therapeutic agents, with retatrutide - a groundbreaking triple agonist targeting GLP-1, GIP, and glucagon receptors - emerging as a key player. Initial findings from clinical studies suggest that retatrutide has the potential to facilitate weight loss exceeding 20%, positioning it as one of the most promising treatment options on the horizon [15]. Its unique mechanism of action, combining appetite control (GLP-1), improvement of insulin sensitivity (GIP), and increased energy expenditure (glucagon), opens new possibilities for the treatment of severe obesity. Moreover, ongoing research is also focusing on the increasingly popular oral formulations of GLP-1 agonists, which have great potential to improve patient adherence to therapy and increase accessibility to modern treatments [19]. The remarkable advancements that have been made in the field of pharmacology are closely linked with the ongoing progress in the field of personalized medicine, which consequently enables healthcare professionals to more effectively customize and adjust therapeutic interventions to precisely meet the unique and varied needs of each individual patient.

Analysis of the efficacy and safety of GLP-1 agonists in obesity

GLP-1 agonists are gaining increasing importance in the treatment of obesity, offering new therapeutic possibilities. Their effects go beyond mere weight reduction, also influencing metabolic processes. However, like any new treatment method, they require thorough evaluation of both efficacy and safety. Only through careful analysis is it possible to fully understand their potential and limitations. The efficacy of GLP-1 agonists in body weight reduction has been well documented in numerous randomized clinical trials. Results from multiple meta-analyses suggest a significant advantage of GLP-1 agonists over placebo in terms of weight loss, supported by data including over 25, 000 patients [20]. Semaglutide proved to be the most effective, causing a body weight reduction of 14.9% at doses of 2.4 mg/week compared to 2.4% in the placebo group [14]. When it comes to the aspect of safety, it is important to note that the most frequently observed adverse effects primarily involve the gastrointestinal system, which can manifest as symptoms such as nausea experienced by approximately 20–40% of patients, vomiting occurring in about 5–15% of individuals, and diarrhea reported by roughly 10–20% of those affected, all of which are typically transient in nature and tend to resolve spontaneously within a matter of a few weeks [21]. In exceptional instances (<1%), pancreatitis has been reported; nonetheless, the causal link remains uncertain [22]. Contrary to previous worries, extensive studies over the long term have not established a heightened risk of thyroid cancer in humans, although such risks were observed in studies involving rodents [23]. From a clinical standpoint, it is crucial to choose the medication not solely based on effectiveness but also taking into account tolerability and the preferences of the patient (for example, oral form vs. injectable form).

Table 1. Comparison of Clinical Efficacy of Selected GLP-1 Agonists in Obesity Treatment

Drug	Dose	Weight Loss (%)	Duration (weeks)	≥5% Weight Loss (%)	HbA1c ↓ (%)	Other Metabolic Effects	Common Adverse Effects
Liraglutide	3.0 mg/day	~8	56	63–70	~1.2–1.5	↓TG, ↓SBP	Nausea, diarrhea
Semaglutide	2.4 mg/week	14.9	68	86	~1.7–1.8	↓TG, ↓SBP, ↓LDL	Nausea, vomiting
Tirzepatide	15 mg/week	20.9	72	91	~2.0	↓TG, ↑ insulin sensitivity	Nausea, vomiting
Retatrutide	Investigational (prelim.)	>20	48	n.a.	n.a.	↑ energy expenditure	n.a.

Legend: TG – triglycerides, SBP – systolic blood pressure, LDL – LDL cholesterol, n.a. – not available

Source: based on [13, 14, 15, 16, 20, 26, 32]

Barriers and Challenges in the Use of GLP-1 Agonists

Despite their high efficacy, the use of GLP-1 agonists is associated with certain limitations. The high cost of therapy (approximately 800-1000 USD per month) represents a significant barrier in many healthcare systems [24], especially given the long-term nature of obesity treatment. Moreover, the need for injectable administration may discourage some patients; however, it is worth noting that the introduction of extended-release formulations (e.g., once-weekly injections) has improved treatment acceptance [25]. Another significant challenge lies in the requirement for prolonged usage of these medications - research indicates that most patients tend to gradually regain the lost body weight after stopping the treatment. This is supported by findings from the SURMOUNT clinical program, which revealed that to preserve metabolic benefits, continuous therapy with GLP-1 agonists is essential. In the instance of tirzepatide, which can facilitate weight loss of up to 20%, the cessation of treatment was linked to a gradual return to baseline body weight for the majority of patients. This

underscores the chronic nature of obesity and the vital need for ongoing, long-term treatment [26]. An important limitation also includes medical restrictions, such as a personal or family history of medullary thyroid carcinoma and multiple endocrine neoplasia syndrome type 2 (MEN 2) [27]. In the context of public health, it is crucial to identify patients who are likely to benefit the most from treatment, in order to make optimal use of limited resources [28]. It is important to keep in mind that pharmacological treatment inherently involves the possibility of specific side effects or the existence of contraindications. Consequently, it is crucial to thoughtfully evaluate if anti-obesity pharmacotherapy represents the most suitable choice for a particular patient and if alternative weight loss methods have been thoroughly investigated.

Socio-health implications of obesity treatment with GLP-1 agonists

The implementation of effective pharmacotherapy for obesity could greatly influence public health. Projections derived from mathematical models indicate that the extensive adoption of semaglutide among individuals with obesity and prediabetes might lead to a reduction in the occurrence of type 2 diabetes by nearly 50% within a decade [29]. Economic analyses indicate that, although the cost of therapy is relatively high, the reduction in obesity-related complications - such as diabetes, coronary artery disease, and non-alcoholic fatty liver disease - may result in substantial long-term healthcare savings. It is estimated that each one-percent reduction in body weight at the population level translates into approximately a 2–3% decrease in obesity-related healthcare costs [31]. Fully harnessing the potential of GLP-1 agonists requires addressing treatment accessibility through reimbursement policies, monitoring programs, and the education of both physicians and patients [32]. It is important to highlight and emphasize the fact that GLP-1 agonists have the potential to contribute significantly to the reduction of health disparities, especially considering that obesity tends to be particularly widespread and disproportionately affects individuals belonging to populations that are categorized as having lower socioeconomic status, who, in addition, often face significant barriers that limit their access to effective and necessary treatments for this condition [33]. Beyond their advantages for public health, the influence of GLP-1 agonists on energy balance, appetite control, and metabolic efficiency prompts further inquiry into their overall physiological effects. These processes, initially examined in relation to disease, could have consequences for athletic performance, body composition, and recovery - elements that are gaining greater attention within the field of sports science.

The role of physical activity in modulating the effects of GLP-1

In recent years, there has been an increasing curiosity regarding the potential interplay between GLP-1 receptor agonist pharmacotherapy and physical activity in addressing obesity. Both incretin-based therapies and consistent exercise offer positive impacts on glucose-insulin metabolism, appetite control, and the body’s energy expenditure. Many studies indicate that combining these therapies may enhance results beyond what each can achieve individually. This section will explore how physical activity affects the incretin system and its relationship with GLP-1 agonists for weight loss and metabolic improvement.

Physical exercise has been demonstrated to have a beneficial effect on endogenous GLP-1 levels, aiding in enhanced metabolic regulation, especially in those with type 2 diabetes. Different types of physical activity, such as both aerobic exercises and resistance training, can boost incretin levels depending on the intensity, duration, and frequency of the workouts. A significant mechanism behind this phenomenon is the rise in interleukin-6 (IL-6) triggered by exercise, a cytokine recognized for promoting GLP-1 release from intestinal L-cells and pancreatic α-cells. This process involves the upregulation of proglucagon and prohormone convertase 1/3 expression, both crucial for GLP-1 biosynthesis. Growing clinical evidence supports the idea that physical activity can influence the secretion of incretin hormones. Short sessions of acute exercise in healthy individuals have been shown to raise lactate and interleukin-6 (IL-6) levels. These increases are believed to stimulate GLP-

1 release, which helps regulate appetite and support energy balance. After exercise, a temporary reduction in hunger is often observed. This is accompanied by a decrease in ghrelin, the hormone responsible for stimulating appetite, and a rise in circulating GLP-1 levels. In individuals with type 2 diabetes, extended periods of moderate-intensity physical activity, approximately 90 minutes long, have demonstrated encouraging results. Levels of IL-6 rise significantly, while the concentrations of GLP-1 and GIP remain elevated for as long as 24 hours following exercise. Even with these hormonal fluctuations, postprandial levels of insulin, glucagon, and glucose generally stay stable. These observations imply that exercise may exert a prolonged influence on incretin activity, irrespective of immediate variations in blood glucose. While existing research indicates a favorable link between physical activity and GLP-1 secretion, the extent of this relationship seems to be influenced by the length and intensity of the exercise. It is suggested that more than 30 minutes of exercise at an intensity above 70% of the ventilatory threshold may be necessary to elicit a measurable increase in GLP-1 levels. However, additional research is required to identify the most effective exercise strategies for boosting GLP-1 secretion and optimizing metabolic advantages in individuals with type 2 diabetes and obesity [34], especially given that the combination of semaglutide with lifestyle changes, including physical activity, has been shown to produce clinically meaningful and sustained weight loss. This suggests that physical activity may enhance the therapeutic effects of GLP-1 agonists such as semaglutide, leading to improved outcomes in weight management [35]. It is essential to recognize that individuals might react differently to treatment. Personal factors such as adherence to lifestyle modifications, initial metabolic condition, and sensitivity to side effects can greatly influence results. Although semaglutide has demonstrated considerable effectiveness, it may not be the ideal option for everyone. Importantly, while semaglutide-induced weight loss is largely attributed to reductions in fat mass, emerging data suggest that some of the lost weight may also come from lean tissue. This becomes particularly relevant in physically active individuals and athletes. For these populations, preserving muscle mass is essential. It supports performance, prevents injury, and plays a key role in metabolic health. Extensive clinical trials have reported reductions in lean body mass while undergoing semaglutide therapy. This underscores the importance of adopting measures that safeguard muscle health. Including resistance training or regular physical activity in the therapeutic approach may help offset this effect. Doing so can promote healthier body composition and enhance outcomes in individuals aiming to balance weight loss with physical performance [36].

GLP-1 Pharmacotherapy in Physically Active Individuals: From Medical Treatment to Aesthetic and Performance-Oriented Use

The interest surrounding GLP-1 agonists is not only expanding within the confines of their traditional medical applications but is also beginning to reach into various other realms of health and fitness. A growing number of physically active individuals and competitive athletes are increasingly turning to these pharmacological agents in their pursuit of improved body composition and enhanced athletic performance. Nevertheless, the off-label utilization of these medications inevitably carries inherent risks and raises significant ethical considerations that cannot be overlooked. There is a societal trend towards favoring pharmacological solutions over lifestyle interventions, which may overshadow the importance of diet and exercise in sustainable weight management. The increasing interest in GLP-1 receptor agonists within the training community stems from their ability to enhance appetite control and facilitate weight reduction while potentially preserving strength. These drugs, by mimicking the action of GLP-1, promote satiety and influence hunger-regulating pathways, making them appealing for those seeking weight loss. This trend is driven by the relative simplicity and availability of medications, along with the belief that they can produce quick and noticeable outcomes. Pharmaceutical companies have reacted to this demand by developing a range of weight-loss drugs, many of which are derived from the actions of GLP-1 receptor agonists. However, this emphasis on pharmacotherapy may overshadow the crucial importance of nonpharmacological strategies in the prevention and management of chronic diseases [37]. Despite this, the physiological mechanisms that

these drugs influence have gained attention from athletes and physically active individuals. Enhanced energy regulation and improved fat oxidation are crucial elements. Tirzepatide seems particularly intriguing in this regard. It is appreciated not only for facilitating weight loss but also for its potential to enhance metabolic efficiency during endurance exercises. This drug stands out among the new GLP-1/GIP receptor agonists due to its ability to optimize fat metabolism. It has a beneficial effect on aerobic endurance by delaying the depletion of glycogen stores, which supports the maintenance of exercise intensity over extended periods. The fundamental biological mechanisms that are at play involve a significant enhancement of mitochondrial function along with an increase in biogenesis, which in turn contributes to a heightened intensity of oxidative phosphorylation, a crucial energy-producing process that is particularly vital in endurance sports disciplines such as long-distance running, competitive cycling, or the demanding activity of swimming. Furthermore, the activation of GIP receptors by the therapeutic agent tirzepatide encourages thermogenesis as well as the process of fat oxidation, which collectively leads to a notable improvement in overall metabolic efficiency, thereby facilitating better energy utilization in the body. In addition to its beneficial effects on metabolism, tirzepatide may support recovery after intense physical exertion. Due to its anti-inflammatory properties and enhanced insulin sensitivity, this medication alleviates oxidative stress and minimizes muscle injury resulting from exercise. Increased glucose availability and accelerated glycogen resynthesis have also been observed, which speeds up the restoration of muscle energy, especially in athletes undergoing heavy training loads or competing with short recovery intervals. Tirzepatide can thus enhance recovery efficiency, lessen fatigue, and decrease the likelihood of overtraining [38]. Nevertheless, it is equally crucial to take into account possible negative impacts - particularly in athletes, where even the slightest change in muscle mass and electrolyte levels can be significant. Research has indicated a decline in lean body mass, which encompasses a reduction in muscular fat tissue. This decrease in muscle mass and strength could adversely affect athletic performance [39]. Furthermore, there is a small but real risk of exercise-induced hypoglycemia, particularly during high-intensity training or when carbohydrate intake is insufficient. Additionally, risks such as electrolyte imbalances and delayed gastric emptying should not be overlooked, as they can affect hydration and nutrient absorption.

Legal and Ethical Aspects of GLP-1 Use in Physically Active and Athletic Populations

Glucagon-like peptide-1 (GLP-1) receptor agonists such as liraglutide, semaglutide, and tirzepatide have been approved by regulatory authorities including the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of obesity in individuals with a body mass index (BMI) ≥30 kg/m², or ≥27 kg/m² in the presence of obesity-related comorbidities such as type 2 diabetes or hypertension. Their therapeutic uses are specifically restricted to populations at metabolic risk and do not encompass healthy individuals, recreational athletes, or professional sportspeople who possess normal or slightly elevated BMI values. Consequently, employing GLP-1 receptor agonists in individuals with a BMI of less than 30 and without qualifying comorbidities is regarded as off-label, thus falling outside the sanctioned regulatory framework. At present, there is no official endorsement for their use in areas like performance enhancement, physical rehabilitation, or aesthetic body modification. Although their popularity is increasing in these fields, the lack of clinical approval for such purposes raises ethical and legal issues concerning their regular or preventive application in sports medicine and fitness practices. Additionally, ethical concerns arise regarding the potential classification of GLP-1 agonists as a form of doping, especially in cases where they are used by physically active individuals or athletes without obesity. While these medications are not presently part of the World Anti-Doping Agency (WADA) banned substances list, their potential to enhance body composition, metabolic adaptability, and recovery could indirectly boost athletic performance, prompting concerns regarding the adherence to fair play principles. Another issue is the inequality in access to these medications. Their high cost and off-label status may give an advantage to wealthier athletes or those affiliated

with well-funded clubs and sports organizations. Consequently, there is an immediate necessity for well-defined ethical and legal guidelines to tackle the increasing fascination with the non-medical application of metabolic drugs in the sports community. In the absence of such regulation, their usage may become rampant and jeopardize the principles of fair competition [40, 41].

Conclusions

Obesity is a chronic metabolic disease that poses a significant challenge to modern medicine. In recent years, a breakthrough in its treatment has been achieved with drugs targeting the hormonal system, particularly GLP-1 receptor agonists. This class of medications mimics the action of natural gut hormones, offering comprehensive benefits—from weight reduction to improvement in metabolic parameters. Clinical studies confirm their effectiveness, demonstrating not only substantial weight loss (reaching even double-digit percentages) but also improvements in glycemic control, lipid profile, and blood pressure. Importantly, the therapy has a relatively favorable safety profile, although it requires regular monitoring, mainly due to potential gastrointestinal side effects. Moreover, the impact of GLP-1 agonists on public health is significant. By reducing obesity-related complications such as type 2 diabetes and cardiovascular diseases, they may contribute to lessening the burden on healthcare systems. Although the high cost of therapy poses a challenge, economic analyses suggest that investing in this form of treatment can yield long-term savings by reducing expenditures on managing obesity complications. GLP-1 receptor agonists have thus opened new possibilities in the fight against the global obesity epidemic, combining clinical benefits with a positive impact on population health. Analyses indicate that combining GLP-1 receptor agonist therapy with physical activity may provide synergistic benefits in the treatment of obesity and metabolic improvement. Physical exercise, especially of moderate to high intensity, stimulates the secretion of endogenous GLP-1, which supports appetite control and energy balance. However, the effectiveness of this interaction depends on the type, duration, and intensity of exercise, requiring further research to optimize training protocols.

It has been shown that pharmacotherapy combined with lifestyle modification, including regular physical activity, leads to sustained weight loss. However, the use of GLP-1 agonists is also associated with loss of lean body mass, which may negatively affect physical performance, particularly in athletes. Therefore, resistance training is recommended to minimize muscle mass loss. The increasing off-label use of GLP-1 agonists among active individuals and athletes raises ethical and legal controversies. Despite potential benefits such as improved metabolism and faster recovery, their off-label use for aesthetic or ergogenic purposes poses risks of inequality in sports and may undermine the principles of fair play. Therefore, clear regulations regarding the use of these drugs in populations outside approved medical indications are necessary.

Disclosures

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