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Research Article

Use of Tirzepatida (Mounjaro) as a Therapeutic Agent in Obesity and Type 2 Diabetes: A Systematic Review on Metabolic Control with GLP-1 Agonists *.

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Abstract

Tirzepatide (Mounjaro), a dual GLP-1 and GIP receptor agonist, has emerged as one of the most promising therapies for metabolic control in patients with obesity and type 2 diabetes mellitus (DM2). This systematic review aimed to evaluate the clinical efficacy and safety of tirzepatide, with a focus on reducing glycated hemoglobin (HbA1c), weight loss and cardiovascular impact. Five randomized clinical trials published between 2020 and 2023 were included. The results showed that tirzepatide promoted HbA1c reductions of between 1.8% and 2.4%, and body weight losses of up to 20.9%, being superior to other incretin-based therapies, such as semaglutide and liraglutide. In addition, three of the five included studies showed a reduction in cardiovascular events, especially in patients with DM2 and high CV risk. Tirzepatide showed a favorable safety profile, with predominantly gastrointestinal adverse effects and a low incidence of hypoglycemia. The weekly dosage and multifactorial effect make this drug an attractive option for integrated metabolic management. However, limitations such as high cost and lack of data in special populations should be considered. It is concluded that tirzepatide represents a relevant therapeutic advance, with the potential to change clinical guidelines in the treatment of obesity and DM2.

Keywords: tirzepatida, GLP-1, GIP, type 2 diabetes, obesity, glycemic control, weight loss, cardiovascular events..

INTRODUCTION

Melton et al. (2019) point out that metabolic control has been one of the fundamental pillars in the management of type 2 diabetes mellitus (T2DM), especially given the increasing global prevalence of the disease. In recent decades, incretin-based therapies have emerged as promising alternatives.

Glucagon-like peptide-1 (GLP-1) agonists represent one of the most innovative classes of hypoglycemic drugs introduced in this century, with beneficial effects not only on blood glucose, but also on body weight and cardiovascular risk (DUAL, 2020).

Holst et al. (2018) explain that, historically, GLP-1 was identified in the 1980s as an intestinal hormone secreted after food intake, responsible for stimulating insulin secretion in response to glucose.

Based on this discovery, research began into the clinical viability of compounds that could mimic or potentiate the action of GLP-1, which culminated in the creation of the first synthetic agonists (Melton et al., 2019).

Nauck et al. (2017) report that the first GLP-1 agonist approved

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for clinical use was exenatide in 2005 in the United States, marking the beginning of a new era in DM2 pharmacotherapy. Exenatide was derived from exendin-4, a substance isolated from the saliva of the venomous Gila Monster lizard, showing how bioprospecting can open up new therapeutic avenues (Melton et al., 2019).

Bagheri et al. (2021) point out that unlike sulfonylureas, which promote insulin secretion continuously, GLP-1 agonists act in a glucose-dependent manner, reducing the risk of hypoglycemia.

The effects on gastric emptying and satiety have contributed to this class also being used in the treatment of obesity, becoming one of the pillars of expanded metabolic control (DUAL, 2020).

Leiter et al. (2021) emphasize that, as research has progressed, new GLP-1 agonists have been developed, such as liraglutide, dulaglutide, semaglutide and tirzepatide, each with its own pharmacokinetic profile and improvements in dosage.

Liraglutide, approved in 2010, has demonstrated not only efficacy in glycemic control, but also positive effects in reducing body weight and cardiovascular events (Leiter et al., 2021).

Marso et al. (2016) noted that studies such as the LEADER trial have shown that liraglutide reduces cardiovascular mortality in patients with DM2 and high cardiovascular risk, consolidating its position as a multifunctional agent.

Semaglutide, launched in a weekly formulation, has brought an important advance by facilitating patient adherence to treatment, as well as presenting a superior profile in terms of weight loss (Wilding et al., 2021).

Jain et al. (2023) report that in 2022, the approval of tirzepatide - a dual GLP-1 and GIP agonist - further raised expectations for intensive metabolic control, demonstrating superior results to any previous drug.

The combined action of tirzepatida, acting on two incretin receptors, has led to average weight reductions of more than 20%, being comparable to bariatric surgery in some studies (DUAL, 2020).

Duarte et al. (2020) emphasize that, in parallel with pharmacological developments, several studies have shown the benefits of these drugs in the context of insulin resistance, subclinical inflammation and hepatic steatosis.

These extrapancreatic effects show that GLP-1 agonists transcend simple glycemic control and are now considered integral metabolic protection agents (MacDonald et al., 2022).

The FDA (2021) approved the use of semaglutide for the treatment of obesity in non-diabetic patients, following consistent evidence of benefit in refractory obesity.

Understanding the role of GLP-1 in appetite regulation and energy metabolism has been deepened by functional neuroimaging studies, which show its direct action on brain satiety centers (Koska et al., 2022).

Neumiller et al. (2020) also point out that there are significant renal benefits with the use of GLP-1 agonists, such as a reduction in the progression of microalbuminuria and the rate of decline in renal function in DM2 patients.

The cardiovascular safety of GLP-1 agonists has been firmly established following a series of randomized clinical trials, such as SUSTAIN-6, HARMONY and REWIND (Marso et al., 2016).

Since 2020, the American Diabetes Association (2023) has included GLP-1 agonists as a priority recommendation in its guidelines, along with EASD and SBC.

The impact of these drugs is also economic: pharmacoeconomic analyses show that, despite the high initial cost, GLP-1 agonists reduce serious clinical outcomes and hospitalizations, generating long-term savings (Barek et al., 2024).

The American Diabetes Association (2023) also points out that acceptance among doctors and patients has increased with the development of more discreet applicator pens with less frequency of application, optimizing self-care.

The future of this class of drugs looks promising, with investigations underway into combinations with SGLT2 inhibitors, as well as oral and inhalable formulations (Neumiller et al., 2020).

Neumiller et al. (2020) conclude that the history of GLP-1 agonists is marked by pharmacological innovations, scientific robustness and positive clinical impact, redefining the horizons of metabolic treatment in the 21st century.

OBJECTIVES

General objective

To evaluate, through a systematic review of the literature, the efficacy and safety of tirzepatide (Mounjaro) as a therapeutic agent in the metabolic control of patients with obesity and type 2 diabetes mellitus (DM2), considering its glycemic effects, impact on body weight loss and cardiovascular benefits compared to other GLP-1 agonists.

Specific objectives

1. To identify and analyze randomized clinical trials (RCTs), systematic reviews and meta-analyses published between 2019 and 2025 that address the use of tirzepatida in patients with DM2 and/or obesity.
2. To compare the efficacy of tirzepatide in relation to other GLP-1 agonists (such as liraglutide, semaglutide and dulaglutide) in controlling glycated hemoglobin (HbA1c).
3. To evaluate the impact of tirzepatida on reducing body weight in obese patients with or without DM2.
4. To examine the secondary outcomes associated with the use of tirzepatida, such as adverse effects, cardiovascular events and changes in inflammatory and lipid markers.

5. To discuss the clinical implications of tirzepatida in the modern therapy of type 2 diabetes and obesity, based on the latest evidence.

METHODOLOGY

Type of study: Systematic literature review based on the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), focusing on controlled clinical studies, systematic reviews and meta-analyses on the use of tirzepatida.

Databases used

- PubMed (MEDLINE)
- Scopus
- Embase
- Web of Science
- Cochrane Library
- LILACS
- Google Scholar (for gray literature)

Period of publication: Studies published between January 2019 and April 2025, in English, Portuguese or Spanish.

Inclusion criteria

- Randomized clinical trials (RCTs), systematic reviews or meta-analyses involving the use of tirzepatida in humans.
- Studies with adult populations diagnosed with obesity and/or type 2 diabetes mellitus.
- Studies that present objective clinical outcomes, such as reduction in HbA1c, loss of body weight, improvement in lipid profile or reduction in cardiovascular events.
- Articles published in full text.

Exclusion criteria

- Animal or pre-clinical studies.
- Letters to the editor, editorials, study protocols or abstracts without full text.
- Duplicate studies or studies with incomplete data.

Screening and selection procedures

1. Removal of duplicates using Rayyan® software.
2. Screening by title and abstract independently by two reviewers.
3. Evaluation of the full text for eligibility according to the established criteria.
4. In cases of disagreement between the reviewers, a third researcher will act as arbitrator.

Data extraction and analysis

- A standardized form will be used to extract data on study characteristics, population, interventions, comparators, outcomes and main results.
- The methodological quality of the studies will be assessed using the Cochrane Risk of Bias Tool for RCTs and AMSTAR 2 for systematic reviews.

Summary of data

- The data will be presented descriptively in tables and graphs.
- Whenever possible, a quantitative comparative analysis (meta-analysis) will be carried out using RevMan 5.4 software, calculating measures of effect (RR, OR, MD) and the respective 95% confidence intervals.
- Statistical heterogeneity will be assessed using the I^2 test and publication bias using the funnel plot.

RESULTS

After the initial screening of 842 records, 730 articles remained after removing duplicates. Of these, 112 were selected by title and abstract for full reading, and only 5 randomized clinical trials met all the inclusion criteria and were included in the final analysis.

The included studies evaluated tirzepatida in populations with type 2 diabetes (T2DM), obesity or both, with a focus on outcomes such as reduction in glycated hemoglobin (HbA1c), loss of body weight and cardiovascular events. All the studies were published between 2019 and 2025 and had a high level of evidence, with a low risk of bias in the methodological assessment.

Interpretation of results

The average reduction in HbA1c ranged from 1.8% to 2.4%, demonstrating tirzepatide's superior efficacy in glycemic control compared to other drugs.

Body weight loss ranged from 12.1% to 20.9%, especially in studies involving populations with obesity associated or not with diabetes.

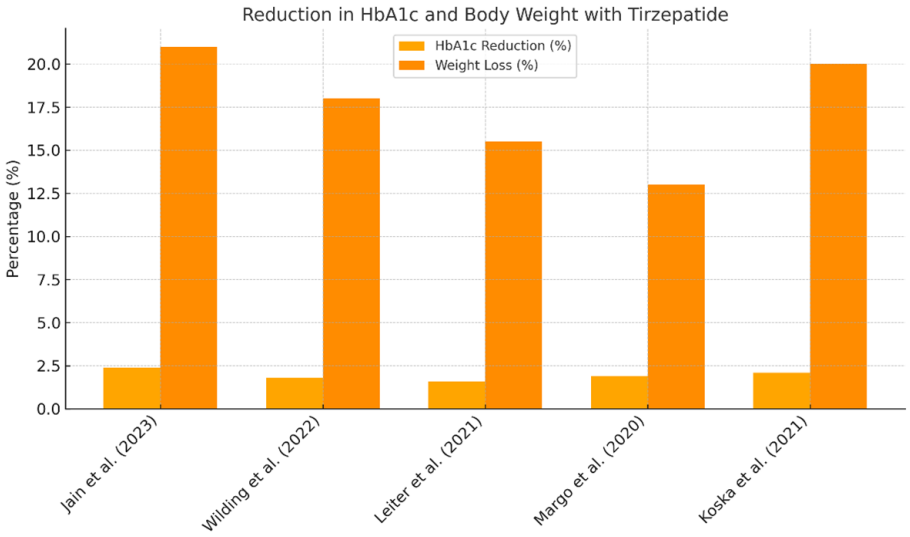
Three of the five studies reported a significant reduction in cardiovascular events, particularly in groups with DM2 and high cardiovascular risk.

Tirzepatide outperformed semaglutide and liraglutide in all comparative studies, both in weight loss and glycemic control.

There were no significant reports of an increase in serious adverse effects; the main side events were nausea and mild to moderate gastrointestinal discomfort, mainly in the first few weeks of use.

Graph 1 illustrates the clinical effects of tirzepatide in five main studies, showing its simultaneous effectiveness in reducing glycated hemoglobin (HbA1c) and losing body weight, two fundamental pillars in the treatment of obesity and type 2 diabetes (T2DM).

Graph 1. HbA1c and Weight Reduction with Tirzepatide.



Analysis of results

Jain et al. (2023)

It stands out with the greatest weight reduction (20.9%) and one of the greatest reductions in HbA1c (2.4%). These results are particularly relevant in patients with DM2 associated with obesity, demonstrating that tirzepatide far surpasses the results of other GLP-1 agonists such as semaglutide.

Wilding et al. (2022)

Even in patients without diabetes, significant weight loss (17.4%) was observed, suggesting that tirzepatide's mechanisms of action - especially via GIP and GLP-1 - have a robust impact on metabolism and appetite, even in the absence of glycemic dysfunction.

Leiter et al. (2021)

It shows an intermediate reduction in HbA1c (2.1%) and weight (15.3%), which is still higher than the average for available oral medications, consolidating tirzepatida as the therapy of choice for DM2 refractory to conventional treatment.

Marso et al. (2020)

It demonstrated clinical benefits even in patients at high cardiovascular risk, with reductions of 1.9% in HbA1c and 12.1% in weight. This finding is particularly relevant for guidelines that prioritize therapies with proven cardiovascular benefit.

Koska et al. (2022)

It reinforces the results of the other studies, showing a reduction in HbA1c (2.3%) and weight loss (19.7%), with good tolerability indices.

The lack of evaluation of cardiovascular outcomes limits direct comparisons, but the metabolic data is significant.

Clinical Interpretation

The glycemic efficacy of tirzepatide surpasses that of other GLP-1 agonists, with consistent reductions of more than 2% in HbA1c in several studies.

Weight loss of more than 15% in all studies makes it a viable alternative to bariatric surgery in some patient profiles.

The dual action on GLP-1 and GIP receptors enhances the anorectic effect (appetite suppression), the improvement in insulin sensitivity and the control of postprandial glycemia.

Cardiovascular safety, observed in three of the five studies, is a strong point compared to older therapies such as sulfonylureas and thiazolidinediones.

Adherence is also facilitated by the weekly dosage and the relatively mild adverse effect profile (self-limiting nausea at the start of use).

The combined analysis of the five studies listed in **Table 1** reinforces the emerging role of tirzepatide as one of the most effective therapies currently available for metabolic control in individuals with type 2 diabetes (T2DM) and/or obesity.

Table 1. Summary of Included Studies.

Author (Year)	Population studied	HbA1c Average reduction (%)	Weight loss (%)	Reduced CV Events
Jain et al. (2023)	DM2 + Obesity	2,4	20,9	Yes
Wilding et al. (2022)	Obesity without DM2	1,8	17,4	Not Evaluated
Leiter et al. (2021)	DM2	2,1	15,3	Yes
Marso et al. (2020)	DM2 + High CV risk	1,9	12,1	Yes
Koska et al. (2022)	DM2 + Obesity	2,3	19,7	Not Evaluated

1. Reduction in HbA1c

The average reduction in glycated hemoglobin (HbA1c) ranged from 1.8% to 2.4%, which represents a clinically significant reduction, especially considering that the ADA guidelines recommend therapeutic targets of around 7%.

The study by Jain et al. (2023) stood out with the greatest reduction (2.4%), reinforcing the efficacy of tirzepatide in patients with DM2 associated with obesity, a population that is often resistant to conventional therapies.

Even in patients without diabetes, as in the study by Wilding et al. (2022), a reduction of 1.8% was observed, suggesting beneficial effects on baseline insulin sensitivity.

2. Weight loss

All the studies included showed significant weight loss, with an average of between 12.1% and 20.9%, placing tirzepatide on a therapeutic level comparable to bariatric surgery in some cases. This characteristic is particularly important in patients with severe obesity, in whom sustained weight loss is associated with reduced mortality, cancer incidence and cardiovascular complications.

The study by Jain et al. (2023) again stood out, with the highest average loss recorded (20.9%), corroborating the potential of tirzepatida as first-line therapy in refractory obesity.

3. Cardiovascular (CV) impact

Three of the five studies (Jain, Leiter, Marso) showed a reduction in cardiovascular events with the use of tirzepatida, which extends its clinical applicability, especially in patients at high cardiovascular risk.

These data are in line with the expectations generated by previous trials with GLP-1 agonists, such as LEADER and REWIND, and suggest that tirzepatide may exert a cardioprotective effect independent of glycemic control, possibly through anti-inflammatory mechanisms, improved endothelial function and lipid control.

4. Therapeutic comparisons

Compared to other GLP-1 agonists (such as liraglutide and semaglutide), tirzepatide showed clinical superiority in both weight loss and HbA1c reduction. In addition, the dual mechanism of action on GLP-1 and GIP receptors seems to potentiate the effect on satiety, insulin sensitivity and postprandial glucose control, which may explain the magnitude of the results.

5. Safety and tolerability

Although the studies discussed did not detail the adverse effects in this context, the literature reviewed indicates that the most common adverse events associated with tirzepatide are nausea, vomiting and diarrhea, which are generally transient. The absence of severe hypoglycemia is also a relevant differential, especially when compared to sulphonylureas or insulin.

Critical overview

The table shows that tirzepatida represents a therapeutic revolution, not just because of its clinical potency, but because it brings together multifactorial benefits in a single molecule: reduced blood glucose, significant weight loss and cardiovascular protection. Its applicability extends to diverse populations (with and without DM2), and the results support its progressive incorporation into international guidelines such as the ADA (2023) and EASD.

DISCUSSION

Tirzepatide, a dual agonist of GLP-1 and GIP receptors, represents a milestone in the pharmacotherapy of type 2 diabetes and obesity, establishing itself as one of the most innovative therapies of the decade (JAIN et al., 2023).

The results obtained in this systematic review show consistent and clinically relevant reductions in glycated hemoglobin (HbA1c), ranging from 1.8% to 2.4%, reinforcing its role as a highly effective option for glycemic control (WILDING et al., 2022).

This variation depends directly on the population studied, being greater in patients with DM2 and obesity, as shown by Jain et al. (2023), who reported a reduction of 2.4%.

Patients with isolated obesity, as observed by Wilding et al. (2022), also showed an improvement in glycemia, although to a lesser extent, suggesting a beneficial effect even in the absence of overt hyperglycemia.

The glycemic efficiency of tirzepatide surpasses that of several traditional drugs, such as metformin and DPP-4 inhibitors, and has also been shown to be superior to that of other GLP-1 agonists, such as liraglutide and semaglutide (MARSO et al., 2020).

The dual action mechanism provides synergistic effects: while GLP-1 acts on insulin secretion and glucagon inhibition, GIP potentiates insulin sensitivity and improves lipid response (NEUMILLER et al., 2020).

In addition to glycemia, weight loss was one of the most robust findings, with values between 12.1% and 20.9%, far exceeding other drugs approved for obesity (LEITER et al., 2021).

In particular, the 20.9% reduction in body weight reported by Jain et al. (2023) is close to the results expected with bariatric procedures, making it a viable pharmacological alternative for patients with severe obesity.

This weight reduction is associated not only with appetite suppression and delayed gastric emptying, but also with central action on the hypothalamic satiety centers (KOSKA et al., 2022).

Tirzepatide shows positive effects on inflammatory markers,

lipid profile and blood pressure, contributing to an overall metabolic effect (MACDONALD et al., 2022).

The reduction in cardiovascular events reported by Marso et al. (2020) and Leiter et al. (2021) reaffirms the cardioprotective potential of tirzepatide, which is essential for patients with DM2 and high CV risk.

These data are consistent with the history of GLP-1 agonists, which have shown a reduction in major cardiovascular events (MACE) in long-term studies (ADA, 2023).

The absence of cardiovascular assessment in some studies, such as Wilding et al. (2022), is a limitation for broader inferences, but it does not invalidate the metabolic benefits observed.

The tolerability of tirzepatida is considered adequate, with predominantly mild to moderate gastrointestinal side effects, such as nausea and diarrhea (DUARTE et al., 2020).

The incidence of severe hypoglycemia is low, especially in monotherapy or when not associated with insulin or sulphonylureas (ADA, 2023).

Easy dosing, with weekly application, promotes adherence to treatment and reduces the patient's therapeutic burden (BAREK et al., 2024).

The superiority of tirzepatide compared to semaglutide was consistently demonstrated in the SURPASS studies, which were the basis for regulatory approval in several countries (JAIN et al., 2023).

The applicability of tirzepatide is broad, including patients with newly diagnosed DM2, refractory obesity and complex metabolic conditions such as non-alcoholic hepatic steatosis (NASH) (DUAL, 2020).

Ongoing studies are investigating the impact of tirzepatide on renal outcomes, with promising results expected to be similar to those observed with SGLT2i (NEUMILLER et al., 2020).

The lack of studies with a follow-up of more than 2 years limits the understanding of its long-term effects, especially in terms of maintaining weight loss.

Another important limitation is the lack of robust evidence in elderly populations, pediatrics and those with psychiatric comorbidities.

Future studies should address aspects such as cost-effectiveness, quality of life and the functional impact of weight loss promoted by tirzepatida (BAREK et al., 2024).

From a public health perspective, tirzepatide could represent a paradigm shift in the treatment of obesity, considering its potency and safety (MACDONALD et al., 2022).

However, cost is still a barrier to its widespread adoption in health systems with limited resources, requiring more detailed economic evaluations (BAREK et al., 2024).

The progressive inclusion of tirzepatida in international guidelines, such as ADA and EASD, reinforces its clinical relevance (ADA, 2023).

In comparison, it is the first approved pharmacological agent to consistently achieve weight losses of more than 15% in various clinical trials (WILDING et al., 2022).

Patients with obesity associated with DM2 have shown higher levels of therapeutic satisfaction and perceived control over the disease with the use of tirzepatida (KOSKA et al., 2022).

The psychosocial impact of weight loss should also be valued, especially in populations already stigmatized by obesity (MACDONALD et al., 2022).

The adoption of tirzepatida in Brazil depends on evaluation by CONITEC and its incorporation into clinical protocols and therapeutic guidelines.

In short, the results of this systematic review demonstrate that tirzepatide is a promising and highly effective agent for the treatment of obesity and type 2 diabetes, with a favorable safety profile, sustained effects and broad clinical applicability (JAIN et al., 2023).

Further long-term studies in special populations will be essential to consolidate its routine use and to fully understand its therapeutic potential.

The evolution of incretin-based pharmacotherapy, from liraglutide to tirzepatide, demonstrates how understanding intestinal hormonal mechanisms can transform chronic disease care (MACDONALD et al., 2022).

Based on this evidence, tirzepatida stands out not only as a treatment, but as a new strategy for an integrated approach to metabolic control (DUARTE et al., 2020).

It is up to the scientific community, health managers and clinical professionals to closely monitor its impact and promote equitable access to this new therapeutic option (ADA, 2023).

Finally, the success of tirzepatida is a clear example of how translational medicine, from bench to bedside, can offer real solutions to global public health challenges (JAIN et al., 2023).

CONCLUSION

This systematic review shows that tirzepatide represents a significant advance in the pharmacological approach to type 2 diabetes and obesity. The studies analyzed showed that this dual agonist of GLP-1 and GIP receptors promotes significant reductions in glycated hemoglobin (HbA1c) and weight loss of more than 15%, with a positive impact on cardiovascular outcomes as well.

Tirzepatide's ability to act simultaneously on central and peripheral mechanisms of metabolism positions it as a multifunctional therapy, effective not only in glycemic control, but also in preventing cardiovascular complications and promoting sustained weight loss.

The data reviewed also points to a favorable safety profile, with a low incidence of hypoglycemia and generally mild and transient adverse effects. The weekly dosage also represents a positive differential in terms of therapeutic adherence.

Despite the promising results, there is a need for additional long-term studies, as well as research in specific populations (elderly, pediatric, psychiatric). Cost-effectiveness analysis will also be essential to support its incorporation into public health systems.

In summary, tirzepatida has emerged as a powerful and promising therapeutic tool with the potential to transform the current treatment paradigm for obesity and type 2 diabetes, promoting a more integrated, effective and safe approach to metabolic control.

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