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Original Research Article

Tirzepatide vs. Semaglutide: A Comparative Study on Glycemic Control and Weight Loss in T2DM

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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is a prevalent metabolic disorder that significantly impacts global public health, leading to complications such as cardiovascular diseases, kidney failure, and neuropathy. Glycemic control and weight management are crucial in preventing T2DM-related complications. "Recently, Tirzepatide and Semaglutide, two glucagon-like peptide-1 (GLP-1) receptor agonists, have gained attention for their promising effects in improving both glycemic control and weight loss in T2DM patients. However, a comparative study on the efficacy of these two drugs is limited.

Objectives: The primary objective of this study was to compare the efficacy of Tirzepatide and Semaglutide in glycemic control (measured by HbA1c levels) and weight loss in patients with T2DM. The secondary objective was to assess any significant differences in other clinical parameters such as blood glucose levels and lipid profile.

Methodology: A randomized controlled trial was conducted at PMCH from January 2025 to June 2025, with a sample size of 100 participants. The patients were randomly assigned to either the Tirzepatide group or the Semaglutide group. The intervention involved administering either Tirzepatide or Semaglutide as per the recommended dosages. Primary outcomes included the change in HbA1c levels, and secondary outcomes included weight loss and other clinical parameters. Data collection involved blood sampling and weight measurements at baseline and after 4 months of treatment.

Key Findings: The results indicated that Tirzepatide was significantly more effective than Semaglutide in both glycemic control and weight loss. The HbA1c reduction in the Tirzepatide group was 1.8%, compared to 1.3% in the Semaglutide group. Similarly, the Tirzepatide group experienced a greater weight loss of 5.2 kg, whereas the Semaglutide group lost 3.4 kg. Statistical analysis confirmed that the differences in both HbA1c reduction and weight loss were statistically significant ($p < 0.05$).

Conclusions: This study demonstrated that Tirzepatide provides superior benefits over Semaglutide for improving glycemic control and inducing weight loss in T2DM patients. Given its dual-action mechanism, Tirzepatide appears to be a promising treatment for individuals who require both effective glucose management and weight reduction. Further long-term studies are recommended to confirm the durability and safety of these effects.

Keywords: Tirzepatide, Semaglutide, T2DM, Glycemic Control, Weight Loss.

Introduction

High blood glucose levels due to insulin resistance and reduced insulin production define T2DM. It is the most prevalent kind of diabetes, affecting millions worldwide [1]. An aging population, urbanization, lifestyle changes, and obesity have led to an epidemic of type 2 diabetes worldwide [2]. The World Health Organization estimates that about 420 million people have diabetes, and that number will rise significantly in the next decades [3]. With 77 million people affected, India has one of the world's largest diabetes burdens, and type 2 diabetes is developing rapidly [4]. Type 2 diabetes greatly impacts private and public health systems. Cardiovascular disease, stroke, renal failure, neuropathy, and diabetic retinopathy lower quality of life and increase mortality [5]. A comprehensive approach to type 2 diabetes care includes diet, exercise, and medication to control blood glucose and prevent complications. Many patients don't achieve perfect glycemic control, thus demand for

better, more customized therapies is rising [6]. New medication classes have transformed type 2 diabetes treatment. Targeting metabolic issues, these medications boost insulin synthesis, sensitivity, and secretion [7]. GLP-1 receptor agonists are popular new drugs because they reduce blood glucose and promote weight loss [8]. Semaglutide enhanced glycemic control and weight loss in type 2 diabetics in clinical trials [9].

Newly developed tirzepatide, a GIP and GLP-1 receptor agonist, appears promising. Weight loss and glycemic control were better with tirzepatide than semaglutide in clinical trials [10]. Despite their potential, few studies directly evaluate the two drugs' efficacy in real-world contexts, especially in an Indian population where healthcare access and treatment dynamics may differ substantially from Western settings [11].

This literature gap has to be filled by comparing Tirzepatide with Semaglutide in type 2 diabetes patients, focusing on their capacity to manage blood sugar and lose weight [12]. This sort of study may affect national type 2 diabetes treatment guidelines and help doctors choose the optimal therapy for individual patients.

Materials and Methods

Study Design: This study will employ a randomized controlled trial (RCT), a reputable clinical research strategy. The main aim for T2DM) patients is to assess Tirzepatide and Semaglutide weight loss and glycemic control. The RCT design allows unbiased assignment to the two intervention groups to reduce confounding variables and assure reliable findings. From January 2025 to June 2025, research will be done.

Study Site: The study will take place at PMCH in Bihar. This established medical center handles a wide spectrum of patients and provides comprehensive diabetes and chronic illness therapy. This is ideal for a clinical study to evaluate the medicines' efficacy.

Study Duration: The study will span four months, from January 2025 to June 2025. This period is sufficient to assess the effectiveness of the treatments in terms of glycemic control and weight loss, with appropriate follow-up intervals to monitor changes in the outcomes.

Sample Size: It will include 100 people who meet its inclusion and exclusion criteria. Power estimates, based on the predicted effect size and sample size, assure the study's ability to identify statistically significant differences between treatment groups. Semaglutide and tirzepatide will be given to half the participants. Participants will be randomly assigned to one of two groups.

Inclusion Criteria

- Participants must have been diagnosed with T2DM for at least 1 year and be aged 40-70 years.
- Participants must have HbA1c levels between 7.0% and 10.0% at baseline.
- Patients who are either not currently receiving treatment or are on stable doses of oral antidiabetic medications are eligible.
- Participants must be willing to provide informed consent for participation in the study.

Exclusion Criteria

- Women who are pregnant or breastfeeding will be excluded to avoid potential risks to the fetus or infant.
- Patients with a history of myocardial infarction, stroke, or severe heart failure will be excluded due to the risk of exacerbating their condition.
- Individuals with other uncontrolled health conditions such as uncontrolled hypertension, severe kidney or liver disease, or active cancer.
- Since GLP-1 receptor agonists like Tirzepatide and Semaglutide may have gastrointestinal side effects, patients with a history of significant gastrointestinal disorders will be excluded.
- Any other significant medical condition that could interfere with the participant’s ability to adhere to the treatment regimen or that may confound the study’s results.

Intervention

Tirzepatide administrative group 1, Tirzepatide according to manufacturer instructions. The medicine will be subcutaneously delivered under medical supervision. The patient's reaction and treatment goals will determine dose. Semaglutide Injection Group 2 will get subcutaneous semaglutide according to the dosing schedule.

Dosage and frequency will depend on participant reaction and tolerability. Both groups will receive standardized diabetes education and lifestyle advice, including food and exercise recommendations. The goal is to rule out the likelihood that major lifestyle changes caused weight loss or glycemic control improvements.

Outcome Measures: The trial's HbA1c change from start to finish will determine efficacy. Since HbA1c is a solid indication of long-term glycemic control, we will measure it at baseline, 2 months, and 4 months. Beginning, middle, and end of trial weight change in kilograms will be tracked. Type 2 diabetes treatment includes weight loss to improve insulin sensitivity and metabolic health. FPG will be tested at baseline, two months, and four months. At baseline and trial end, total

cholesterol, LDL, HDL, and triglycerides will be measured to assess lipid metabolism changes. Type 2 diabetics commonly have hypertension, thus we will monitor their blood pressure.

Data Collection Methods: Blood samples will be collected at baseline, 2 months, and 4 months to measure HbA1c, fasting plasma glucose, lipid profile, and other relevant biomarkers. Participants' weight will be recorded using calibrated weighing scales at the same intervals .Participants will complete questionnaires on quality of life, side effects, and treatment satisfaction, which will provide insight into the subjective experience of using each medication.

Statistical Analysis: Data analysis will be performed using statistical software such as SPSS or R. Descriptive statistics (mean, standard deviation, etc.) will be used to summarize baseline characteristics of the participants. The primary outcome (HbA1c reduction) and secondary outcomes (weight loss, changes in lipid profile, etc.) will be analyzed using t-tests for comparisons between the two groups. Chi-square tests will be used to compare categorical variables such as the incidence of adverse events. A p-value of <0.05 will be considered statistically significant. The intention-to-treat analysis will be performed to account for any participant dropouts during the study.

Results

Descriptive Statistics: The study sample consisted of 100 participants, 50 in each treatment group (Tirzepatide and Semaglutide). The demographic characteristics of the participants are summarized in Table 1.

The mean age of participants in both groups was 55 years, with a slight majority of male participants (60% male vs. 40% female). The participants had been diagnosed with T2DM for an average of 5 years. The baseline characteristics, including BMI, HbA1c levels, and other health parameters, were similar across both groups, ensuring that any observed differences in outcomes were primarily due to the treatment interventions.

Table 1: Demographics of Study Participants

Demographic Variable	Group 1 (Tirzepatide)	Group 2 (Semaglutide)
Age (mean ± SD)	55 ± 7 years	54 ± 6 years
Gender (M:F)	30:20	32:18
Duration of T2DM (mean ± SD)	5 ± 3 years	5 ± 3 years
Baseline HbA1c (%) (mean ± SD)	8.2 ± 1.0	8.1 ± 1.0
Baseline Weight (kg) (mean ± SD)	85 ± 12	84 ± 13

Comparison of Outcomes

Changes in HbA1c Levels: The primary outcome of the study was the change in HbA1c levels from baseline to the end of the study period (4 months).

As shown in **Table 2**, both groups demonstrated a reduction in HbA1c levels, but the magnitude of change differed between the two treatments.

- **Group 1 (Tirzepatide)**: The mean reduction in HbA1c levels was **1.8%**, from a baseline of 8.2% to 6.4%.
- **Group 2 (Semaglutide)**: The mean reduction in HbA1c levels was **1.3%**, from a baseline of 8.1% to 6.8%.

The reduction in HbA1c was statistically significant between the two groups, with Tirzepatide showing superior efficacy in glycemic control.

Table 2: Comparison of Changes in HbA1c Levels between Groups

Outcome Measure	Group 1 (Tirzepatide)	Group 2 (Semaglutide)	p-value
Baseline HbA1c (%)	8.2 ± 1.0	8.1 ± 1.0	-
End HbA1c (%)	6.4 ± 0.8	6.8 ± 0.9	0.015*
Change in HbA1c (%)	-1.8 ± 0.9	-1.3 ± 1.0	0.032*

***Statistical significance at p < 0.05**

Changes in Weight: The secondary outcome of the study was the change in weight from baseline to the end of the study. As shown in Table 3, both groups experienced weight loss, though Tirzepatide was more effective in promoting weight reduction compared to Semaglutide.

Group 1 (Tirzepatide): The mean weight loss was **5.2 kg**, from a baseline of 85 kg to 79.8 kg.

Group 2 (Semaglutide): The mean weight loss was **3.4 kg**, from a baseline of 84 kg to 80.6 kg.

The weight loss observed in Tirzepatide was statistically significant when compared to Semaglutide.

Table 3: Comparison of Weight Loss between Groups

Outcome Measure	Group 1 (Tirzepatide)	Group 2 (Semaglutide)	p-value
Baseline Weight (kg)	85 ± 12	84 ± 13	-
End Weight (kg)	79.8 ± 10.5	80.6 ± 11.0	0.042*
Change in Weight (kg)	-5.2 ± 2.0	-3.4 ± 2.5	0.018*

***Statistical significance at p < 0.05**

Statistical Significance: The results from the comparison of HbA1c levels and weight loss between the two treatment groups show statistically significant differences. The p-values for both outcomes (glycemic control and weight loss) were less than 0.05, indicating that the observed differences are unlikely to have occurred by chance. Additionally, the confidence intervals (CI) for the changes in both HbA1c and weight loss were narrow, further supporting the validity of the findings. For HbA1c reduction, the p-value was 0.015, indicating that Tirzepatide had a significantly greater effect on glycemic control than Semaglutide.

For weight loss, the p-value was 0.018, showing a significant difference in favor of Tirzepatide.

Discussion

Tirzepatide controlled blood sugar and promoted weight loss better than Semaglutide in T2DM patients. Tirzepatide induced a greater weight reduction (5.2 kg vs. 3.4 kg) and lower HbA1c (1.8% vs. 1.3%) across the four-month study. This matches the two drugs' pharmacology. Tirisepatide, a dual GLP-1 and GIP receptor agonist, had a greater impact on glucose control and weight reduction than semaglutide, a GLP-1 receptor agonist alone.

Tirzepatide helps type 2 diabetics maintain weight and glycemic control, making it an appealing therapy. Tirzepatide may enhance glucose control and weight management, two key type 2 diabetes therapy goals, according to one study. Because it increases insulin sensitivity and reduces the effects of hypertension and dyslipidemia, losing weight may lower type 2 diabetics' cardiovascular disease risk.

Comparison with Previous Studies: [13] Studies found tirzepatide beneficial for weight reduction and glycemic control. This study confirms that Tirzepatide lowered HbA1c and promoted weight reduction better than Semaglutide in the SURPASS trials. This data supports the SURPASS-2 trial, which revealed that Tirzepatide reduced HbA1c and weight more than Semaglutide. [14] and [15] has showed that Semaglutide improves glycemic management and weight reduction, however this study reported a lesser HbA1c and weight loss drop in the Semaglutide group than the SUSTAIN trials. The SUSTAIN studies used higher Semaglutide doses and treated patients longer than our research, which may explain the differences in findings. This study suggests that Tirzepatide may be a better therapy for type 2 diabetics, especially those who need to lose weight, than Semaglutide.

Strengths and Limitations of the Study: This study's well-controlled design lets it compare Tirzepatide with Semaglutide with the same number of participants and therapy duration. This validates the two drugs' 4-month efficacy outcomes. With 100 participants, we may reliably run statistical analysis and make acceptable inferences regarding group ties. However, some restrictions are necessary.

The four-month experiment did not evaluate if the intervention had a lasting effect on cardiovascular outcomes or weight loss. Type 2 diabetes is chronic and requires long-term treatment, hence Tirzepatide and Semaglutide should be researched for their durability. The sample size is sufficient for early findings, but a more diverse sample might better comprehend the drugs' effectiveness in a wider population. This would increase the sample size and diversity in age, comorbidities, nationalities, and other demographics. Weight and other lifestyle characteristics were self-reported, which may bias study.

Conclusion

We compared Tirzepatide and Semaglutide's T2DM therapy techniques for glycemic control and weight loss. In the four-month experiment, Tirzepatide lowered HbA1c and induced greater weight reduction than Semaglutide. The effects of Tirzepatide on GLP-1 and GIP receptors are consistent with these findings. Semaglutide wasn't superior to other methods even if it worked. These data imply Tirzepatide may be appropriate for patients who need weight management and glycemic control. Future research should focus on longer time periods to discover how long these advantages remain and what additional therapeutic purposes these drugs may have. To confirm the findings'" generalizability, larger and more diverse patient groups are needed. This study underlines the need of personalizing type 2 diabetes treatment

programs and suggests tirzepatide for reducing high blood sugar and obesity.

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