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Original Research Article

COMPARATIVE ANALYSIS OF TRADITIONAL INSULIN THERAPY VERSUS GLP-1 RECEPTOR AGONISTS IN TYPE 2 DIABETES MANAGEMENT

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ABSTRACT

Background: Aim: This study aims to compare the efficacy and safety of traditional insulin therapy versus GLP-1 receptor agonists (GLP-1 RAs) in managing type 2 diabetes mellitus (T2DM), focusing on glycemic control, weight changes, lipid profile, and adverse events.
Materials and Methods: A comparative observational study was conducted at a tertiary care hospital, involving 110 patients with T2DM randomized into two groups: Insulin Therapy Group (n=55) and GLP-1 RA Group (n=55). Patients were monitored for 36 weeks, with assessments at 4, 12, 24, and 36 weeks. Primary outcomes included changes in HbA1c, fasting blood glucose (FBG), and postprandial blood glucose (PPG). Secondary outcomes measured BMI, lipid profile, hypoglycemia incidence, and other adverse effects.
Results: At 36 weeks, HbA1c reduction was significantly greater in the GLP-1 RA group (6.8% ± 0.4) compared to the insulin group (7.3% ± 0.5, p=0.001). Similarly, FBG and PPG levels were significantly lower in the GLP-1 RA group (FBG: 121.8 ± 15.7 mg/dL vs. 136.4 ± 17.2 mg/dL, p=0.002; PPG: 165.2 ± 19.8 mg/dL vs. 184.6 ± 22.4 mg/dL, p=0.001). The GLP-1 RA group also showed greater weight reduction (BMI: 26.7 ± 3.1 vs. 28.1 ± 2.9, p=0.001) and improved lipid profile, with significant decreases in LDL (p=0.004) and triglycerides (p=0.002). Hypoglycemia was more common in the insulin group (32.73%) than in the GLP-1 RA group (10.91%, p=0.002), whereas nausea (21.82%), vomiting (14.55%), and diarrhea (12.73%) were more frequent in the GLP-1 RA group.
Conclusion: GLP-1 receptor agonists demonstrated superior glycemic control, weight loss benefits, and improved lipid parameters compared to insulin therapy, with a lower incidence of hypoglycemia. However, gastrointestinal side effects were more common with GLP-1 RAs, potentially affecting patient adherence. These findings support GLP-1 RAs as a preferred alternative to insulin therapy in overweight or cardiovascular-risk patients with T2DM.
Keywords: Type 2 diabetes mellitus, GLP-1 receptor agonists, insulin therapy, glycemic control, adverse events.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels resulting from impaired insulin secretion, insulin resistance, or a combination of both. Type 2 diabetes mellitus (T2DM), the most prevalent form of diabetes, is primarily associated with lifestyle factors, genetic predisposition, and progressive β-cell dysfunction. As the global burden of T2DM continues to rise, effective management strategies are crucial to preventing complications such as cardiovascular disease, nephropathy, neuropathy, and retinopathy. Among the various therapeutic approaches, insulin therapy and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) play a

pivotal role in glycemic control, yet they differ significantly in their mechanisms, efficacy, safety profiles, and overall impact on patient outcomes.[1]

Traditional insulin therapy has long been the cornerstone of diabetes management, especially for patients with advanced T2DM who fail to achieve glycemic control through oral antidiabetic medications. Insulin therapy includes various formulations, such as rapid-acting, short-acting, intermediate-acting, and long-acting insulins, allowing for tailored treatment regimens. Insulin functions by directly lowering blood glucose levels through enhanced glucose uptake in peripheral tissues and suppression of hepatic glucose production. However, despite its efficacy, insulin therapy presents challenges, including the risk of hypoglycemia, weight gain, and the need for multiple daily injections, which can contribute to patient non-adherence.[2]

In contrast, GLP-1 receptor agonists represent a relatively newer class of injectable agents that have gained prominence due to their glucose-dependent mechanism of action. These drugs mimic the effects of endogenous GLP-1, a hormone secreted by the intestine in response to food intake. GLP-1 RAs enhance insulin secretion, suppress glucagon release, delay gastric emptying, and promote satiety, leading to better postprandial glucose control and weight reduction. Unlike insulin, GLP-1 RAs are associated with a lower risk of hypoglycemia and offer additional benefits such as improved cardiovascular outcomes. Their once-daily or once-weekly dosing options further enhance adherence and patient satisfaction compared to the frequent injections required in insulin therapy.[3]

A comparative analysis of traditional insulin therapy and GLP-1 receptor agonists in T2DM management is essential for guiding clinical decisions and optimizing patient outcomes. While insulin remains indispensable for patients with severe β-cell failure or acute hyperglycemia, GLP-1 RAs are increasingly favored for individuals seeking weight loss, cardiovascular protection, and a reduced risk of hypoglycemia. The selection of an appropriate therapy depends on multiple factors, including disease progression, comorbidities, patient preferences, and healthcare accessibility.

The clinical outcomes associated with these two treatment modalities also warrant examination. Insulin therapy is highly effective in achieving glycemic targets, but its use is often hindered by the burden of self-monitoring, dose adjustments, and potential adverse effects. On the other hand, GLP-1 RAs, while not as potent in reducing glucose levels as insulin, provide a more physiological approach by enhancing endogenous insulin secretion in a glucose-dependent manner. The weight-neutral or weight-reducing properties of GLP-1 RAs make them particularly appealing for overweight and obese patients, addressing a crucial aspect of T2DM pathophysiology.[4]

Beyond glycemic control, the impact of these therapies on long-term health outcomes is a crucial consideration. Emerging evidence suggests that GLP-1 RAs have cardioprotective properties, reducing major adverse cardiovascular events in patients with T2DM. This benefit is particularly relevant given the high prevalence of cardiovascular disease in this population. In contrast, insulin therapy, while effective in managing hyperglycemia, does not confer inherent cardiovascular benefits and may even contribute to adverse effects such as weight gain and increased insulin resistance over time.[5]

Another important aspect of this comparison is the impact on patient quality of life and adherence. The complexity of insulin regimens, frequent blood glucose monitoring, and the fear of hypoglycemia can significantly affect patient adherence and psychological well-being. Conversely, the user-friendly administration of GLP-1 RAs, along with their favorable safety profile, offers a more convenient alternative for many individuals. However, gastrointestinal side effects, including nausea and vomiting, remain a challenge for some patients initiating GLP-1 RA therapy.[6]

From a healthcare perspective, cost considerations and accessibility also influence treatment decisions. Insulin therapy, particularly human insulin formulations, is widely available and often more affordable than GLP-1 RAs, making it a preferred option in resource-limited settings. In contrast, GLP-1 RAs, despite their advantages, are relatively expensive and may not be accessible to all patients due to insurance limitations or high out-of-pocket costs. These economic factors play a significant role in determining treatment choices, highlighting the need for cost-effectiveness analyses to guide policy and clinical practice.

MATERIALS AND METHODS

This study is a comparative observational analysis evaluating the effectiveness and safety of traditional insulin therapy versus GLP-1 receptor agonists (GLP-1 RAs) in the management of type 2 diabetes mellitus (T2DM). The study was conducted at tertiary care hospital, following ethical approval from the institutional review board. Written informed consent was obtained from all participants before enrollment. A total of 110 patients diagnosed with T2DM were recruited for the study.

Patients were selected based on the following inclusion criteria

- Age between 40-75 years.
- Diagnosed with T2DM for at least five years.
- HbA1c levels between 7.5% and 10% at baseline.
- Not on any GLP-1 RAs or insulin therapy for at least six months before the study.
- Willing to comply with study protocols, including follow-up visits.

Exclusion Criteria

- Patients with type 1 diabetes or secondary diabetes.
- Pregnant or lactating women.
- History of severe hypoglycemia or ketoacidosis within the past year.
- Severe renal impairment (eGFR <30 mL/min/1.73m²) or end-stage liver disease.
- Patients with a history of gastrointestinal disorders that may affect GLP-1 RA absorption.

Study Groups and Treatment Protocol

The enrolled patients were divided into two groups:

- **Insulin Therapy Group (n = 55):** Patients in this group were initiated on a basal-bolus insulin regimen (e.g., insulin glargine/detemir as basal insulin and insulin aspart/lispro as prandial insulin). Dosage titration was performed based on self-monitored blood glucose levels and HbA1c trends.
- **GLP-1 Receptor Agonist Group (n = 55):** Patients in this group were prescribed GLP-1 RAs (e.g., liraglutide, semaglutide, or dulaglutide) based on clinical recommendations and patient-specific factors. Dosage adjustments followed standard guidelines and patient tolerance.

All patients underwent comprehensive baseline evaluations, which included assessments of glycemic control, metabolic parameters, and potential adverse events. Glycemic control was measured using HbA1c levels, fasting blood glucose (FBG), and postprandial blood glucose (PPG). Metabolic parameters such as lipid profiles, including total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides, were recorded alongside body mass index (BMI) and blood pressure measurements. Additionally, the incidence of hypoglycemia, gastrointestinal side effects, and other drug-related adverse events was carefully monitored.

Follow-up visits were scheduled at 4, 12, 24, and 36 weeks after treatment initiation. During each visit, glycemic parameters, body weight, blood pressure, and lipid profiles were reassessed. Adverse effects were documented to evaluate treatment safety, while patient adherence and satisfaction were measured using structured questionnaires.

The primary outcome of the study was the change in HbA1c levels at 36 weeks from baseline. Secondary outcomes included changes in FBG and PPG levels, variations in body weight and BMI, the frequency and severity of hypoglycemia, alterations in lipid profile parameters, and the incidence of adverse events. These outcomes provided a comprehensive assessment of the comparative efficacy and safety of traditional insulin therapy versus GLP-1 receptor agonists in the management of type 2 diabetes.

Statistical Analysis

Data analysis was conducted using SPSS Version 25.0. Descriptive statistics were used to summarize baseline characteristics. Paired t-tests and ANOVA were used for within-group and between-group comparisons of continuous variables, while Chi-square tests were applied to categorical variables. A p-value < 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics of Study Participants (Table 1)

The baseline characteristics of the study participants were comparable between the insulin therapy group and the GLP-1 receptor agonist (GLP-1 RA) group, as shown in Table 1. The average age of patients in both groups was similar (58.2 ± 7.4 years in the insulin group vs. 57.6 ± 6.9 years in the GLP-1 RA group, p=0.621), and the male-to-female ratio was nearly identical (30/25 vs. 28/27, p=0.735). The duration of type 2 diabetes mellitus (T2DM) was also consistent between groups (8.5 ± 3.2 years vs. 8.7 ± 3.5 years, p=0.804), indicating that the patient populations were comparable in terms of disease progression. Baseline glycemic parameters, including HbA1c (8.9% ± 0.8 vs. 8.8% ± 0.7, p=0.531), fasting blood glucose (FBG) (178.5 ± 23.6 mg/dL vs. 176.2 ± 21.9 mg/dL, p=0.678), and postprandial glucose (PPG) (245.3 ± 31.2 mg/dL vs. 241.7 ± 29.8 mg/dL, p=0.521), were not significantly different between groups. Similarly, body mass index (BMI) and blood pressure values were also statistically similar at baseline, ensuring that any observed differences in treatment outcomes were likely due to therapeutic intervention rather than baseline disparities.

Glycemic Control at Follow-Up Intervals (Table 2)

HbA1c levels showed a significant reduction in both treatment groups over time, but the decrease was more pronounced in the GLP-1 RA group. At 12 weeks, the HbA1c reduction was significantly greater in the GLP-1 RA group (7.5% ± 0.6) compared to the insulin therapy group (8.1% ± 0.7, p=0.003). This trend continued at 24 weeks (7.1% ± 0.5 vs. 7.6% ± 0.6, p=0.002) and 36 weeks (6.8% ± 0.4 vs. 7.3% ± 0.5, p=0.001), with the GLP-1 RA group achieving superior glycemic control.

Changes in Fasting and Postprandial Blood Glucose (Table 3)

Fasting and postprandial blood glucose levels improved significantly in both treatment groups, but the GLP-1 RA group consistently showed superior results. At 12 weeks, fasting blood glucose (FBG) levels dropped from 176.2 ± 21.9 mg/dL to 148.7 ± 18.2 mg/dL in the GLP-1 RA group, whereas in the insulin group, FBG decreased from 178.5 ± 23.6 mg/dL to 160.2 ± 20.5 mg/dL (p=0.007). Similarly, at 36 weeks, the GLP-1 RA group had significantly lower FBG (121.8 ± 15.7 mg/dL) compared to the insulin therapy group (136.4 ± 17.2 mg/dL, p=0.002).

Postprandial glucose (PPG) levels followed the same trend. By 36 weeks, PPG levels decreased from 241.7 ± 29.8 mg/dL to 165.2 ± 19.8 mg/dL in the GLP-1 RA group and from 245.3 ± 31.2 mg/dL to 184.6 ± 22.4 mg/dL in the insulin therapy group (p=0.001).

Changes in BMI and Lipid Profile (Table 4)

A key advantage of GLP-1 RAs was their ability to reduce body weight, as reflected in BMI changes. At baseline, BMI values were similar between groups (28.6 ± 3.1 kg/m² for insulin vs. 28.4 ± 3.3 kg/m² for GLP-1 RAs, p=0.743). However, after 36 weeks, BMI remained almost unchanged in the insulin group (28.1 ± 2.9 kg/m²), whereas a significant reduction was observed in the GLP-1 RA group (26.7 ± 3.1 kg/m², p=0.001). This indicates that GLP-1 RAs were effective in promoting weight loss, likely due to their appetite-suppressing effects.

Lipid profile parameters also showed significant improvement in the GLP-1 RA group. Total cholesterol levels reduced more substantially in the GLP-1 RA group (196.7 ± 25.5 mg/dL to 178.2 ± 22.6 mg/dL) compared to the insulin therapy group (198.4 ± 26.7 mg/dL to 190.3 ± 24.2 mg/dL, p=0.003). Similarly, LDL cholesterol decreased more in the GLP-1 RA group (117.9 ± 21.7 mg/dL to 105.4 ± 19.8 mg/dL, p=0.004), and HDL cholesterol increased significantly (42.9 ± 5.9 mg/dL to 46.8 ± 6.4 mg/dL, p=0.002). Triglycerides also showed a more pronounced decrease in the GLP-1 RA group compared to the insulin therapy group (p=0.002). These findings highlight the additional cardiovascular benefits of GLP-1 RAs beyond glycemic control.

Adverse Events Comparison Between Groups (Table 5)

Adverse events varied between the two treatment groups, with hypoglycemia being significantly more frequent in the insulin therapy group (32.73%) compared to the GLP-1 RA group (10.91%, p=0.002). This is a crucial finding, as hypoglycemia is a major concern in insulin-treated patients and can lead to serious complications.

On the other hand, gastrointestinal side effects were more common in the GLP-1 RA group. Nausea was reported in 21.82% of patients in the GLP-1 RA group compared to only 5.45% in the insulin therapy group (p=0.011). Vomiting (14.55% vs. 3.64%, p=0.023) and diarrhea (12.73% vs. 1.82%, p=0.017) were also significantly higher in the GLP-1 RA group. These adverse effects are consistent with the known gastrointestinal profile of GLP-1 RAs and may limit their tolerability in some patients. Injection site reactions were slightly more frequent in the insulin group (10.91% vs. 3.64%, p=0.089), but the difference was not statistically significant.

Table 1: Baseline Characteristics of Study Participants

Parameter	Insulin Therapy Group (n=55)	GLP-1 RA Group (n=55)	p-value
Age (years)	58.2 ± 7.4	57.6 ± 6.9	0.621
Gender (Male/Female)	30/25	28/27	0.735
Duration of T2DM (years)	8.5 ± 3.2	8.7 ± 3.5	0.804
Baseline HbA1c (%)	8.9 ± 0.8	8.8 ± 0.7	0.531
Fasting Blood Glucose (mg/dL)	178.5 ± 23.6	176.2 ± 21.9	0.678
Postprandial Glucose (mg/dL)	245.3 ± 31.2	241.7 ± 29.8	0.521
BMI (kg/m²)	28.6 ± 3.1	28.4 ± 3.3	0.743
Systolic BP (mmHg)	132.5 ± 10.2	130.7 ± 9.8	0.514
Diastolic BP (mmHg)	80.6 ± 6.4	81.2 ± 6.1	0.692

Table 2: Glycemic Control at Follow-Up Intervals

Time Point	Insulin Therapy Group (HbA1c %)	GLP-1 RA Group (HbA1c %)	p-value
Baseline	8.9 ± 0.8	8.8 ± 0.7	0.531
12 Weeks	8.1 ± 0.7	7.5 ± 0.6	0.003
24 Weeks	7.6 ± 0.6	7.1 ± 0.5	0.002
36 Weeks	7.3 ± 0.5	6.8 ± 0.4	0.001

Table 3: Changes in Fasting and Postprandial Blood Glucose

Time Point	Insulin Therapy Group (FBG, mg/dL)	GLP-1 RA Group (FBG, mg/dL)	p-value	Insulin Therapy Group (PPG, mg/dL)	GLP-1 RA Group (PPG, mg/dL)	p-value
Baseline	178.5 ± 23.6	176.2 ± 21.9	0.678	245.3 ± 31.2	241.7 ± 29.8	0.521
12 Weeks	160.2 ± 20.5	148.7 ± 18.2	0.007	215.8 ± 27.6	198.3 ± 25.1	0.002
24 Weeks	145.7 ± 18.4	132.9 ± 16.5	0.004	198.4 ± 23.9	179.6 ± 22.3	0.001
36 Weeks	136.4 ± 17.2	121.8 ± 15.7	0.002	184.6 ± 22.4	165.2 ± 19.8	0.001

Table 4: Changes in BMI and Lipid Profile

Parameter	Baseline (Insulin Group)	36 Weeks (Insulin Group)	Baseline (GLP-1 RA Group)	36 Weeks (GLP-1 RA Group)	p-value
BMI (kg/m²)	28.6 ± 3.1	28.1 ± 2.9	28.4 ± 3.3	26.7 ± 3.1	0.001
Total Cholesterol (mg/dL)	198.4 ± 26.7	190.3 ± 24.2	196.7 ± 25.5	178.2 ± 22.6	0.003
HDL (mg/dL)	42.5 ± 5.7	43.2 ± 6.1	42.9 ± 5.9	46.8 ± 6.4	0.002
LDL (mg/dL)	118.6 ± 22.3	112.8 ± 21.2	117.9 ± 21.7	105.4 ± 19.8	0.004
Triglycerides (mg/dL)	152.8 ± 27.4	145.3 ± 25.9	151.2 ± 26.5	132.7 ± 23.1	0.002

Table 5: Adverse Events Comparison Between Groups

Adverse Event	Insulin Therapy Group (n=55)	GLP-1 RA Group (n=55)	p-value
Hypoglycemia	18 (32.73%)	6 (10.91%)	0.002
Nausea	3 (5.45%)	12 (21.82%)	0.011
Vomiting	2 (3.64%)	8 (14.55%)	0.023
Diarrhea	1 (1.82%)	7 (12.73%)	0.017
Injection Site Reaction	6 (10.91%)	2 (3.64%)	0.089

DISCUSSIONS

The findings of this study suggest that GLP-1 receptor agonists (GLP-1 RAs) provide superior glycemic control, promote weight loss, improve lipid profiles, and reduce the risk of hypoglycemia compared to traditional insulin therapy in type 2 diabetes mellitus (T2DM) patients. However, gastrointestinal side effects were more frequently observed in patients receiving GLP-1 RAs. These results align with existing literature, including randomized controlled trials and meta-analyses, further strengthening the case for GLP-1 RAs as a viable alternative to insulin therapy in diabetes management.

A significant reduction in HbA1c levels was observed in both treatment groups over the 36-week period, with the GLP-1 RA group demonstrating a superior reduction compared to the insulin therapy group (6.8% ± 0.4 vs. 7.3% ± 0.5, p=0.001). This trend aligns with the SUSTAIN 4 trial conducted by Pratley et al. (2018), which compared semaglutide to insulin glargine in patients inadequately controlled on metformin and sulfonylureas. The study reported that semaglutide reduced HbA1c by 1.21% compared to 0.74% with insulin glargine ($p<0.001$), confirming the greater efficacy of GLP-1 RAs in reducing glycemic levels.[6]

The greater reduction in glycemic parameters observed with GLP-1 RAs is attributed to their dual mechanism of enhancing glucose-dependent insulin secretion and suppressing glucagon release (Madsbad, 2016).[7] The 2019 ADA-EASD consensus report also recognizes GLP-1 RAs as a preferred treatment for T2DM due to their potent glucose-lowering effects and reduced risk of hypoglycemia (Buse et al., 2020).[8]

The study demonstrated significant improvements in fasting blood glucose (FBG) and postprandial glucose (PPG) levels in both groups, with a more pronounced reduction in the GLP-1 RA group. At 36 weeks, FBG decreased to 121.8 ± 15.7 mg/dL in the GLP-1 RA group compared to 136.4 ± 17.2 mg/dL in the insulin therapy group (p=0.002), while PPG decreased to 165.2 ± 19.8 mg/dL in the GLP-1 RA group versus 184.6 ± 22.4 mg/dL in the insulin group (p=0.001).

These findings are consistent with the UKPDS and Holman et al. (2007) studies, which demonstrated that insulin therapy effectively reduces fasting glucose levels but does not significantly impact postprandial hyperglycemia compared to incretin-based therapies.[9] Moreover, Mellbin et al. (2013) found that while insulin is effective in glycemic control, it may not significantly impact postprandial glucose excursions.[10]

A major advantage of GLP-1 RAs observed in this study was the significant reduction in BMI, from 28.4 ± 3.3 kg/m² at baseline to 26.7 ± 3.1 kg/m² at 36 weeks (p=0.001), whereas the insulin group showed minimal change (28.6 ± 3.1 kg/m² to 28.1 ± 2.9 kg/m²). This supports findings from Nissen et al. (2009), which demonstrated that liraglutide treatment resulted in an average weight loss of 2.5 kg compared to weight gain with insulin therapy.[11] Furthermore, the EMPAREG-OUTCOME trial (Zinman et al., 2015) demonstrated that T2DM patients with obesity benefit more from GLP-1 RAs, as these drugs reduce weight by promoting satiety and delaying gastric emptying.[12] In contrast, insulin therapy has been associated with weight gain, a concern for many patients with T2DM.

The study observed a significant reduction in total cholesterol, LDL, and triglycerides in the GLP-1 RA group, while HDL levels increased significantly. Similar improvements were observed in the SUSTAIN 6 trial (Marso et al., 2016), which reported a 5% reduction in LDL and a 6% reduction in total cholesterol with semaglutide therapy.[13]

GLP-1 RAs have been linked to improved cardiovascular outcomes, as shown in meta-analyses by Russell-Jones et al. (2012) and Mannucci & Monami (2017), which concluded that GLP-1 RA treatment reduces cardiovascular risk factors, particularly lipid levels and body weight.[14,15]

One of the most critical findings of this study was the significantly lower incidence of hypoglycemia in the GLP-1 RA group (10.91%) compared to the insulin therapy group (32.73%, p=0.002). This aligns with results from Eng et al. (2014), who demonstrated that GLP-1 RA therapy was associated with a 75% lower risk of hypoglycemia compared to insulin-based regimens. The reduced risk of hypoglycemia with GLP-1 RAs is likely due to their glucose-dependent insulin secretion mechanism, which prevents excessive insulin release in normoglycemic states.[16]

However, gastrointestinal side effects, including nausea (21.82% in the GLP-1 RA group vs. 5.45% in the insulin group, p=0.011), vomiting (14.55% vs. 3.64%, p=0.023), and diarrhea (12.73% vs. 1.82%, p=0.017), were more prevalent among patients receiving GLP-1 RAs. These findings are consistent with the adverse event profiles reported in randomized trials such as the LEADER trial and meta-analyses of GLP-1 RA therapies. Despite these side effects, patient adherence to GLP-1 RAs

remained high due to their benefits in glycemic control and weight loss.[11,15]

CONCLUSION

This study demonstrates that GLP-1 receptor agonists (GLP-1 RAs) provide superior glycemic control, greater reductions in fasting and postprandial blood glucose, and significant weight loss compared to traditional insulin therapy in patients with type 2 diabetes. Additionally, GLP-1 RAs improved lipid profiles and had a significantly lower risk of hypoglycemia, making them a safer alternative to insulin. However, gastrointestinal side effects were more prevalent in the GLP-1 RA group, which may impact patient adherence. Overall, these findings support the preferential use of GLP-1 RAs over insulin therapy, particularly in overweight patients and those at risk of cardiovascular complications.

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