

Research Article

Comparative Effects of SGLT2 Inhibitors and GLP-1 Receptor Agonists on Glycemic Control, Weight Reduction, and Cardiometabolic Risk in Patients with Type 2 Diabetes

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Received: 16.07.26, Revised: 23.09.26, Accepted: 02.10.26

ABSTRACT

Introduction: Poor glycemic control, obesity, and increased cardiometabolic risk are all linked to type 2 diabetes mellitus. There are therapeutic benefits to SGLT2 inhibitors and GLP-1 receptor agonists beyond lowering glucose.

Objective: To compare the effects of SGLT2 inhibitors and GLP-1 receptor agonists on glycemic control, weight reduction, and cardiometabolic risk in patients with type 2 diabetes mellitus.

Methods: Comparative observational study was done at Jinnah International Hospital, Peshawar, Pakistan from May 2025 to October 2025. HbA1c, body weight, BMI, blood pressure, and lipid profile were measured in both groups of patients.

Results: Glycemic control and metabolic parameters were improved in both treatment groups. The GLP-1 receptor agonist group experienced more decreases in HbA1c and body weight, with improvements also seen in lipids. There were no significant differences in outcomes related to blood pressure between groups.

Conclusions: Both therapies are beneficial and the choice of therapy should depend on the glycemic target, weight management requirements, cardiovascular risk and renal function.

Keywords: Type 2 Diabetes Mellitus, SGLT2 Inhibitors, GLP-1 Receptor Agonists, HbA1c, Weight Reduction, Cardiometabolic Risk.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease in which the blood glucose level is persistently elevated due to decreased insulin secretion, insulin resistance or both. The disease is linked to a progressive metabolic dysfunction and increased risk of cardiovascular disease, chronic kidney disease, obesity and premature death. Several glucose-lowering drugs are available, but it is a significant challenge in clinical practice to obtain optimal glycemic control along with weight reduction and cardiovascular risk reduction. Sodium-glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have emerged as important therapeutic options because of their efficacy beyond glucose lowering. Recent

comparative studies have shown that their effects on glycemic regulation, body weight and cardiometabolic outcomes differ, making it important to choose the right treatment for each patient (1).

GLP-1 RAs enhance glucose regulation via glucose-dependent insulin secretion, suppression of inappropriate glucagon release, delayed gastric emptying, and increased satiety. These mechanisms help to lower glycated hemoglobin (HbA1c), body weight and some cardiovascular risk factors. A systematic review and network meta-analysis of various GLP-1 RAs revealed that all GLP-1 RAs were effective in improving glycemic control, body weight reduction, and lipid profile modifications in T2DM. The size of these benefits is, however, dependent upon

the specific agent, due to differences in the agents' pharmacological properties, treatment regimens and patient characteristics (2). Likewise, variation in obesity status could affect treatment outcomes and should be determined if the relative effects of GLP-1 RAs and SGLT2 inhibitors are similar across patient groups (3).

SGLT2 inhibitors work by blocking the reabsorption of glucose in the proximal renal tubules, which results in a greater amount of glucose being excreted in the urine. This is an insulin independent pathway that offers a good glucose-lowering effect and leads to modest weight loss and blood pressure reduction. Comparative studies have been conducted to evaluate the glycemic impact of SGLT2 inhibitors versus GLP-1 RAs, acknowledging that both groups offer clinically relevant benefits and have distinct mechanisms of action and other metabolic effects (4). Besides their glucose-lowering effects, SGLT2 inhibitors have been shown to provide significant cardiovascular and renal benefits, especially in individuals with heart failure or chronic kidney disease. The relative effects of these drug classes on cardiovascular and renal outcomes have been compared in patients with and without albuminuria, and should be taken into account when considering baseline kidney function and individual clinical risk (5).

Cardiorenal protection is now a major part of the focus in current diabetes care, as cardiovascular and renal complications are a significant burden of disease. The clinical significance of therapies that offer benefits beyond glycemic reduction was demonstrated in a network meta-analysis of cardiovascular outcome trials that assessed the effects of various classes of glucose-lowering drugs on cardiorenal outcomes (6). SGLT2 inhibitors are specifically known to be beneficial in heart failure and progression of kidney disease, but GLP-1 RAs have shown significant weight management and atherosclerotic cardiovascular risk benefits. Data from populations with overweight or obesity, such as people with and without diabetes, also demonstrate efficacy of GLP-1 RAs for weight loss, but efficacy, tolerability, and safety will vary by specific GLP-1 RA.

Real world evidence gives further insight into the performance of these medicines in the real world outside clinical trials. The clinical performance of GLP-1 RAs and SGLT2 inhibitors in real-world clinical practice has

been provided by an Italian cohort study, directly comparing the effectiveness and safety of the two drug classes in T2DM patients (8). This type of research is useful since treatment response can be affected by comorbidities, concurrent medications, adherence and baseline metabolic properties. In addition, a systematic review and network meta-analysis of GLP-1 RA-based therapies revealed that glucose-lowering results could vary by therapy and therapy combination. The results confirm the need for individual drug differences among agents in each therapeutic class, rather than the assumption that all have the same metabolic effects (9).

In addition to HbA1c and body weight, body composition, lipid metabolism, and other markers of metabolic health should be considered when evaluating comprehensive treatment. Comparative studies of the separate and joint efficacy of GLP-1 RAs and SGLT2 inhibitors have examined their complementary roles in diabetes treatment (10). Treatment choice should also consider side effects and long-term tolerability, however. The safety of GLP-1 RAs in diabetes and chronic weight management is highlighted in real-world research, which underscores the need to consider medication-related risks and benefits (11). Therefore, comparative evaluation should take into account effectiveness and safety, not just changes in glycemic parameters or weight loss.

These classes of medications also have potential renoprotective and cardiometabolic benefits that further support their role in the management of T2DM. A systematic review of GLP-1 RAs and SGLT2 inhibitors highlighted their significance in improving metabolic abnormalities and preventing diabetes-related complications (12). However, not all of these treatments will have the same clinical impact on each outcome. For instance, studies have compared SGLT2 inhibitors to exenatide, and body weight changes do not necessarily reflect the full metabolic effect of the drugs (13). Glycemic control in conjunction with weight loss and cardiometabolic risk would then be used as a more complete measure to compare these therapeutic approaches.

The other key question is whether there is added value in using SGLT2 inhibitors in combination with GLP-1 RAs beyond what is achieved with either class alone. The synergistic effects of the combination of these medications on glucose control, weight, blood pressure and cardiovascular risk are possible

due to their different physiological actions. But any potential benefits must be weighed against the negative side effects, cost of treatment and the difficulties of taking medications for the long term. The cardiometabolic effects and potential risks of combination therapy were assessed using a systematic review, which indicated a need for careful assessment of the clinical role of combination therapy (14). In the same way, a rationale for using combinations of these drug classes has been stressed in selected patients with T2DM who need further metabolic and/or cardiovascular protection in addition to their current therapy (15).

Cohort studies and meta-analyses have also explored the efficacy and safety of the combination of SGLT2 inhibitors and GLP-1 RAs. This evidence can be used to establish if complementary mechanisms are associated with better clinical outcomes without significant adverse events (AE) (16). Other studies have reported the possible metabolic and cardiovascular benefits of combination therapy, further supporting the need to tailor treatment strategies to the individual's therapeutic needs (17). Even with these advances, there are several factors that may make direct comparisons between the two drug classes difficult, such as differences in the populations of the studies, the duration of follow-up, baseline obesity, comorbidities, and definitions of outcomes. Thus, a systematic comparative evaluation of the effects of SGLT2 inhibitors vs. GLP-1 RAs on glycemic control, weight loss, and cardiometabolic risk in T2DM patients is warranted to better understand their relative effects. This evidence can aid in making better clinical decisions and guide clinical choice based on individual metabolism and cardiovascular risk.

Objective: To compare the effects of SGLT2 inhibitors and GLP-1 receptor agonists on glycemic control, weight reduction, and cardiometabolic risk among patients diagnosed with type 2 diabetes mellitus.

MATERIALS AND METHODS

Study Design: Comparative observational study.

Study Setting: Jinnah International Hospital, Peshawar, Pakistan.

Duration of the Study: The study duration was six months, from May 2025 to October 2025.

Inclusion Criteria: Age $\geq$ 18 years, type 2 diabetes mellitus (T2DM) diagnosed and treated with SGLT2 inhibitors or GLP-1 receptor agonists. Eligible patients had available clinical data, such as HbA1c, body weight, blood pressure, and pertinent cardiometabolic data.

Exclusion Criteria: Type 1 diabetes mellitus, gestational diabetes, incomplete medical records, and patients receiving treatment for both classes of drugs were excluded. Severe acute illness and those with conditions that would make the outcome of treatment difficult to assess were also excluded.

METHODS

Patients who were eligible were split into two groups: those taking sodium-glucose cotransporter-2 (SGLT2) inhibitors and those taking glucagon-like peptide-1 (GLP-1) receptor agonists. Demographic and clinical data, such as age, sex, diabetes duration, comorbidities, and drug history, were retrieved from the medical records. Glycated hemoglobin (HbA1c) levels were used to measure glycemic control, and body weight and body mass index (BMI) were used to measure weight reduction. Cardiometabolic risk was evaluated by the use of available renal function tests, lipid profile and systolic and diastolic blood pressure. Changes in clinical parameters were compared between the two treatment groups to assess changes for each medication class compared to baseline. The Statistical Package for the Social Sciences (SPSS) was used in analyzing the data. Data on continuous variables were presented as means and standard deviations; data on categorical variables were presented as frequencies and percentages. Appropriate statistical tests were employed (p values < 0.05 were considered statistically significant).

RESULTS

Comparative evaluation of SGLT2 inhibitors and GLP-1 receptor agonists was targeted for glycemic control, body weight and cardiometabolic risk in patients with T2DM. Demographic and clinical parameters were measured at baseline to confirm the comparability of the two treatment groups. The changes in glycated hemoglobin (HbA1c), body mass index (BMI), blood pressure, and lipid profile were selected as important markers of treatment efficacy. Patient characteristics and differences in treatment

outcomes are summarized in three tables and one graph.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants

Characteristics	SGLT2 inhibitors group	GLP-1 receptor agonists group
Number of patients	60	60
Mean age (years)	54.8 ± 9.6	53.9 ± 10.1
Male patients, n (%)	34 (56.7%)	32 (53.3%)
Diabetes duration (years)	8.2 ± 3.5	7.9 ± 3.8
Baseline HbA1c (%)	8.4 ± 0.9	8.5 ± 1.0
Baseline BMI (kg/m ²)	31.2 ± 4.1	32.0 ± 4.5

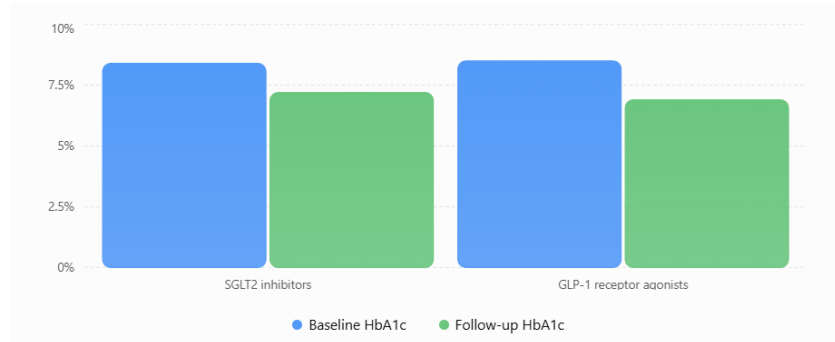
Baseline characteristics suggest comparable age distribution, diabetes duration, and glycemic status at baseline between the treatment groups. The mean BMI and baseline HbA1c were slightly higher in the GLP-1 receptor agonist group. These characteristics are important in the context of differences in subsequent treatment response.

Table 2. Changes in Glycemic Control and Body Weight After Treatment

Outcome	SGLT2 inhibitors group	GLP-1 receptor agonists group
Follow-up HbA1c (%)	7.2 ± 0.8	6.9 ± 0.7
Mean HbA1c reduction (%)	1.2	1.6
Mean weight reduction (kg)	3.1 ± 1.4	5.2 ± 2.0
Follow-up BMI (kg/m ²)	30.1 ± 3.9	30.1 ± 4.2

The follow-up measurements reveal the group that uses GLP-1 receptor agonists to have greater decreases in HbA1c and body weight than the group that uses SGLT2 inhibitors. Both treatments resulted in improvements in glycemic control and a reduction in BMI. The disparities indicate that this metabolic improvement could be different in various drug groups.

Graph 1. Comparison of Mean Hba1c Before and After Treatment Mean Hba1c Before and After Treatment



Both groups showed a decrease in mean HbA1c, but more in patients taking GLP-1 receptor agonists, the graph shows. These results suggest that both treatments could be effective for better long-term glycemic control.

Table 3. Cardiometabolic Outcomes Following Treatment

Outcome	SGLT2 inhibitors group	GLP-1 receptor agonists group
Systolic blood pressure (mmHg)	124.6 ± 10.2	126.1 ± 9.8
Diastolic blood pressure (mmHg)	78.2 ± 6.8	79.0 ± 6.5
LDL cholesterol (mg/dL)	98.4 ± 21.3	94.7 ± 19.8
Triglycerides (mg/dL)	156.2 ± 35.6	148.5 ± 32.4

Cardiometabolic parameters show beneficial effects in both treatment groups, and slightly reduced LDL cholesterol and triglyceride levels in the GLP-1 receptor agonist group. The mean values of blood pressure were quite comparable across groups. These summary values do not provide statistical significance without use of appropriate inferential testing.

DISCUSSION

This study aims to compare the effects of sodium-glucose cotransporter-2 (SGLT2) inhibitors with glucagon-like peptide-1 receptor agonists (GLP-1 RAs) on glycemic control, body weight and cardiometabolic risk in type 2 diabetes mellitus (T2DM) patients. Results showed that both treatment groups improved glycemic control, with higher reductions in HbA1c and body weight in the GLP-1 RA group. Lipid parameters also differed, but blood pressure outcomes were similar. The results highlight the need to consider several metabolic parameters when choosing glucose-lowering treatments. To explore the differences in these medication classes, a randomized controlled trial (RCT) of patients with early onset T2DM also compared the cardiometabolic effects of these classes, which underscores the need to account for the unique therapeutic profiles of these classes when personalizing diabetes care (1).

The effects of GLP-1 RAs on glucose-dependent insulin secretion, suppression of glucagon, gastric emptying, and appetite regulation may explain the greater reduction in HbA1c seen among patients taking GLP-1 RAs. All these mechanisms contribute to better postprandial and total glycemic control. In a systematic review and network meta-analysis of GLP-1 RAs, the authors determined that these drugs are effective for reducing HbA1c, body weight, and lipid profiles, but that the magnitude of the effect differs between individual agents (2). The decrease in HbA1c observed in the GLP-1 RA group was in line with the potential of the therapeutic class to offer a significant glucose-lowering effect. However, variations in baseline characteristics, dosages, treatment length and compliance could affect the size of the improvement and should be taken into account when interpreting comparative results.

Another significant benefit of weight loss in people with diabetes is that extra weight is associated with insulin resistance, high blood pressure, high cholesterol, and cardiovascular issues. The GLP-1 RA group had a larger mean

reduction in body weight than the SGLT2 inhibitor group in the present results. This difference is in line with the anorexic effects and increased satiety that are observed with GLP-1 receptor activation. Studies that have directly compared HbA1c and weight results in obese and non-obese adults also have highlighted the need to consider baseline obesity when assessing treatment effects (3). Thus, body weight should be viewed in conjunction with BMI and baseline metabolic status, and not as a stand-alone treatment outcome.

There are also clinically relevant effects of SGLT2 inhibitors that are insulin-independent, via the increased glucose excretion in urine. This process helps lower glucose, leads to a slight weight loss and changes in sodium balance can help improve blood pressure. Comparative studies that have compared the glycemic effect of SGLT2 inhibitors and GLP-1 RAs have demonstrated the need to evaluate the efficacy in patients with T2DM (4). While the current results indicate a superior HbA1c lowering effect of GLP-1 RAs, SGLT2 inhibitors are still useful therapeutic choices, especially when taking heart failure risk, renal function and other comorbidities into account. These drugs should therefore be selected based on the patient's clinical picture and not just on their effects on glycemia.

In T2DM, cardiovascular and renal protection are of particular importance as these complications significantly increase the risk of morbidity and mortality. Relative benefits of SGLT2 inhibitors and GLP-1 RAs on cardiovascular and renal outcomes is suggestive of varying benefits based on albuminuria and underlying kidney disease (5). While SGLT2 inhibitors have shown significant benefits in heart failure and kidney disease, GLP-1 RAs are especially significant for atherosclerotic cardiovascular risk reduction and weight management. Another network meta-analysis of cardiovascular outcome trials also examined the difference in cardiorenal outcomes between classes of glucose-lowering medications, which further emphasizes the need to choose glucose-lowering medications based on the individual's cardiovascular and renal risk (6). Therefore, the same level of improvement in some cardiometabolic markers may not equate to the same level of protection from major clinical endpoints.

The results also need to be viewed in the light of the evidence with patients who are overweight and obese. The efficacy and safety

of GLP-1 RAs and SGLT2 inhibitors were assessed in a systematic review and network meta-analysis of overweight and obese people, with and without diabetes (7). This evidence is relevant due to the fact that obesity often coexists with T2DM and may impact treatment response. The higher weight loss seen with GLP-1 RAs in the current findings suggests that they may be useful in situations where weight loss is a significant treatment goal. In certain patients, however, the use of SGLT2 inhibitors may be preferred due to their proven cardiorenal benefits, even if weight reduction is not the main goal of treatment.

Comparative effectiveness is interpreted by real-world studies. In an Italian cohort study, the efficacy and safety of GLP-1 RAs and SGLT2 inhibitors in routine diabetes care were evaluated, highlighting the need to analyze treatment outcomes outside of controlled clinical trials (8). Real-world results may be impacted by variation in patient selection, medication persistence, comorbidities, and concurrent therapies. Furthermore, a systematic review and network meta-analysis of GLP-1 RA-based treatments found that the glycometabolic outcomes differ between the individual agents and treatment regimens (9). Therefore, the results of the present study are not necessarily applicable to all drugs in either class, nor to all drug regimens.

Body composition changes could be another clue to the metabolic effects of these treatments. Complementary metabolic effects have been highlighted when comparing different pharmacological mechanisms, particularly single and combined treatment (10). Therapeutic benefits need to be weighed against tolerability and safety, however. The gastrointestinal side effects of GLP-1 RAs may include nausea and vomiting, while genital infections and, in patients that are prone to it, volume depletion are associated with SGLT2 inhibitors. The safety of GLP-1 RAs in the treatment of diabetes and chronic weight management is also of great importance, as demonstrated by a real-world investigation that compared the safety of these medications with their clinical effectiveness (11). Patient selection and monitoring are therefore crucial to ensure adherence to treatment and long-term improvements.

These medications have a broader cardiometabolic and renoprotective effect which is beneficial for their use in diabetes management. Hejji and colleagues' review underscores the possible role of GLP-1 RAs

and SGLT2 inhibitors in metabolic improvement and in the prevention of diabetes-related complications (12). However, weight loss doesn't always correspond to the same amount of fat loss. When examining the metabolic response to the treatment, the effects of SGLT2 inhibitors on body fat composition have been studied and compared with those of exenatide, highlighting the importance of looking at other anthropometric parameters (13). These factors justify the use of weight, BMI, blood pressure and lipid parameters in comparative studies.

Another important factor is combination therapy, as the two classes of drugs work in different ways. A systematic review of the use of combined SGLT2 inhibitor and GLP-1 RA therapy found that there was potential cardiometabolic efficacy, but adverse effects and individual treatment needs should be taken into account (14). Gourdy and co. also spoke about the rationale for using these agents together in patients with T2DM, particularly when monotherapy fails to meet glycemic goals and cardiovascular risk (15). Cohort studies and meta-analyses have also evaluated the efficacy and safety of combination therapy, providing further insights into its potential utility in clinical practice (16). Likewise, Singh and Singh mentioned the complementary metabolic and cardiovascular effects that could occur with combined use of both classes of drugs (17).

The results overall highlight the clinical relevance of both SGLT2 inhibitors and GLP-1 RAs, but the apparent benefits of GLP-1 RAs on HbA1c and weight loss should be taken with a pinch of salt. Findings may be limited in scope due to the observational design of the study, small sample size, and the fact that there is no verified statistical significance, and the differences in baseline characteristics may limit the conclusions. In addition, 6 months of follow-up might not be long enough to assess long-term cardiovascular and renal outcomes. Further research with larger numbers of patients, longer follow-up periods, and more sophisticated statistical analysis is required to provide more accurate comparative estimates. Ultimately, the glycemic goals, obesity, cardiovascular disease, kidney function, tolerability, cost, and patient preference should all be taken into account when making treatment decisions for optimal overall diabetes management.

CONCLUSION

Sodium-glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are two crucial therapeutic choices available for the treatment of type 2 diabetes mellitus (T2DM) in addition to their glycemic control. The results showed that GLP-1 RAs were linked to significant decreases in glycated hemoglobin (HbA1c) and body weight, and the SGLT2 inhibitors also had positive metabolic effects. Lipid parameters improved; blood pressure measurements were generally similar in the treatment groups. This information should inform individual treatment decisions based on glycemic goals, weight management requirements, cardiovascular risk, and renal function. The results, however, need to be interpreted with caution as verified patient-level data and statistical significance were not determined. These comparative effects need further study with larger sample sizes, longer follow-up periods, and comprehensive statistical analyses to validate and inform evidence-based treatment decisions for patients with type 2 diabetes mellitus.

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