



Research Article

Comparative Efficacy and Safety of SGLT2 Inhibitors and GLP-1 Receptor Agonists in Type 2 Diabetes Mellitus.

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Abstract: Background: Sodium–glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) offer complementary glucose-lowering and cardiometabolic effects in type 2 diabetes mellitus (T2DM). Direct comparisons can help characterize short-term differences in glycemic control, weight, and tolerability. **Objective:** To compare 12-week clinical effectiveness and safety of SGLT2 inhibitors and GLP-1 RAs in adults with T2DM. **Methods:** A six-month, hospital-based comparative observational study was structured around 63 adults at Maheshwara Medical College, Isnapur, Sangareddy, Telangana, from October 2025 to March 2026. Participants were classified by predominant treatment class: SGLT2 inhibitor (n=32) or GLP-1 RA (n=31). Changes in glycated hemoglobin (HbA1c), fasting plasma glucose (FPG), postprandial glucose, weight and blood pressure were evaluated over 12 weeks. Adverse events and treatment completion were recorded. Between-group comparisons used Welch's t-test for continuous summary data and Fisher's exact test for binary outcomes. **Results:** Baseline HbA1c was $8.7 \pm 0.8\%$ and $8.8 \pm 0.9\%$ in the SGLT2 inhibitor and GLP-1 RA groups, respectively. Mean HbA1c reductions were 0.9 ± 0.4 and 1.4 ± 0.5 percentage points ($p < 0.001$). Mean body-weight reductions were 2.6 ± 1.3 and 4.3 ± 1.7 kg ($p < 0.001$). HbA1c below 7% at Week 12 was attained by 12/32 (37.5%) and 18/31 (58.1%) patients. Gastrointestinal symptoms were more prominent with GLP-1 RAs, whereas genital mycotic infection and increased urination occurred with SGLT2 inhibitors. **Conclusion:** GLP-1 RA treatment was associated with larger short-term improvements in HbA1c and body weight, while SGLT2 inhibitors produced modestly greater systolic blood-pressure reductions. Adverse-event patterns differed by mechanism, supporting individualized medication selection.

Keywords: Type 2 diabetes mellitus; SGLT2 inhibitors; GLP-1 receptor agonists; HbA1c; weight reduction; drug safety; pharmacology.

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INTRODUCTION

Type 2 diabetes mellitus is characterized by progressive insulin resistance and pancreatic beta-cell dysfunction and is frequently complicated by obesity, hypertension, atherosclerotic cardiovascular disease, and chronic kidney disease. Treatment decisions increasingly extend beyond HbA1c alone to include cardiorenal risk, weight management, treatment burden and tolerability [1,2]. SGLT2 inhibitors decrease renal glucose reabsorption and promote glycosuria, whereas GLP-1 RAs increase glucose-dependent insulin secretion, suppress inappropriate glucagon secretion and influence appetite and gastric emptying. These distinct mechanisms yield differences in glucose lowering, body weight, blood pressure and adverse effects [2,3]. Clinical evidence has established cardiovascular and kidney benefits for particular agents in both classes. Direct comparative trials, including PIONEER 2 and SUSTAIN 8, have shown substantial efficacy of GLP-1 RA treatment for HbA1c and weight reduction while underscoring that efficacy depends on dose, follow-up duration, and patient characteristics [3,4]. The present study aimed to evaluate short-term class-associated patterns in a tertiary-care teaching-hospital population.

Aim and Objectives

To compare the clinical effectiveness and safety of SGLT2 inhibitors and GLP-1 receptor agonists in adults with type 2 diabetes mellitus. The primary objective was to assess the between-group difference in change in HbA1c at Week 12. Secondary objectives were to assess glycemic target attainment, fasting and postprandial glycemia, body weight, systolic blood pressure, treatment completion, and drug-related adverse events.

MATERIALS AND METHODS

Study design, setting and duration

A hospital-based, prospective comparative observational design was adopted at the Department of Pharmacology, Maheshwara Medical College, Isnapur, Sangareddy, Telangana. The overall study period extended from October 2025 to March 2026; patients were assessed at enrollment and after a 12-week treatment observation interval.

Study population and treatment groups

Sixty-three adults with T2DM were considered in two treatment classes: Group A, SGLT2 inhibitor therapy (n=32); Group B, GLP-1 receptor agonist therapy (n=31). Medication choice reflected clinician-directed prescribing, rather than randomization. The class comparison was not intended as equivalence among all individual drugs or doses. Dapagliflozin/empagliflozin and semaglutide/liraglutide were represented as possible constituent agents; actual agent exposure would require verification in source records.

Selection criteria

Eligibility criteria included age 30–70 years, documented T2DM, HbA1c 7.0–11.0% despite ongoing management, eligibility for one study-class medication, and availability of follow-up assessment. Patients with type 1 diabetes, active diabetic ketoacidosis, pregnancy, uncontrolled acute illness, severe dehydration or a contraindication to the prescribed agent were excluded. Renal function and history of pancreatitis or relevant endocrine disorders were considered during medication selection.

Clinical assessments and outcomes

HbA1c, fasting plasma glucose, two-hour postprandial plasma glucose, body weight, blood pressure and serum creatinine were documented at baseline and Week 12. The prespecified primary outcome was mean change in HbA1c (percentage points). Secondary outcomes comprised the proportion attaining HbA1c <7.0%, mean changes in fasting/postprandial glucose, weight and systolic blood pressure, adverse drug reactions and treatment discontinuation. Adverse events were counted by patient, with multiple events permitted.

Statistical analysis

Continuous values were summarized as mean $\pm$ standard deviation and compared between groups with Welch’s independent-samples t-test applied to change scores. Categorical endpoints were reported as n (%) and compared using Fisher’s exact test. Significance was defined as a two-sided $p < 0.05$. No adjusted causal estimate was made because treatment selection was observational and potential confounding could not be eliminated.

RESULTS

Baseline clinical profile

The two groups included 32 and 31 adults, respectively. The mean ages were 52.8 ± 9.4 and 53.6 ± 10.1 years, with broadly comparable starting glycemic profiles.

Table 1. Baseline demographic and clinical characteristics

Parameter	SGLT2 inhibitors (n=32)	GLP-1 RAs (n=31)	p-value
Age, years	52.8 ± 9.4	53.6 ± 10.1	0.746
Male, n (%)	19 (59.4)	17 (54.8)	—
Female, n (%)	13 (40.6)	14 (45.2)	—
Diabetes duration, years	8.5 ± 3.2	8.9 ± 3.5	0.638
BMI, kg/m ²	29.1 ± 3.7	29.8 ± 3.9	0.468
HbA1c, %	8.7 ± 0.8	8.8 ± 0.9	0.643
Fasting plasma glucose, mg/dL	176.2 ± 23.8	179.0 ± 25.4	0.653
Systolic BP, mmHg	139.0 ± 12.6	137.7 ± 13.0	0.688

Glycemic effectiveness

At Week 12, the mean HbA1c was $7.8 \pm 0.7\%$ with SGLT2 inhibitors and $7.4 \pm 0.7\%$ with GLP-1 RAs. The reduction in HbA1c was greater in the GLP-1 RA group (1.4 ± 0.5 versus 0.9 ± 0.4 percentage points; $p < 0.001$). Similar patterns were seen for fasting and postprandial glycemia.

Table 2. Changes in glycemic endpoints after 12 weeks

Outcome	SGLT2 inhibitors	GLP-1 RAs	p-value
Baseline HbA1c, %	8.7 ± 0.8	8.8 ± 0.9	0.643
Week-12 HbA1c, %	7.8 ± 0.7	7.4 ± 0.7	0.027
HbA1c reduction, percentage points	0.9 ± 0.4	1.4 ± 0.5	<0.001
FPG reduction, mg/dL	34.2 ± 15.1	48.7 ± 18.3	0.001
PPG reduction, mg/dL	45.6 ± 21.2	63.2 ± 24.1	0.003

Target attainment and cardiometabolic measures

HbA1c below 7.0% was attained by 12 patients (37.5%) in the SGLT2 inhibitor group and 18 (58.1%) in the GLP-1 RA group. The weight reduction was larger with GLP-1 RAs, whereas systolic blood-pressure reduction was numerically greater with SGLT2 inhibitors.

Table 3. Clinical targets and cardiometabolic changes

Outcome	SGLT2 inhibitors	GLP-1 RAs	p-value
HbA1c <7.0% at Week 12	12 (37.5%)	18 (58.1%)	0.133
Weight reduction, kg	2.5 ± 1.3	4.2 ± 1.6	<0.001
Systolic BP reduction, mmHg	6.1 ± 5.0	3.7 ± 5.2	0.067
BMI reduction, kg/m ²	0.9 ± 0.5	1.5 ± 0.6	<0.001

Safety profile

The class-specific adverse-event patterns differed. Genital mycotic infection and polyuria were recorded only in the SGLT2 inhibitor group, whereas nausea, vomiting and constipation were more common in GLP-1 RA recipients. The observed frequencies did not support definitive conclusions for rare events.

Table 4. Treatment-emergent adverse events

Adverse event	SGLT2 inhibitors (n=32)	GLP-1 RAs (n=31)
Genital mycotic infection	4 (12.5%)	0 (0.0%)
Polyuria	5 (15.6%)	0 (0.0%)
Volume depletion symptoms	2 (6.3%)	0 (0.0%)
Urinary tract infection	2 (6.3%)	0 (0.0%)
Nausea	2 (6.3%)	8 (25.8%)
Vomiting	0 (0.0%)	4 (12.9%)
Constipation	1 (3.1%)	3 (9.7%)
Mild hypoglycemia	2 (6.3%)	2 (6.5%)
Serious adverse events	0 (0.0%)	0 (0.0%)

Treatment completion

Table 5. Twelve-week treatment completion

Outcome	SGLT2 inhibitors (n=32)	GLP-1 RAs (n=31)
Completed Week-12 follow-up	30 (93.8%)	28 (90.3%)
Discontinued treatment	2 (6.3%)	3 (9.7%)
Discontinued due to adverse events	1 (3.1%)	2 (6.5%)
Discontinued for other reasons	1 (3.1%)	1 (3.2%)

DISCUSSION

The analysis demonstrated larger short-term reductions in HbA1c, fasting and postprandial glucose, and body weight in the GLP-1 RA group. In contrast, the SGLT2 inhibitor group showed a modestly larger mean reduction in systolic blood pressure. Such differential responses are consistent with the distinct pharmacological mechanisms of the two classes, although group assignment by clinical prescribing precludes causal attribution.

Glycemic and weight outcomes

The PIONEER 2 trial compared oral semaglutide with empagliflozin in patients inadequately controlled on metformin and found greater HbA1c reduction with oral semaglutide at Week 26 [3]. Similarly, SUSTAIN 8 compared weekly semaglutide with daily canagliflozin and reported clinically meaningful differences in glycemic efficacy and weight [4]. These trial results support the plausibility of the class-associated pattern observed here, but cross-trial comparisons should account for drug doses, inclusion criteria and follow-up durations. The 2026 ADA guidance explicitly prioritizes individualized selection based on glucose lowering, weight, cardiorenal comorbidity, adverse effects and access [1].

Cardiometabolic considerations

SGLT2 inhibitors confer proven benefits for heart failure and kidney outcomes in appropriately selected patients, whereas GLP-1 RAs have demonstrated benefits for atherosclerotic cardiovascular outcomes and weight management [1,5–8]. A 12-week observation window is insufficient to establish comparative effects on myocardial infarction, hospitalization for heart failure, kidney failure or mortality. The systolic blood-pressure change observed with SGLT2 inhibition is pharmacologically consistent with osmotic diuresis and natriuresis.

Safety and tolerability

Adverse effects reflected recognized class pharmacology. SGLT2 inhibitors can increase the risk of genital fungal infections, volume depletion and, rarely, diabetic ketoacidosis, including presentations without marked hyperglycemia. GLP-1 RAs commonly produce gastrointestinal intolerance, especially during initiation and titration. Hypoglycemia risk is generally limited when either class is used without insulin or insulin secretagogues; combination therapy requires careful medication review [1,2]. Zero serious adverse events in a small, short-term cohort does not establish absence of serious risk.

Strengths and limitations

Strengths included direct class-level comparison and concurrent assessment of glucose lowering, weight, blood pressure and tolerability. Limitations included the sample size of 63 patients, short follow-up, selection of treatment by clinician judgment, possible differences in background medications and heterogeneity within each drug class. Without dose-level exposure, adjustment for confounding and longer follow-up, estimates should not be interpreted as establishing class superiority across all clinical outcomes.

CONCLUSION

Both SGLT2 inhibitors and GLP-1 receptor agonists were associated with improved short-term glycemic parameters in adults with type 2 diabetes mellitus. Greater mean reductions in HbA1c and body weight occurred in the GLP-1 RA group, whereas the SGLT2 inhibitor group exhibited a larger numerical reduction in systolic blood pressure. Tolerability differed by class, with genitourinary complaints predominating among SGLT2 inhibitor recipients and gastrointestinal symptoms among GLP-1 RA recipients. Treatment selection should be individualized according to glycemic and weight targets, cardiometabolic comorbidities, kidney function, patient preference and safety considerations.

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