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Original Research Article

THE EFFICACY AND SAFETY OF DAPAGLIFLOZIN AND SITAGLIPTIN IN PATIENTS WITH UNCONTROLLED TYPE 2 DIABETES: A QUASI EXPERIMENTAL STUDY

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Abstract: *Type 2 diabetes mellitus (T2DM) is a prevalent metabolic disorder that requires effective glycemic control to prevent complications. Dapagliflozin, a sodium-glucose cotransporter-2 (SGLT2) inhibitor, and Sitagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, are commonly used in combination with Metformin for patients with uncontrolled T2DM. However, there is limited comparative data on the efficacy and safety of these two therapeutic regimens* ***Objectives:*** *To compare the efficacy and safety of Dapagliflozin and Sitagliptin in patients with uncontrolled type 2 diabetes.* ***Methods:*** *After approval from the ethical committee of Islamabad Medical Complex, 250 patients meeting the selection criteria were enrolled. Written informed consent was obtained from patients or their guardians. The patients were divided into two groups: Group A received Dapagliflozin with Metformin, while Group B received Sitagliptin with Metformin. Baseline lab tests were performed and repeated after 12 weeks, along with safety and tolerability assessments. Changes in HbA1c and other parameters were recorded. Efficacy was measured by changes in HbA1c, and safety was evaluated based on reported side effects. Data were collected using a predesigned questionnaire.* ***Results:*** *The study population had a mean age of 45.32 years and a mean BMI of 26.02; 54% were male and 46% female. Most participants (62.4%) were aged 31-50, and 33.2% were over 50. BMI distribution showed 45.6% were of normal weight, while 27.6% were obese. Group A's HbA1c dropped from 9.51 to 7.30 (mean difference: 2.20), and Group B's from 9.39 to 8.16 (mean difference: 1.23), both with p=0.00. Adverse effects included more UTIs in Group A (40.8% vs. 14.4%) and more diarrhea in Group B (38.4% vs. 4.8%), with small differences in other symptoms.* ***Conclusion:*** *The study concluded that both dapagliflozin and sitagliptin effectively reduce HbA1c in uncontrolled type 2 diabetes. Dapagliflozin showed a greater HbA1c reduction but had a higher rate of urinary tract infections, while sitagliptin had fewer UTIs but more gastrointestinal side effects. Further studies are needed to confirm these results and assess long-term safety and efficacy.*

Keywords: Dapagliflozin, Sitagliptin, Metformin, Uncontrolled Diabetes Type 2, HbA1c

Introduction

Diabetes mellitus is a major global health issue, affecting roughly 9% of adults worldwide [(1)] and leading to an estimated 1.5 million deaths annually from related complications, underscoring its substantial impact on public health. [(2)] The World Health Organization (WHO) anticipates that diabetes may become the seventh leading cause of death by 2030. [(3)] Individuals with uncontrolled T2DM are at high risk of complications, including cardiovascular disease, kidney dysfunction, neuropathy, and other metabolic disorders.(4) Managing T2DM effectively requires not only controlling blood glucose levels but also ensuring that treatments are safe and well-tolerated. The increasing prevalence of Type 2 diabetes mellitus (T2DM) globally underscores the need for effective and safe therapeutic options, particularly for patients with uncontrolled blood glucose levels who are at heightened risk of serious complications. Standard management strategies, which often include lifestyle modifications and metformin therapy, may be insufficient for achieving optimal glycemic control in a substantial subset of patients. In such cases, additional pharmacological interventions are warranted to improve outcomes and reduce the risk of complications. Dapagliflozin, an SGLT-2 inhibitor, and Sitagliptin, a DPP-4 inhibitor, represent two distinct pharmacological classes with mechanisms that address hyperglycemia through different pathways.(5) Dapagliflozin lowers blood glucose by promoting renal glucose excretion, and it has also been associated with beneficial effects on weight and blood pressure.(6) Sitagliptin, on the other hand, enhances insulin secretion and reduces glucagon levels, thus improving glycemic control without a significant risk of hypoglycemia.(7) Both drugs have shown potential in managing T2DM, but comparative evidence on their efficacy and safety in patients with uncontrolled diabetes remains limited. This study aims to evaluate the relative efficacy and safety of Dapagliflozin and Sitagliptin in patients whose blood glucose levels remain poorly controlled. A quasi-experimental design allows for practical, real-world insights into how each drug impacts glycemic control and safety profiles, offering valuable data to guide personalized diabetes treatment decisions and improve outcomes in this high-risk population.

Objective: To compare the efficacy and safety of Dapagliflozin and Sitagliptin in patients with uncontrolled type 2 diabetes.

Methodology

Quasi-experimental study Department of Medicine, Islamabad Medical Complex. The duration of the study was 6 month .Non-probability Consecutive sampling were used for the recruitment of patients. All patient with uncontrolled type 2 diabetes (on ≥ 1500mg of Metformin daily with or

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without sulfonylureas) and normal renal function presenting to the medical OPD of IMC. Patients of age 18-70 years. Both gender (male and female).Patients with Type 1 diabetes mellitus. History of heart failure or recent cardiovascular events within the last 6 months. Patients with decompensated liver disease, or those with suppressed immune functions along with the patients who discontinue the recommended drug regimen prematurely. Patients with uncontrolled hypertension (blood pressure > 180/110 mmHg).Individuals with severe cognitive impairment that may affect their ability to provide accurate information. Pregnant or breastfeeding women. Estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m².Following approval from the ethical committee of Islamabad Medical Complex, patients meeting the selection criteria were enrolled in the study. Written informed consent was obtained from the patients or their guardians after providing a clear explanation of the study's purpose, benefits, and potential risks. A total of 250 patients were enrolled. All the patients were divided into two groups. Group A patients received Dapagliflozin in addition to their baseline Metformin regimen, while Group B received Sitagliptin in addition to Metformin. Baseline laboratory investigations were conducted and were repeated after 12 weeks of follow-up. Patients were also followed up after 12 weeks to assess the safety and tolerability of the drugs. Changes in HbA1c and other parameters were recorded. Efficacy endpoints were defined as the change in HbA1c levels in the two groups from baseline. Safety endpoints were assessed based on the reported side effects of the drugs. Data were collected using a predesigned questionnaire.

The gathered data were entered and analyzed using the computer software Statistical Package for Social Sciences (SPSS) Version 25. The results for all quantitative variables, including age and HbA1C were expressed as mean ± standard deviation. Frequencies and percentages were presented for qualitative data such as gender. Paired samples T-test was used to compared the efficacy of both groups. And chi square test was used to compare the adverse effects of both groups. P value < 0.05 was considered significant.

Results

The study population had an average age of 45.32 ± 10.12 years and a mean BMI of 26.02 ± 4.83. Among the participants, 54% were male (n=135) and 46% were female (n=115). Age distribution showed that 4.4% were in the 18-30 years group, 62.4% in the 31-50 years group, and 33.2% were over 50 years old. BMI classification revealed that 3.2% were underweight, 45.6% had a normal BMI, 23.6% were overweight, and 27.6% were classified as obese (Table 1). In the pre- and post-intervention comparison, Group A showed a significant reduction in HbA1c levels from 9.51 ± 1.20 to 7.30 ± 1.07, with a mean difference of 2.20 ± 0.98 (p-value = 0.00). Group B also experienced a significant decrease, with HbA1c levels dropping from 9.39 ± 1.19 to 8.16 ± 0.99, resulting in a mean difference of 1.23 ± 0.73 (p-value = 0.00) (Table 2). Table 3 presents a comparison of adverse effects between Group A and Group B, showing that urinary tract infections were significantly more common in Group A (40.8%) compared to Group B (14.4%) with a p-value of 0.000. Diarrhea was reported by 4.8% of patients in Group A and 38.4% in Group B, while increased urination occurred in 13.6% of Group A and 12.8% of Group B. Nausea was noted in 15.2% of Group A and 8.8% of Group B, headaches in 16.0% of Group A and 15.2% of Group B, and mild dizziness in 9.6% of Group A and 10.4% of Group B.

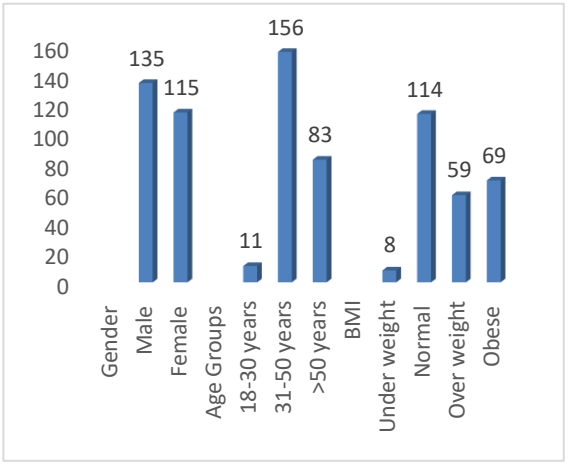

Fig 1: Frequency of patients on the basis of different variables

Table 1: Characteristics of enrolled patients *(n=250)*

Variables	
Age (Years)	45.32±10.12
BMI	26.02±4.83
Gender	
Male	135(54.0%)
Female	115(46.0%)
Age Groups	
18-30 years	11(4.4%)
31-50 years	156(62.4%)
>50 years	83(33.2%)
BMI	
Under weight	8(3.2%)
Normal	114(45.6%)
Over weight	59(23.6%)
Obese	69(27.6%)

Table 2: Pre-intervention and post-intervention comparison

Groups	**Pre intervention**	**Post intervention**	**Difference**	**p-value**
Group A	9.51±1.20	7.30±1.07	2.20±0.98	0.00
Group B	9.39±1.19	8.16±.99	1.23±0.73	0.00

Table 3: Comparison of Reported Adverse Effects between Group A and Group B

	Group A	**Group B**	**p-value**
Urinary tract infection	51(40.8%)	18(14.4%)	0.000
Diarrhea	6(4.8%)	48(38.4%)	
Increased urination	17(13.6%)	16(12.8%)	
Nausea	19(15.2%)	11(8.8%)	
Headache	20(16.0%)	19(15.2%)	
Mild dizziness	12(9.6%)	13(10.4%)	

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Discussion

The quasi-experimental study on the efficacy and safety of Dapagliflozin and Sitagliptin in patients with uncontrolled Type 2 diabetes (T2DM) addresses a critical aspect of diabetes management by comparing two distinct pharmacological approaches. Uncontrolled T2DM is a challenging condition, associated with high risks of complications, including cardiovascular disease, kidney dysfunction, and neuropathy, which necessitates effective glycemic management options.(8) This study specifically focuses on patients who have not achieved adequate glucose control with standard therapies, making them ideal candidates for alternative or adjunctive treatments. Sitagliptin and dapagliflozin belong to two different classes of oral antihyperglycemic agents (AHAs) used in the treatment of patients with type 2 diabetes (T2D).(9) Dapagliflozin, a SGLT-2 inhibitor, works by inhibiting glucose reabsorption in the kidneys, promoting glucose excretion through urine, which can lead to reduced blood glucose levels, improved glycemic control, and additional benefits like weight loss and blood pressure reduction.(10) Sitagliptin, a DPP-4 inhibitor, has a different mechanism; it enhances insulin secretion and decreases glucagon release, thereby aiding glycemic control with minimal risk of hypoglycemia.(11) Both agents are generally well-tolerated, but their side effect profiles differ, with Dapagliflozin sometimes associated with an increased risk of urinary tract infections and Sitagliptin linked to gastrointestinal symptoms in some patients.(12) Previous studies have examined the safety and/or efficacy of either sitagliptin or dapagliflozin in older patients, however, none have specifically assessed these treatments in an older population with mild renal insufficiency.(13-15)

In comparing these two treatments in a quasi-experimental study design, this research evaluates not only the efficacy of each drug in reducing HbA1c levels but also the safety profiles based on reported side effects and adverse events over a defined period. Such comparisons can provide valuable insights into which drug might be more suitable for patients with specific clinical characteristics or comorbidities, supporting personalized treatment strategies. In the pre- and post-intervention comparison, both Group A and Group B showed statistically significant reductions in HbA1c levels, indicating improved glycemic control following the interventions. Group A exhibited a more substantial decrease in HbA1c, with levels falling from 9.51 ± 1.20 to 7.30 ± 1.07. This reduction yielded a mean difference of 2.20 ± 0.98, with a highly significant p-value of 0.00, demonstrating the effectiveness of the intervention in this group. Similarly, Group B experienced a notable reduction in HbA1c levels, from 9.39 ± 1.19 to 8.16 ± 0.99, with a mean difference of 1.23 ± 0.73 and a p-value of 0.00. While both groups showed improvement, the reduction in HbA1c levels was more pronounced in Group A, as evidenced by the greater mean difference. These findings suggest that while both interventions effectively lowered HbA1c, the approach in Group A may offer a more impactful improvement in glycemic control for patients. The findings of the present study are consistent with those of Sarah L. Anderson et al.(16), who reported that dapagliflozin is effective both as a monotherapy and when used in combination with other oral antihyperglycemic agents and insulin. Their study demonstrated that dapagliflozin can reduce HbA1c levels by approximately 6 mmol/mol (0.5%) to 8 mmol/mol (0.7%), supporting its efficacy in improving glycemic control. This aligns with the HbA1c reductions observed in our study, reinforcing the role of dapagliflozin as an effective treatment option in managing blood glucose levels. Another study also supported our finding.(17)

The analysis of adverse effects between the two groups revealed notable differences. Urinary tract infections (UTIs) were significantly more prevalent in Group a, affecting 40.8% of patients, compared to only 14.4% in Group B, with a highly significant p-value of 0.000. This suggests a strong association between the intervention used in Group A and a higher incidence of UTIs.

Diarrhea was reported more frequently in Group B, where 38.4% of patients experienced this side effect, compared to only 4.8% in Group A. This marked difference may indicate that the intervention in Group B is more likely to cause gastrointestinal discomfort. Increased urination was relatively similar in both groups, with 13.6% of Group A and 12.8% of Group B reporting this effect, suggesting it is a common but minor issue in both interventions.

Other adverse effects, such as nausea, headaches, and mild dizziness, showed less pronounced differences between the groups. Nausea was reported by 15.2% of patients in Group A and 8.8% in Group B, while headaches affected 16.0% in Group A and 15.2% in Group B. Mild dizziness was observed in 9.6% of Group A and 10.4% of Group B. These findings indicate that, apart from UTIs and diarrhea, most side effects were comparable in frequency across the two groups. The results suggest that while both treatments have distinct side effect profiles, they are generally well-tolerated with relatively low incidences of severe adverse events.

Conclusion

It was concluded that both dapagliflozin and sitagliptin effectively reduce HbA1c levels in patients with uncontrolled type 2 diabetes, supporting their roles in improving glycemic control. Dapagliflozin was associated with a more significant reduction in HbA1c levels, highlighting its potential efficacy in managing blood glucose. However, it was also linked to a higher incidence of urinary tract infections, indicating a distinct side effect profile that should be considered when selecting treatment options. Sitagliptin showed efficacy with fewer urinary tract infections but a higher incidence of gastrointestinal side effects such as diarrhea. Further research involving larger and more diverse patient populations is recommended to confirm these findings and to explore the long-term safety and efficacy of these medications in various clinical settings.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-TVCH-023/23)

Consent for publication

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The authors declared absence of conflict of interest.

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