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Original Research Article

Efficacy and Safety of Once Weekly Oral Trelagliptin Switched From Once Daily Sitagliptin in the Glycaemic Control of Type 2 Diabetes Mellitus

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Abstract: *Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder requiring effective long-term glycaemic control. Dipeptidyl peptidase-4 (DPP-4) inhibitors such as sitagliptin are commonly used for glucose regulation. Trelagliptin, a once-weekly oral DPP-4 inhibitor, offers the potential for improved patient compliance.* ***Objective:*** *To evaluate the efficacy (glycaemic control) and safety of once-weekly oral trelagliptin in comparison to once-daily sitagliptin in patients with T2DM.* ***Methods:*** *This quasi-experimental (pre-post intervention) study was conducted at the Diabetes and Endocrine Unit, Nishtar Hospital, Multan, from November 2024 to April 2025. A total of 35 patients aged >12 years with well-controlled HbA1c (6.5–8.5%) on sitagliptin therapy were enrolled. Patients with a history of hypoglycaemia, diabetic ketoacidosis, or diabetic coma in the preceding 6 months were excluded. After switching from sitagliptin to trelagliptin, HbA1c levels were recorded to assess glycaemic control. Data were analysed using SPSS version 26. Quantitative variables were summarized using means and standard deviations, and categorical variables using frequencies and percentages. A paired-samples t-test was used to compare pre- and post-intervention HbA1c values.* ***Results:*** *The mean age of the participants was 49.8 ± 10.5 years, with females comprising 60% of the study population. Mean HbA1c prior to switching (sitagliptin) was 7.37 ± 0.61%, and after switching to trelagliptin was 7.41 ± 0.68% (p > 0.05), indicating comparable glycaemic control. Improved compliance was noted with once-weekly trelagliptin. Minor side effects were reported in 17.1% of patients, with no major or life-threatening adverse events observed.* ***Conclusion:*** *Once-weekly oral trelagliptin demonstrated comparable glycaemic control to daily sitagliptin, with good patient compliance and an acceptable safety profile, making it a viable alternative in the management of T2DM.*

Keywords: Compliance, Dipeptidyl Peptidase IV Inhibitors, Glycated Hemoglobin A, Hypoglycemia, Sitagliptin Phosphate, Trelagliptin, Type 2 Diabetes Mellitus

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Introduction

Diabetes mellitus is a chronic metabolic condition marked by persistently high blood glucose levels. This occurs either due to insufficient insulin production or because the body's cells do not respond effectively to insulin, a state known as insulin resistance (1). Type 2 diabetes mellitus (T2DM) specifically involves multiple metabolic disturbances, including reduced insulin sensitivity in peripheral tissues, an inadequate insulin response from the pancreas, and increased hepatic glucose production during fasting (2). If left untreated or poorly controlled, diabetes can lead to numerous complications—both short- and long-term—affecting the eyes, kidneys, nerves, heart, and blood vessels, contributing significantly to patient suffering and increased risk of death (3, 4).

Managing T2DM effectively requires a holistic, multidisciplinary approach that combines lifestyle changes—such as diet and exercise—with pharmacological treatments. The goal is to achieve and maintain optimal glycemic control tailored to the needs of each individual (5, 6). Over the years, various classes of antidiabetic drugs have been developed, one of which is the DPP-4 (dipeptidyl peptidase-4) inhibitor group.

DPP-4 inhibitors work by preventing the breakdown of incretin hormones, including GLP-1, which are involved in stimulating insulin release and lowering blood glucose levels. These medications are well-tolerated, associated with minimal risk of hypoglycemia, and do not typically cause weight gain. While clinical trials have confirmed their cardiovascular safety, they have not shown significant cardiovascular benefits (7).

DPP-4 inhibitors are available in both daily and weekly formulations. Common daily options include sitagliptin, vildagliptin, and linagliptin, while trelagliptin is a once-weekly alternative. Trelagliptin, a derivative of alogliptin, has emerged as a promising once-weekly oral DPP-4 inhibitor. The standard dose is 100 mg weekly for patients with normal to mildly impaired renal function (8). With a half-life of approximately 54.3 hours, trelagliptin sustains significant enzyme inhibition over seven days. Studies have shown that after 12 weeks of once-weekly treatment, DPP-4 inhibition remained at 77.4% seven days post-dose, compared to only 2.4% in the placebo group. Whether used alone or with other antidiabetic agents, trelagliptin has demonstrated long-term efficacy and safety (9, 10).

Although several international studies have compared once-weekly DPP-4 inhibitors to their daily counterparts, data remains limited in the local context. This study aims to evaluate and compare the glycemic efficacy of daily sitagliptin (100 mg) and weekly trelagliptin (100 mg) in patients with T2DM attending the Diabetes and Endocrine Clinic at Nishtar Hospital, Multan.

Methodology

This was a quasi-experimental (pre-post intervention) study, which was conducted in the Diabetes and Endocrine Unit, Nishtar Hospital, Multan, over six months from November 2024 to April 2025, after approval from the Institutional ethical review board (ERC=18989/NMU on 02-11-24). Informed consent was taken from patients before the collection of their data.

Patients of more than 12 years, diagnosed with type 2 diabetes mellitus, taking sitagliptin 100 mg daily alone or with a combination of other antidiabetics for at least 12 weeks and their HbA1c well controlled, between 6.5 to 8.5, were included in the study. The patients less than 12 years of age, who experienced hypoglycaemia, diabetic acidosis or coma

within 6 months, had major hemoglobinopathy, hepatic impairment, ECG abnormalities (prolonged QT interval), and concomitant use of medicines that may affect efficacy evaluation of the trial drugs e.g. glucocorticoids, estrogens were excluded from the study. The eligible patients were switched to trelagliptin 100 mg once weekly in place of sitagliptin. At the same time, other antidiabetics were continued in the same dose, and their HbA1c was measured after 12 weeks of treatment. A fixed diet and exercise plan for these patients was recommended.

The efficacy of sitagliptin and tregliptin was compared using HbA1c, random blood sugar (RBS), and fasting blood sugar (FBS) values. At the start of the study, HbA1c, RBS, and FBS values were taken while patients were on sitagliptin 100 mg daily treatment for at least 12 weeks. Then patients were switched to trelagliptin 100 mg once weekly for 12 weeks, and again HbA1c, RBS, and FBS values were measured. Treatment compliance by the patient was evaluated by the investigator at each visit based on the following four categories: took the drug majority of the time (compliance rate more than 90%), usually took the medicine (compliance rate 70-89%), took the drug more than half of the time of dosing (compliance rate between 50-69%), took the drug less than half of the time of dosing (compliance rate less than 50%).

The minimum sample size of 31 patients was needed to detect a HbA1c% within 0.18% of the pre-treatment HbA1c of 7.06±0.49% with a 95% confidence level, using the WHO sample size calculator formula for a continuous response variable. Data was entered and analysed on SPSS version 26 and then summarized using descriptive statistics as mean and standard deviation for quantitative data and frequencies and percentages for categorical data. Pre and post-HbA1c (%) were compared through a paired t-test, and a p-value <0.05 was taken as significant.

Results

The mean age of patients was 49.88±10.5 years. Patients up to 40 years were 7 (20%), from 41 to 60 years 22 (62.9%), and above 60 years were 6 (17.1%) in number. Males were 14 (40%) while females were 21 (60%). Patients from rural backgrounds were 5 (14.3%), and from urban areas were 30 (85.7%). The mean BMI of patients was 25.22±2.0 kg/m2 **(Table 1).**

Table 1: Characteristics of Type 2 Diabetes mellitus patients (N=35)

Characteristics	Mean	Standard deviation
Age (years)	49.88	10.46
Body Mass Index (kg/m^2)	25.23	1.99
Age category	Frequency	Percentage
Up to 40 years	7	20
41-60 years	22	62.9
More than 60 years	6	17.1
Gender		
Male	14	40
Female	21	60
Residence		
Rural	5	14.3
Urban	30	85.7

The HbA1c, RBS, and FBS values of patients who were on sitagliptin and after replacement with trelagliptin (12 weeks of use) were compared. The mean FBS value when the patient was on daily sitagliptin is 112.63±14.26 as compared to 112.91±13.64 when on weekly trelagliptin. The mean RBS value with sitagliptin is 153.46±24.61, and with trelagliptin RBS mean is 153.51±24.53. Sitagliptin-treated patients have a 7.37 % mean HbA1c±0.61, and trelagliptin-treated patients have a 7.41 % mean HbA1c±0.68 (Table 2).

Table 2: Comparison of glycemic parameters of Type 2 diabetes patients on Trelagliptin when switched from Sitagliptin (N=35)

Parameters	On Sitagliptin	On Trelagliptin	P-value*
FBS	112.63±14.26	112.91±13.64	0.570
RBS	153.46±24.61	153.51±24.53	0.928
HbA1C	7.37±0.61	7.41±0.68	0.264

***paired t-test**

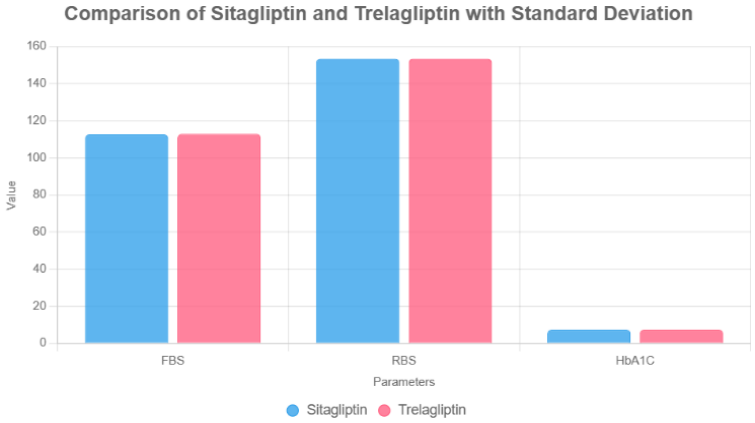

Figure 1: Comparison of glycemic parameters of Type 2 diabetes patients

Patients taking sitagliptin did not show complete compliance, and 21 patients (60%) took medicines with complete compliance, while other patients had some missed doses per week. Patients who were taking trelagliptin had full medicine intake compliance (100%). Out of 35 patients, 29 patients (82.9%) experienced no side effects, and 2 patients (5.7%) felt the feeling of nausea. One patient each experienced vomiting, headache, abdominal pain, and loose motions.

Discussion

Trelagliptin, a long-acting DPP-4 inhibitor, has been developed for the management of type 2 diabetes mellitus. It functions by enhancing the activity of incretin hormones, thereby improving insulin secretion and reducing blood glucose levels. Chemically, trelagliptin is a fluorinated derivative of alogliptin. It differs from daily DPP-4 inhibitors due to its extended half-life, allowing once-weekly dosing, which is a distinct advantage in terms of patient convenience and adherence.

In a Phase 1 clinical study, trelagliptin demonstrated dose-proportional pharmacokinetics over a wide dosing range (3.125–800 mg). The peak plasma concentration was typically reached within 1.0 to 1.5 hours, with an elimination half-life ranging between 38.4 and 54.3 hours. Importantly, a single 100 mg dose resulted in sustained DPP-4 inhibition of approximately 75–80% even seven days post-administration (11). These findings support the drug's potential for effective glycaemic control with weekly administration.

In our study, we compared the efficacy of trelagliptin with sitagliptin in patients who were already following a stable diet and exercise regimen. The results revealed no statistically significant difference in fasting blood glucose, random glucose, or HbA1c between the two groups. This indicates that trelagliptin provides glycaemic control comparable to that of daily sitagliptin, supporting its use as an effective alternative for patients requiring DPP-4 inhibitor therapy.

Our findings are consistent with previous research. A meta-analysis conducted by Deep D. et al. confirmed that trelagliptin offers similar glycaemic efficacy to other antidiabetic medications over a 12- to 24-week period (10). Another meta-analysis by Tomohide Y. et al. demonstrated that weekly DPP-4 inhibitors, including trelagliptin, significantly reduced HbA1c by 0.66%, fasting plasma glucose by 0.72 mmol/L, and postprandial glucose by 1.82 mmol/L compared to placebo. Moreover, the risk of side effects such as pancreatitis, severe hypoglycemia, and gastrointestinal disturbances did not differ significantly from placebo. Importantly, when compared directly to daily DPP-4 inhibitors, there was no notable difference in glycaemic outcomes or adverse effects (12).

Several studies have evaluated the comparative efficacy of sitagliptin and trelagliptin and reached similar conclusions, noting that both drugs deliver comparable metabolic outcomes (13). However, the once-weekly dosing schedule of trelagliptin offers a clear advantage in enhancing treatment adherence.

Poor compliance with oral antidiabetic therapy is a well-documented issue among patients with T2DM. Factors such as complex medication regimens, depression, forgetfulness, and the burden of multiple medications often lead to suboptimal adherence. In this context, a once-weekly oral medication like trelagliptin can play a significant role in simplifying treatment and encouraging regular use (14). Our study found that participants using trelagliptin demonstrated higher medication compliance, a finding echoed by other researchers who reported improved adherence with this weekly formulation (15-17).

Additionally, trelagliptin was well tolerated by our study participants, with no serious adverse events observed. This safety profile aligns with previous studies that have established the long-term tolerability of trelagliptin (18, 19).

One of the strengths of our research lies in its focus on a relatively novel treatment option—once-weekly DPP-4 inhibitors—in a regional context where such studies are scarce. Particularly in South Punjab, limited data exist on the real-world use of trelagliptin. Nevertheless, our study had certain limitations, including a small sample size and its single-center design based in Nishtar Hospital, Multan. Therefore, further large-scale, multi-center research is recommended to validate and expand upon our findings.

Conclusion

From this study, we found that the glycaemic efficacy of once weekly trelagliptin to control type 2 diabetes mellitus is comparable to once daily DPP-4 sitagliptin. Trelagliptin also has the added benefit of an easy dose regimen and increased compliance with medicine. This study will help contribute to the new advancements in the treatment of diabetes mellitus.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned. (IRBEC- ERC=18989/NMU)

Consent for publication
Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

MMN (FCPS Medicine Postgraduate Resident)
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Review of Literature, Data entry, Data analysis, and drafting articles.
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Conception of Study, Development of Research Methodology Design,

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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