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Research Article

Glycemic Control and Safety Profile of Newer Oral Antidiabetic Drugs in Type 2 Diabetes Mellitus

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Abstract

Introduction: Due to poor glycemic control and its complications, type 2 diabetes mellitus (T2DM) is a major global health concern that is associated with a high rate of morbidity and mortality. More modern oral antidiabetic drugs have been introduced, and this has increased the therapeutic options that have better efficacy and safety. Nevertheless, there is limited data on their efficacy and tolerability of them in the local real world.

Materials and Methods: 160 patients with T2DM who were taking newer oral antidiabetic medications participated in this Prospective observational study, which was conducted over a six-month period in a hospital with tertiary care. Glycemic control was assessed using changes in glycated hemoglobin levels and fasting blood glucose (FBG) levels. By documenting the unfavorable follow-up events, the safety was assessed. While independent t-tests and chi-square tests were employed to assess the intergroup and categorical variables, paired t-tests were utilized to compare baseline and follow-up glycemic parameters. Statistically a p-value of less than 0.05 was considered significant.

Results: At baseline, the mean HbA1c was 8.4 ± 1.1%; at follow-up, it was 7.1 ± 0.9% ($p < 0.001$). Additionally, there was a substantial reduction in FBG levels ($p < 0.001$). 61.3% of patients had appropriate glycemic control (HbA1c <7%). HbA1c was reduced more by SGLT-2 inhibitors than by DPP-4 inhibitors ($p = 0.02$). 28.8% of the participants reported complications, the majority of which were minor and controllable.

Conclusion: Newer oral anti-diabetic drugs can manage the level of glycemia and is safe in patients with T2DM, but the SGLT-2 inhibitors have superior effects.

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Introduction

Insulin insensitivity and increasing pancreatic β-cell dysfunctionare hallmarks of T2DM, a chronic metabolic disease that causes persistent hyperglycemia [1]. This is one of the significant global health problems, and its prevalence rate is growing rapidly, especially among the low- and middle-income nations [2]. Microvascular problems, such as neuropathy, nephropathy, and retinopathy, and vascular consequences, such as coronary heart disease and stroke, are closely associated with insufficient blood sugar control in T2DM patients [3]. Therefore, achieving and keeping appropriate blood sugar control to reduce morbidity, death, and health burden is the anticipated outcome of diabetes management [4]. Novel oral antidiabetic medications (OADs), such as dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium-glucose co-transporter-2 (SGLT-2) inhibitors, and novel insulin sensitizers, have significantly altered the treatment of T2DM throughout the past ten years [5].

A number of possible benefits over traditional treatment methods like sulfonylureas and metformin are presented by these agents, including reduced likelihood of hypoglycemia, weight neutrality and reduction of weight, and other renal and cardiovascular advantages [6]. Subsequently, they are becoming part of global and local treatment standards, which are used to manage T2DM [7].

Regardless of their increasing usage, there are still concerns over the effectiveness and safety profile of these new oral antidiabetic agents in practice [8]. Genitourinary infections, gastrointestinal intolerance, and volume depletion were also adverse effects, with unusual but severe complications also reported, with their rate potentially differing among groups of people [9]. Moreover, the majority of evidence on the glycemic efficacy and safety of these medications are based on randomized controlled trials, which might not necessarily be a fully representative of clinical practice in a limited resource setting [10].

Rationale and Objectives

Since more oral antidiabetic medications are being prescribed and there is limited local data information regarding actual performance, there is a need to investigate their efficacy and safety in patients with T2DM. The study aim is therefore to assess the level of glycemic control on newer oral antidiabetic drugs and analyze their safety profile in the clinical care. To determine the glycemic control and safety of the newer oral antidiabetic medications in those affected with T2DM.

Materials and Methods

Study Design and Setting

The current study was a Prospective observational study carried out in the outpatient medical and endocrinology outpatient clinics within a teaching hospital of tertiary care. The study duration was six months and the study sample consisted of qualified patients with T2DM that were on newer oral medications for diabetes and observed to determine the safety and glycemic control results.

Study Population

The study sample comprised of adult patients with T2DM based on the American Diabetes Association (ADA) criteria and those who received newer oral antidiabetic drugs either alone or in conjunction with other oral antidiabetic medications. The recruitment of the patients was done as a part of a consecutive follow-up visit to reduce selection bias. Those patients having type 1 diabetes mellitus, gestational diabetes, severe liver disease, end-stage kidney disease, active infections, or undergoing injectable antidiabetic treatment (insulin or GLP-1 receptor agonist) were excluded. Included were also patients who were unable to follow up or failed to have their consent.

Sample Size Calculation

The formula for calculating a single population proportion was used to get the sample size:

$$n = \frac{Z^2 \times p \times (1 - p)}{d^2}$$

Z is the standard normal deviation corresponding to a 95% confidence level (1.96), p is the expected percentage of patients who were able to achieve sufficient glycemic control using more recent oral antidiabetic medications, d is the degree of error, and n is the necessary sample size.

Since there is no strong local data, p assumed was 50% to acquire the highest sample size with precision 8%. According to these assumptions, 150 patients were the size of the sample. The ultimate

sample size comprised 160 patients to consider the potential dropouts and missing data.

Data Collection Procedure

Informed consent was obtained after which baseline demographic and clinical data were collected like age, gender, body mass index (BMI), duration of diabetes, comorbid conditions and type and period of antidiabetic therapy. The laboratory parameters of FBG, HbA1c and arbitrary blood sugar were recorded in baseline and retested during follow-up visits in accordance with the regular clinical practices.

The safety profile of newer oral antidiabetic drugs was assessed by recording any adverse events that were experienced by patients or noticed in the follow-up period, such as hypoglycemia, gastrointestinal events, genital urinary events, dizziness, and any other drug-related complaints. The adverse events were evaluated by interviewing the patients, conducting physical examination, and analyzing the medical records.

Outcome Measures

Glycemic control, as determined by changes in HbA1c and FBG levels over the study period, was the primary end measure. HbA1c below 7%was taken to be the degree of appropriate glycemic control, as per the conventional clinical premises. The safety profile, assessed by the number and nature of the adverse effects of newer oral antidiabetic drugs, was the secondary outcome. The safety profile was assessed by recording adverse events during follow-up visits. Adverse events were identified through patient interviews, clinical examination, and review of medical records. Hypoglycemia was defined as a blood glucose level of less than 70 mg/dL or the presence of typical hypoglycemic symptoms confirmed by glucose measurement. All events were documented and evaluated by the attending physician.

Statistical Analysis

SPSS version 26.0 was used for analyzing the data. Continuous variables were expressed by mean ± standard deviation, whereas categorical variables were described by frequencies and percentages. Only until the normality of continuous variables was established were parametric tests employed. Paired t-tests were used to do a basic comparison of glycemic parameters at baseline and follow-up. Independent sample t-tests were used to compare drug groups. When applicable, categorical variables were analyzed using the Fisher exact test or the chi-square test. A p-value of below 0.05 is regarded as significant statistically.

Ethical Considerations

The Institutional Review Board granted ethical approval prior to the study's execution. All participants were informed using written consent and confidentiality of patient information was strictly maintained. The research was done by adhering to the principles of the Declaration of Helsinki.

Results

The final analysis included 160 patients with T2DM. All enrolled participants were evaluated for glycemic control and safety outcomes.

The study participants' average age was 52.6 ± 9.8 years. The study population was found to be predominately male. Diabetes lasted an average of 6.9 ± 3.4 years. The majority of patients were overweight or obese, and the most common concomitant illness was hypertension, which was followed by dyslipidemia as shown in Table 1.

Table 1: The study population's baseline clinical and demographic characteristics (n = 160)

Variable	Category	Frequency (%) / Mean ± SD
Age (years)		52.6 ± 9.8
Gender	Male	102 (63.8%)
	Female	58 (36.2%)
Duration of diabetes (years)		6.9 ± 3.4
BMI (kg/m²)		28.1 ± 4.2
Hypertension	Present	96 (60.0%)
Dyslipidemia	Present	72 (45.0%)

Among the newer oral antidiabetic drugs, SGLT-2 inhibitors were prescribed to 68 patients (42.5%), while DPP-4 inhibitors were prescribed to 74 patients (46.3%). The remaining patients received

a combination of two newer oral antidiabetic agents along with metformin. The distribution of patients according to antidiabetic therapy is presented in Figure 1.

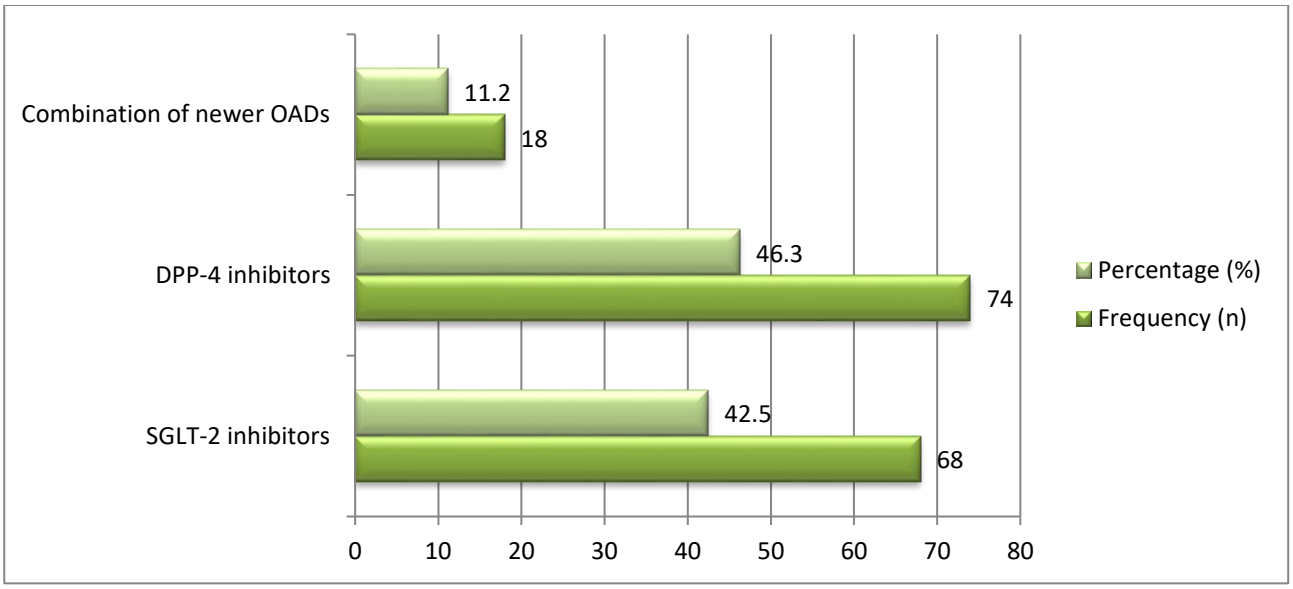

Figure 1: Distribution of Patients According to Antidiabetic Regimen

The mean FBG level was 168.2 ± 32.5 mg/dL and the mean HbA1c level was 8.4 ± 1.1% at baseline. When the follow-up time is over, significant improvements in glycemic parameters were observed. The mean HbA1c decreased to 7.1 ± 0.9%, while the mean FBG reduced to 134.6 ± 24.8 mg/dL.

The HbA1c and FBG levels changed showed statistically significant improvement ($p < 0.001$), according to a paired t-test. All in all, 98 patients (61.3%) attained a sufficient glycemic level, which is viewed as HbA1c below 7%. Table 2 demonstrates the comparison of glycemic parameters in the pre-and post-treatment.

Table 2: Comparison of Glycemic Parameters at Baseline and Follow-up

Parameter	Baseline (Mean ± SD)	Follow-up (Mean ± SD)	p-value
HbA1c (%)	8.4 ± 1.1	7.1 ± 0.9	<0.001
FBG (mg/dL)	168.2 ± 32.5	134.6 ± 24.8	<0.001

Those who were put on SGLT-2 inhibitors showed higher reduction in HbA1c than those put on DPP-4 inhibitors. The SGLT-2 inhibitor group had a mean decrease in HbA1c of 1.5 ± 0.8% with a DPP-4 inhibitor of 1.1 ± 0.7%. This difference was significant statistically ($p = 0.02$) according to the analysis of independent sample t-test. The same was encountered when it came to reducing FBG ($p = 0.03$). Table 3 demonstrates intergroup comparison of glycemic outcomes.

Table 3: Comparison of Glycemic Outcomes between Drug Groups

Parameter	SGLT-2 inhibitors (Mean ± SD)	DPP-4 inhibitors (Mean ± SD)	p-value
HbA1c reduction (%)	1.5 ± 0.8	1.1 ± 0.7	0.02
Fasting glucose reduction (mg/dL)	38.6 ± 21.4	30.1 ± 19.6	0.03

Adverse events were reported in 46 patients (28.8%). The most frequent side effect was genitourinary infections, which were mostly seen in patients on SGLT-2 inhibitors. Gastrointestinal symptoms were more frequently reported in patients receiving DPP-4 inhibitors. Episodes of hypoglycemia were mild and infrequent. The SGLT-2 inhibitor group had a substantially greater incidence of adverse events than the DPP-4 inhibitor group, according to chi-square test analysis ($p = 0.04$). There were no reports of severe adverse medication responses or stopping therapy. Table 4 summarizes the distribution of adverse events.

Table 4: Adverse Events According to Drug Class

Adverse event	SGLT-2 inhibitors n (%)	DPP-4 inhibitors n (%)	p-value
Genitourinary infections	18 (26.5%)	6 (8.1%)	0.01
Gastrointestinal symptoms	7 (10.3%)	14 (18.9%)	0.04
Hypoglycemia	4 (5.9%)	5 (6.8%)	0.82
Any adverse event	29 (42.6%)	21 (28.4%)	0.04

A shorter period of diabetes was substantially correlated with achieving appropriate glycemic control (HbA1c <7%). Compared to patients with longer disease durations, those with shorter disease durations had better glycemic control (χ^2 test, p = 0.01). Gender and BMI did not significantly correlate with glycemic control. Figure 2 goes into detail about these relationships.

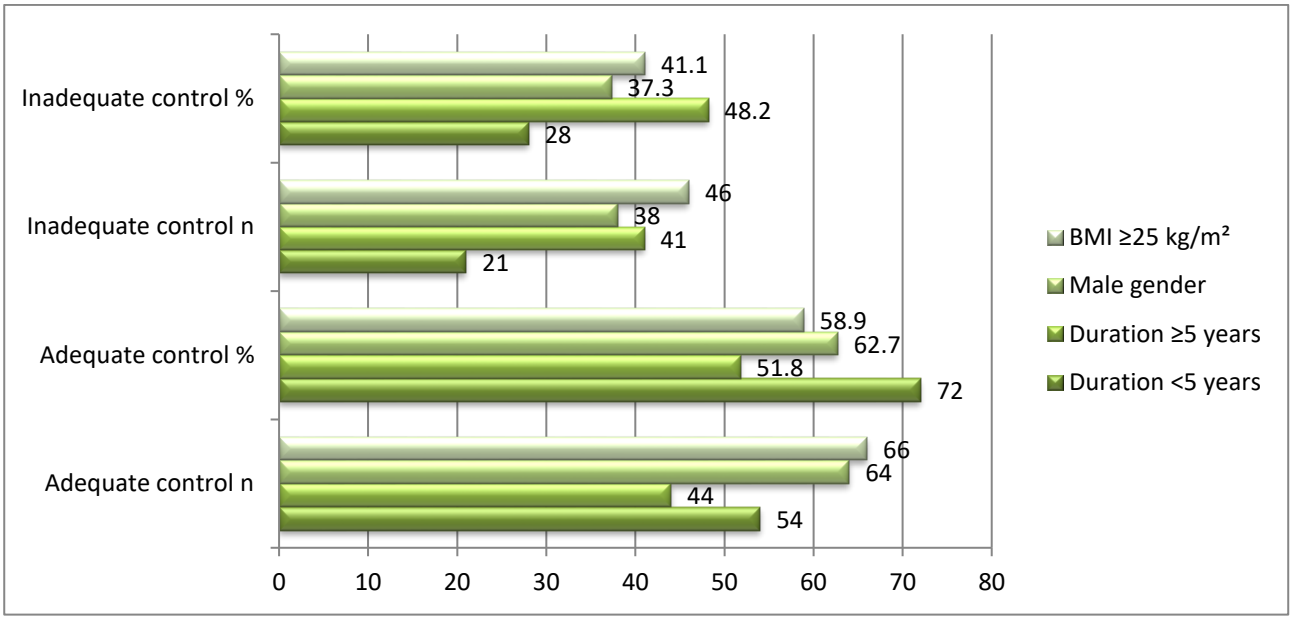

Figure 2: Association of Glycemic Control with Clinical Variables

In general, the results revealed that new oral antidiabetic medications could be used to achieve substantial outcomes in glycemic regulation with a reasonable safety profile across patients with T2DM.

Discussion

According to this study, patients with T2DM may be able to significantly improve their glycemic control with the use of the most recent oral antidiabetic drugs. Following therapy, a statistically significant drop in HbA1c and FBG levels was observed, with over half of the trial population achieving target glycemic control. The findings suggest the increased value of newer oral agents as a useful alternative in clinical practice.

Comparing drug classes, patients who take SGLT-2 inhibitors had a higher decrease in the level of HbA1c and FBG in comparison with drug classes that take DPP-4 inhibitors [11]. This could be clarified by the fact that SGLT-2 inhibitors have an insulin-independent mechanism that enhances the excretion of urinary glucose and causes a long-term effect on glycemic improvement [12]. The greater glycemic control observed in the patients with less time of diabetes also shows the use of effective treatment with early initiation to maintain the remaining β-cell [13].

The safety profile that was evident in this research was in line with the established patterns of adverse effects of newer oral antidiabetic medications [14]. Patients who used SGLT-2 inhibitors were more prone to genitourinary infections and those who used DPP-4 inhibitors were more prone to gastrointestinal symptoms [15]. Notably, majority of the adverse events were mild and did not require the discontinuation of the treatment, and there were no severe cases of drug-related complications [16]. These results imply that the newer oral antidiabetic drugs tend to be better tolerated in most cases provided these

are used properly [17].

When the current study is compared with the existing literature, the extent of the HbA1c reduction has been reported to be similar to previous real-world and clinical trial studies that have provided HbA1c reductions of between 0.8% and 1.5% by newer oral antidiabetic drugs [18]. Parallel research has also shown a better glycemic activity of SGLT-2 inhibitors over that of DPP-4 inhibitors as well as a higher prevalence of genitourinary infections [19]. The safety results of this study are similar to published evidence that shows a low risk of hypoglycemia and tolerability of these agents as acceptable in the context of different patient groups [20].

Limitations and Future Recommendations:

There were some limitations in this study. The observational design did not allow the definition of the causal relationship between drug exposure and outcomes. The comparatively short follow-up time might have failed to record long-term glycemic sustainability and uncommon adverse incidences. The research was also done in one location and this might render the results irrelevant to other population and healthcare systems. It is suggested that future studies that involve larger and multicenter groups and extended follow-up time should be conducted to determine more accurately the long-term effectiveness and safety of newer oral antidiabetic drugs. The evidence base would be further enhanced by comparative randomized studies that would emphasize on cardiovascular and renal outcomes in local populations. Patient-reported outcomes and cost-effectiveness studies can also assist in the process of making customized decisions on treatment in clinical practice.

Conclusion

In individuals with T2DM the more recent oral anti-diabetic medications showed excellent glucose control and a tolerable toxicity profile. Despite having more modest side effects, SGLT-2 inhibitors outperformed DPP-4 inhibitors in terms of glycemic effectiveness. Overall, these medications are safe and efficient substitutes for the standard treatment of T2DM.

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