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Original Research Article

Efficacy and Safety of Metformin and Vildagliptin versus Metformin and Glimepiride in Patients of Type 2 Diabetes Mellitus: A Comparative Study

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Conflict of interest: Nil

Abstract:

Background: The main feature of diabetes mellitus, a varied chronic metabolic illness, is persistent hyperglycemia brought on by abnormalities in insulin secretion or activity. Over time, persistent hyperglycemia and related metabolic abnormalities cause tissue damage that shows up as accelerated atherosclerosis, renoretinal microangiopathy, and neuropathy, which can result in a range of localized, vascular, and neurological problems. The present study aims to compare the safety and effectiveness of metformin and vildagliptin with metformin and glimepiride in individuals with Type 2 diabetes.

Methods: This study is an interventional longitudinal type. The study involved the enrollment of sixty patients in total. The trial comprised patients with poor glycemic control who were currently on 500 mg of metformin daily. These sixty patients were divided up into two groups of thirty each. Patients in Group A were given 500 mg of metformin and 1 mg of glimepiride daily. Patients in Group B were given 500 mg of metformin and 50 mg of vildagliptin bid. The trial lasted for three months in total.

Results: Following three months of therapy, there was a significant decrease in blood glucose levels in both the postprandial (PPBS) and fasting (FBS) groups. The two groups differed significantly in their ability to lower the PPBS and FBS levels. After 12 weeks, there was a notable decrease in both groups' hemoglobin A1c (HbA1c). Following three months of treatment, the group B HbA1C decreased. Between the two groups, there was no statistically significant difference in the HbA1C reduction. After three months of treatment, the group taking metformin and glimepiride experienced more adverse effects. The frequency of negative effects varied significantly between the two groups.

Conclusion: Vildagliptin and metformin combined produced a better adverse effect profile with a lower risk of hypoglycemia and weight gain, and their efficacy was comparable to that of glimepiride and metformin together.

Keywords: Diabetes Mellitus, HbA1C, Fasting Blood Sugar; Postprandial Blood Sugar.

Introduction

Diabetes is a complicated, long-term condition that necessitates ongoing medical supervision and multifaceted risk reduction techniques in addition to glycemic management. Diabetes mellitus, a chronic condition that can be inherited or acquired, is characterized by elevated blood glucose levels brought on by insufficient or inadequate insulin released by the pancreas.

Worldwide, more than half a billion people men, women, and children of all ages have diabetes. In the next 30 years, that figure is expected to more than double to 1.3 billion, with a rise observed in every nation. Diabetes is predicted by the World Health Organization (WHO) to rank seventh among all causes of death by 2030.[1,2] Diabetes is a leading cause of lower limb amputations, heart attacks, strokes, blindness, and renal failure. Diabetes can be managed with diet, exercise, medication, and routine screening and treatment for complications to either prevent or postpone its consequences.[2]

In non-obese diabetics, sulfonylureas are typically the first-choice medication, while metformin is used in obese diabetics. In India, the combination of sulfonylureas and metformin is most frequently used due to its low cost and ability to reduce hemo-

globin A1c (HbA1c) more than either medication alone.[4] Unfortunately, there is a risk of severe hypoglycemia and weight gain with this combo medication. Some Type 2 diabetic patients have poor glycemia control despite well planned dose regimens using oral hypoglycemic agents (OHAs), and many OHAs cause adverse drug reactions (ADRs) such weight gain and hypoglycemia. Better OHAs are currently being sought after.

The function of "incretins," namely glucagon-like peptide (GLP-I), has been well-established in recent times. When plasma glucose levels rise, the peptide GLP-I causes an increase in insulin secretion and a drop in glucagon levels. However, due to its chemical makeup and extremely low plasma t1/2 (2 min), this peptide hormone cannot be taken orally. Therefore, drugs that block dipeptidyl peptidase-4 (DPP 4), the enzyme that breaks down GLP 1, have been created in order to extend the duration of action of endogenous GLP-I. Vildagliptin helps patients with Type 2 diabetes mellitus (T2DM) achieve better glycemic control. It is a strong, specific, and reversible inhibitor of DPP-4.[5-8]

In this case, the current study was conducted to assess and contrast, in T2DM patients, the safety and effectiveness of combinations of metformin and glimepiride and metformin and vildagliptin.

Materials and Methods

From January to June of 2023, the Department of Pharmacology at Jawaharlal Nehru Medical College and Hospital in Bhagalpur, Bihar, collaborated with the Department of Medicine to perform this longitudinal interventional study. For this study, a total of sixty outpatient department patients with T2DM were screened. This trial included patients with poor glycemic control who were already on 500 mg of metformin daily. These sixty patients were split up into two groups, each with thirty individuals. Patients in Group A were given 500 mg of metformin and 1 mg of glimepiride daily. Patients in Group B were given 500 mg of metformin and 50 mg of vildagliptin bid. The trial lasted for three months in total. At the end of each month, periodic blood sugar levels were tested, including postprandial and fasting values. Before and after the study, blood glucose and HbA1c levels were measured.

The study included male and female individuals aged 40 to 70 years who had Type-2 diabetes and were already receiving treatment but had uncontrolled blood sugar levels (fasting blood sugar [FBS] >126 mg/dl and postprandial blood sugar [PPBS] >200 mg/dl), hypertension, and were taking angiotensin-converting enzyme inhibitors.

Version 22 of the Statistical Package for Social Sciences was used to analyze the data. For both groups, mean±standard deviations were computed for the quantitative variables. Using an independent t-test, the statistical significance between the two groups was evaluated. Using an unpaired t-test, an intragroup comparison was performed between baseline and 6 and 12 weeks. A P-value of less than 0.05 was deemed statistically significant.

Results

The study involved the enrollment of sixty patients in total. The highest percentage of patients (n = 20) were in the 50–54 age range. No patients younger than 40 years old were present [Figure 1].

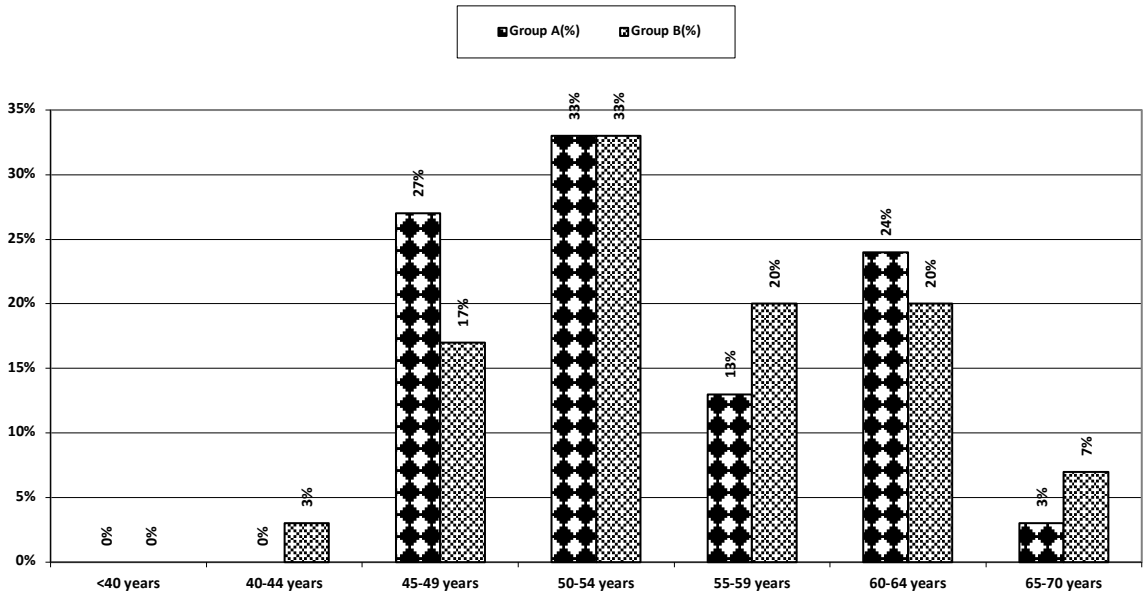

Figure 1: Age wise distribution of cases

Of 60 patients, 47% (n = 28) of patients were males and 53% (n = 32) of patients were females.

Before treatment started, the average FBS in Groups A and B was 215 mg/dl and 204.13 mg/dl, respectively. The average FBS in Groups A and B was lowered to 132.5 mg/dl and 120.97 mg/dl at the conclusion of the third month of treatment. Following a 90-day course of therapy, there was a noteworthy reduction in FBS for both groups.

In terms of lowering the FBS levels, there was a substantial difference (P < 0.0001) between the two groups [Figure 2].

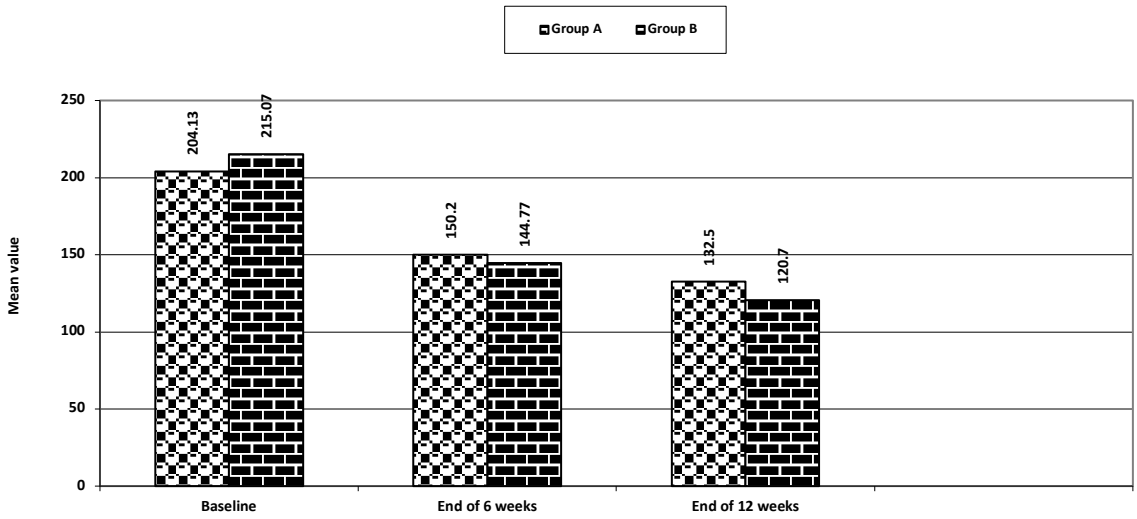

Figure 2: Comparison of fasting blood sugar in Group A and Group B

Before treatment started, the average PPBS in Groups A and B was 288.57 mg/dl and 303.33 mg/dl, respectively. The average PPBS in Groups A and B decreased to 203.47 mg/dl and 199.67 mg/dl at the conclusion of the third month of treatment. Following a three-month course of therapy, the levels of PPBS significantly decreased in both groups. In terms of lowering the PPBS levels, there was no discernible difference between the two groups (P = 0.472) [Figure 3].

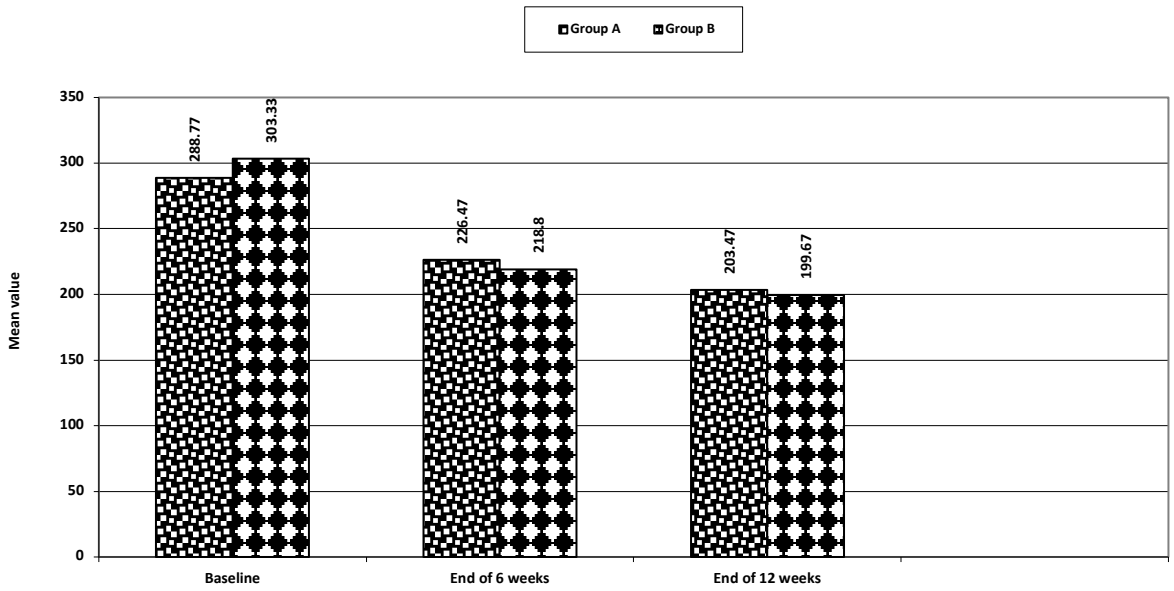

Figure 3:Comparison of postprandial blood sugar in Group A and Group B

Before starting treatment, Group A's baseline mean HbA1C with glimepiride was 8.49, while Group B's baseline mean HbA1C with vildagliptin was 8.83. After 12 weeks, Groups A and B's average HbA1C values were 8.53

and 8.79, respectively. Between the two groups, the decrease in HbA1C was not statistically significant (P = 0.200) [Figure 4].

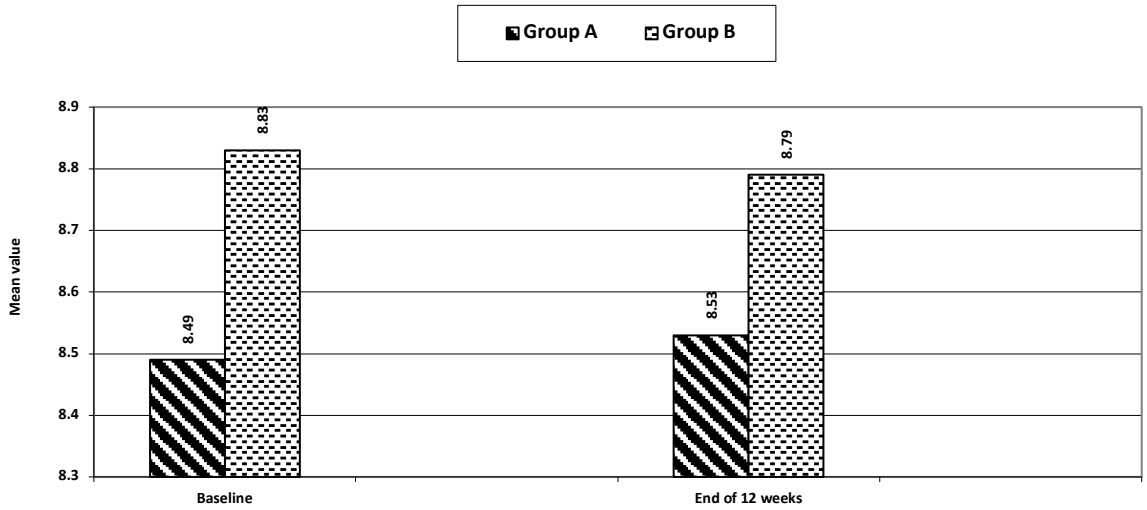

Figure 4:Comparison of HbA1c in Group A and Group B

Hypoglycemia: Mild-to-moderate hypoglycemic symptoms were observed in 53% (*n* = 16) of Group A patients and 3% of Group B patients. Weight gain: Weight gain was observed only in 13% (*n* = 4) of patients on metformin and glimepiride combination. Headache: Headache was reported by 6% (*n* = 2) of patients on metformin and vildagliptin group [Figure 5].

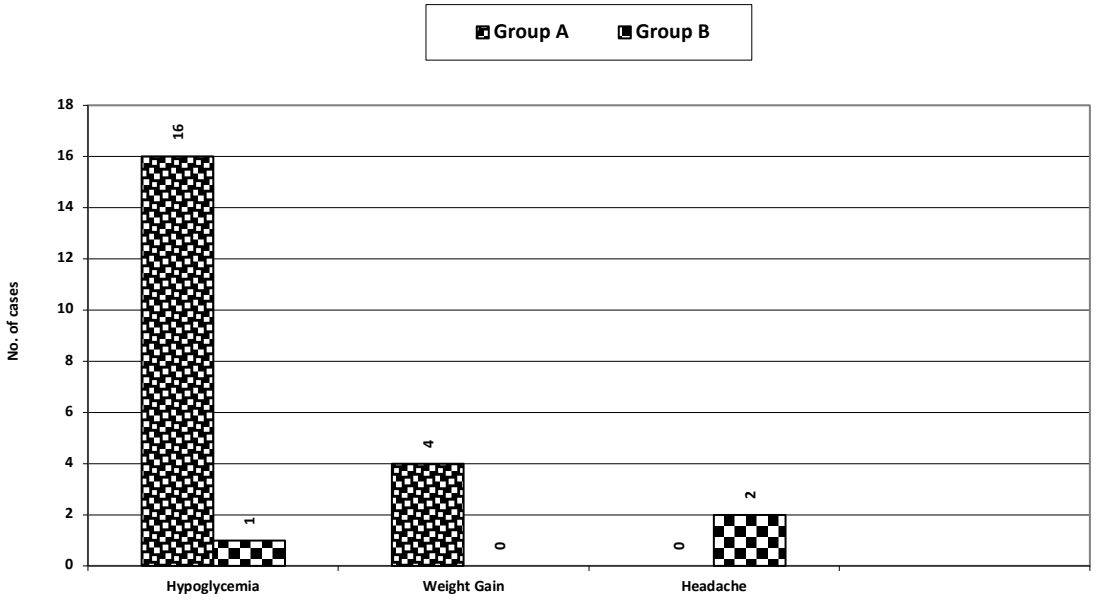

Figure 5: Adverse Effects in Group A and Group B

Discussion

Without causing negative side effects like weight gain or hypoglycemia, the novel method of treating diabetes mellitus through DPP-4 inhibition has the ability to lower and possibly even normalize both fasting and postprandial glucose concentrations. By offering a safe treatment option for patients with reduced glucose tolerance, this strategy also raises the possibility that the therapy will be able to stop, slow down, or even reverse the course of the illness. Finally, because of its reliance on glucose, this method may prove to be intrinsically safer than current insulin secretagogues.

Therefore, DPP-4 inhibitors even when used in conjunction with currently available oral antidiabetic agents have not been linked to any incidence of severe hypoglycemia. The patients in this trial who were taking vildagliptin in addition to met-

formin had a significant decrease in mean PPBS and FBS, reaching a maximum of 199 mg/dl and 120 mg/dl after 12 weeks, respectively ($P < 0.01$). The outcomes align with research conducted by Bosi et al. [9], which revealed a noteworthy reduction in FBS and PPBS levels, and Pan et al. [10], which revealed that the combination of metformin and vildagliptin significantly decreased fasting blood glucose (FBG) levels ($P < 0.001$) at 24 weeks in comparison to metformin placebo.

According to the current study's findings, Chatterjee and Chatterjee [11] demonstrated a substantial decrease in FBS from baseline for both the once-daily and twice-daily regimens of metformin and vildagliptin ($P < 0.0001$). In both groups, there was a significant decrease in the PPBS level ($P < 0.0001$).

Vildagliptin combined to metformin is not less effective than glimepiride in lowering mean HbA1C levels, as demonstrated by Matthewes et al. [12]. The HbA1C change was similar with glimepiride and vildagliptin therapy. Vildagliptin-treated patients had a lower incidence of hypoglycemia (2.3% versus 18.2% with glimepiride), and there was a 14-fold decrease in the number of hypoglycemic incidents (59 versus 838). Vildagliptin produced a positive change in body weight.

FBS and PPBS significantly decreased in patients taking metformin and glimepiride together, reaching a maximum of 204 mg/dl and 132 mg/dl after 12 weeks, respectively ($P < 0.01$). This is in line with research by Charpentier et al., Wang et al., and Pareek et al. [13–15], which shown that metformin or glimepiride alone did not significantly reduce FBS and PPBS from baseline ($P < 0.001$). The current study's findings align with previous research, which showed a significant ($P < 0.01$) decline in FBS and PPBS between baseline and 12 weeks ($P < 0.001$).

Vildagliptin and glimepiride were tested for its efficacy and safety as add-on therapies to metformin by Ferrannini et al. [16]. At the end of 52 weeks, the mean change in baseline HbA1C (7.3%) was −0.44% for vildagliptin and −0.53 for glimepiride in both groups. The groups' FBG reductions (mean and standard error) were similar at −1.01 mmol/lt and −1.14 mmol/lt, respectively. Our findings are consistent with those of Jeon and Oh [17] comparative study of the metformin-vildagliptin and metformin-glimepiride combos. In both groups, a comparable decrease in 2 h-PPBS and FBS was observed.

Between the start of the study and the 12-week mark, the mean HbA1c in both groups significantly decreased ($P < 0.01$). Our findings agree with those of Pan et al., Ved and Shah, and Bosi et al.[10,11,18]

Vildagliptin, when combined with metformin, is well tolerated and results in clinically significant, dose-related drops in FBS and A1C, according to research by Bosi et al. [9]. Of those who reported adverse occurrences, 65% did so. Every day, patients are given 100 mg of vildagliptin. Just 10% of participants in our research who received 50 mg of vildagliptin reported side effects.

Vildagliptin caused a 10-fold decrease in the incidence of hypoglycemia compared to glimepiride and significantly decreased body weight (1.7 vs. 16.2% exhibiting at least one hypoglycemic episode and 39 vs. 554 hypoglycemic events, $P < 0.01$). Compared to 10 glimepiride events, there were no severe hypoglycemic episodes with vildagliptin ($P < 0.01$), and no patient in the vildagliptin group was stopped due to hypoglycemia, while 11 patients in the glimepiride group experienced this condition.[16]

Conclusion

At the conclusion of three months of treatment, metformin + glimepiride and metformin + vildagliptin nearly equally achieved excellent glycemic control in this trial. Regarding the adverse effect profile, hypoglycemia was noted in 3% of the group treated with vildagliptin and 53% of the group treated with glimepiride. The glimepiride group was the only one to report weight gain. The vildagliptin group reported 6% of headache cases. Vildagliptin plus metformin, therefore, provides a benefit and is a significant new therapy option for achieving ideal glycemic control without causing weight gain or raising the risk of hypoglycemia. Vildagliptin is a more effective and well-tolerated medication for treating diabetes mellitus than glimepiride.When combined with metformin, it gradually shown increased efficacy without causing weight gain or hypoglycemia, which are common side effects of other antidiabetic medications (perhaps because GLP-1 induces an increase in beta cell mass and number). Vildagliptin reduces hypoglycemia because of the glucose-dependent insulinotropic action of GLP-1 as well. The reason for satiety following GLP-1 injection may be due to inhibition of stomach emptying.

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