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COMPARATIVE STUDY ON EFFICACY AND SAFETY OF VILDAGLIPTIN-METFORMIN VS GLIMEPIRIDE-METFORMIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS .

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ABSTRACT

The aim of the study was to compare the efficacy and safety of vildagliptin-metformin Vs glimepiride metformin in patients with type 2 DM. A comparative study was conducted over a period of three months in a tertiary care hospital.

In this study the primary goal was a reduction in HbA1c from baseline and secondary goal included fasting plasma glucose (FPG) or postprandial glucose (PPG) reduction from baseline, as well as HbA1c responder rate and HbA1c reduction according to baseline HbA1c category.

Among the study population N=102, comparable HbA1c reduction was observed with a mean±standard deviation change from baseline in the vildagliptin group and -1.00±1.32% in the glimepiride group. A similar reduction in PPG (vildagliptin group 3.53±4.11 mmol/L vs. the glimepiride group 3.72±4.17 mmol/L) was demonstrated, and the decrements in FPG (vildagliptin group 1.54±2.41 mmol/L vs. glimepiride group 2.16±2.51 mmol/L) were not different between groups. The proportion of patients who achieved an HbA1c less than 7% in the vildagliptin group and 56.0% in the glimepiride group. An average body weight gain in the glimepiride group was observed in contrast with the weight gain noted in the vildagliptin group. A 10-fold lower incidence of hypoglycemia was demonstrated in the vildagliptin group, in addition to an absence of severe hypoglycemia.

The study concluded that vildagliptin-metformin treatment provided blood glucose control efficacy

comparable to that of glimepiride-metformin treatment and resulted in better adverse event profiles with lower risks of hypoglycemia and weight gain.

KEYWORDS: DM-Diabetes Mellitus, PPG-Post prandial glucose, FPG-Fasting blood plasma glucose, HbA1c-Hemoglobin A1C

INTRODUCTION

The term diabetes describes a group of metabolic disorders characterized and identified by the presence of hyperglycaemia in the absence of treatment. Diabetes may present with characteristic symptoms such as thirst, polyuria, blurring of vision, and weight loss. The long-term specific effects of diabetes include retinopathy, nephropathy and neuropathy. People with diabetes are also at increased risk of other diseases including heart, peripheral arterial and cerebrovascular disease, obesity, cataracts.

The types of Diabetes Mellitus includes Type 1 Diabetes Mellitus- Autoimmune, Idiopathic, Type 2 Diabetes Mellitus- Predominantly insulin resistance, Predominantly insulin secretory, Gestational Diabetes Mellitus- Diabetes mellitus in pregnancy. Type 2 diabetes mellitus (T2DM) is a massive health problem in India which leads to serious chronic morbidity. While metformin is the first line drug to treat T2DM, in patients not controlled by metformin monotherapy, other OHAs can be added. [1,2]

Recently, several new classes of oral hypoglycemic agents have been introduced [14,15]. Vildagliptin is an oral and highly selective dipeptidyl peptidase-4 (DPP-4) inhibitor which prevents the rapid degradation of endogenous glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) and increases the levels of the intact, active form of endogenous GLP-1. Vildagliptin improves glycemic control in type 2 diabetic patients either as a monotherapy or administered in combination with metformin, sulfonylurea, thiazolidinedione or insulin. Improvements in glycemic control are mediated primarily by increased insulin secretion and the suppression of glucagon secretion. Both of these effects depend on plasma glucose concentration, indicating that insulin secretion is suppressed and glucagon secretion is stimulated under low-blood glucose conditions. Vildagliptin has not demonstrated any effects on body weight and does not evoke severe hypoglycemia.

Sulfonylurea is a potent oral hypoglycemic agent and is commonly prescribed as a monotherapy or as a component of combination therapy for the treatment of type 2 diabetic patients over 60 years of age [3,4]. Although sulfonylurea is well-known as being effective in lowering blood glucose, it also induces body weight gain and severe hypoglycemia. In the present study, the efficacy and safety of vildagliptin-metformin treatment compared to those of glimepiride-metformin treatment were evaluated over 32 weeks in type 2 diabetic patients.

MATERIALS AND METHOD

A retrospective study was conducted over a period of three months in a tertiary care hospital. A total of 102 patient case records satisfying the inclusion criteria were analyzed. Case records were retrospectively reviewed for the demographic data, clinical presentation, investigational management and outcomes. Data analysis was conducted using Microsoft Excel 2010, R software and R studio.

STATICAL ANALYSIS

Statistical analysis will be done using descriptive statistics, Chi square test for attributes. Case records were retrospectively reviewed from MRD for demographic data, clinical presentations, investigations, management .Data analysis was conducted using R software, R studio and Microsoft Excel 2010.

RESULT AND DISCUSSION

TABLE NO 1: DEMOGRAPHICS AND BASELINE CHARACTERISTICS OF PATIENTS

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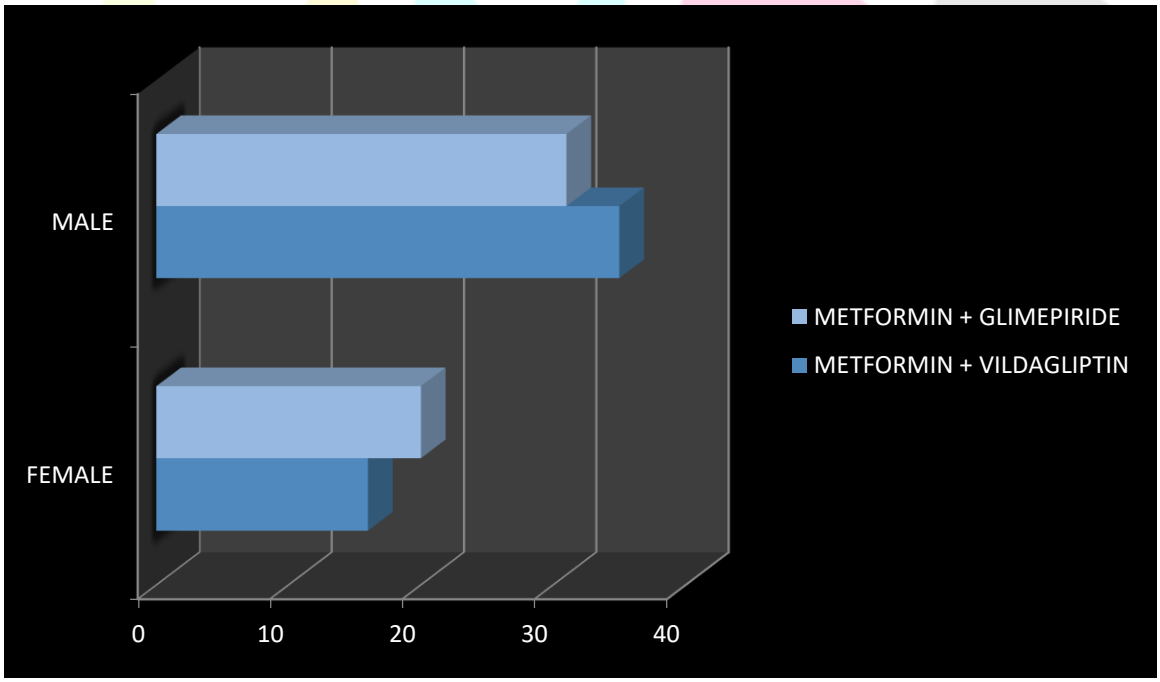
CHARACTERISTIC	METFORMIN+VILDAGLIPTIN (n=51)	METFORMIN+GLIMEPIRIDE (n=51)
Age (years	53.51±10.41	55.38±10.98
Sex, n (%)		
Male	35(68.6%)	31 (60.8%)
Female	16 (31.4%)	20(39.2%)
FPG, mmol/l	8.78±2.32	9.34 ± 2.14
PPG, mmol/l	13.67±3.59	14.44±2.22
HbA1C, %	8.01±1.20	8.13±0.86

FIGURE 1 : GENDER WISE DISTRIBUTION OF PATIENTS TAKING METFORMIN + VILDAGLIPTIN Vs METFORMIN + GLIMEPIRIDE

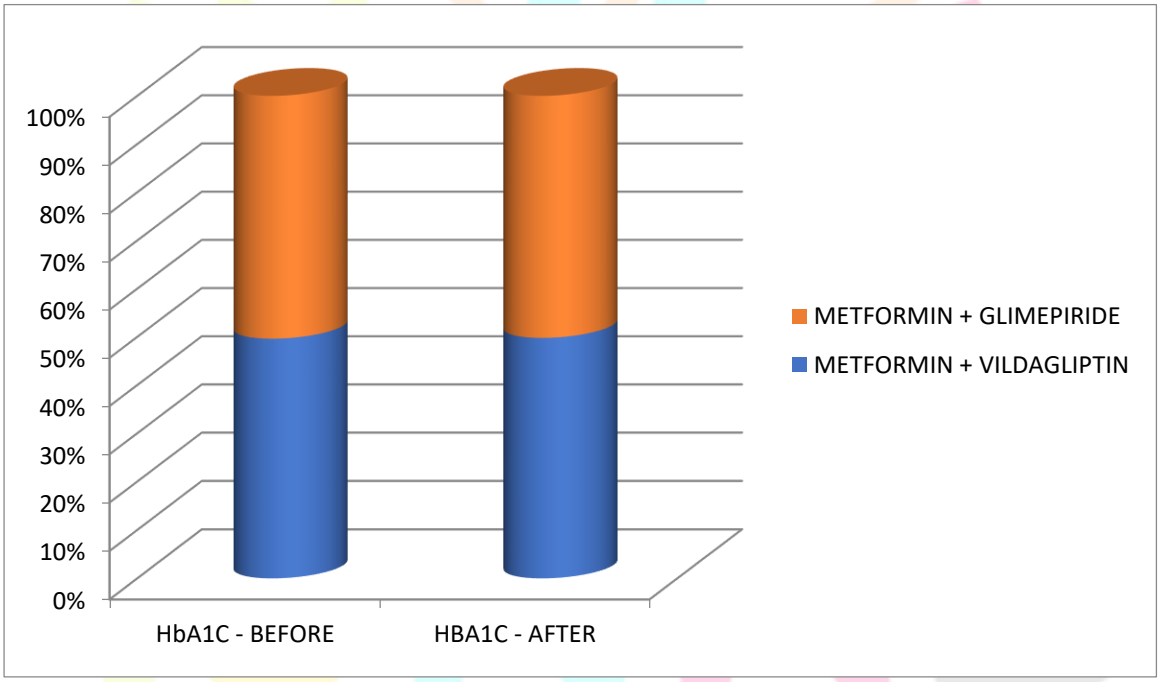


The above Table No 1 and Figure 1 shows that out of 102 patients, 35 males and 16 females were taking Metformin + Vildagliptin and 31 males and 20 females Metformin + Glimepiride.

TABLE NO 2 : VARIATION OF HbA1C BEFORE AND AFTER TAKING THE MEDICATIONS

HbA1C	METFORMIN + VILDAGLIPTIN	METFORMIN + GLIMEPIRIDE	P-VALUE
BEFORE	8.01	8.13	0.00
AFTER	7.07	7.13	

FIGURE 2: VARIATION OF HbA1C BEFORE AND AFTER TAKING THE MEDICATIONS

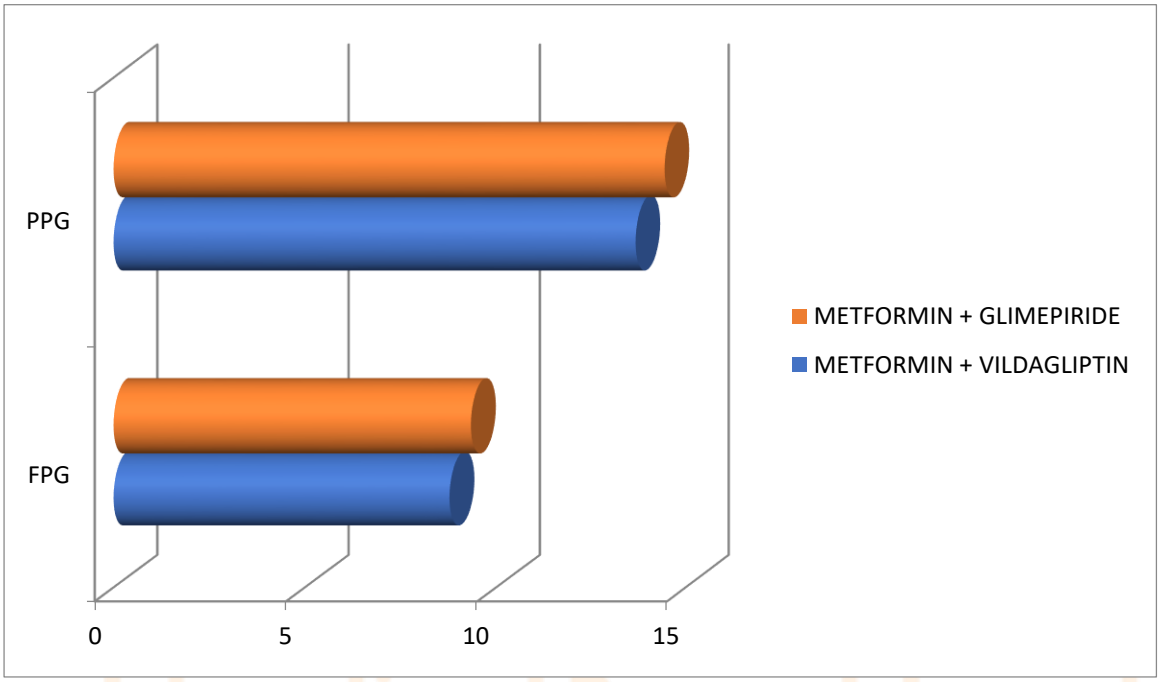


The above Table No 2 and Figure 2 shows the variation of HbA1C before and after taking Metformin + Vildagliptin and Metformin + Glimepiride. The mean HbA1c was decreased from 8.01 to 7.07 (1.21% to 0.81%) in the vildagliptin-metformin group and from 8.13 to 7.13 (0.86% to 0.81%) in the glimepiride-metformin group. The p-value was found to be 0.00. [5.6]

TABLE NO 3: CHANGE FROM BASELINE IN FPG AND PPG (mmol/l)

CHARACTERISTIC	METFORMIN+ VILDAGLIPTIN	METFORMIN+ GLIMEPIRIDE	P-VALUE
FPG, mmol/l	8.78±2.32	9.34 ± 2.14	0.00
PPG, mmol/l	13.67±3.59	14.44±2.22	

FIGURE 3: CHANGE FROM BASELINE IN FPG AND PPG (mmol/l)

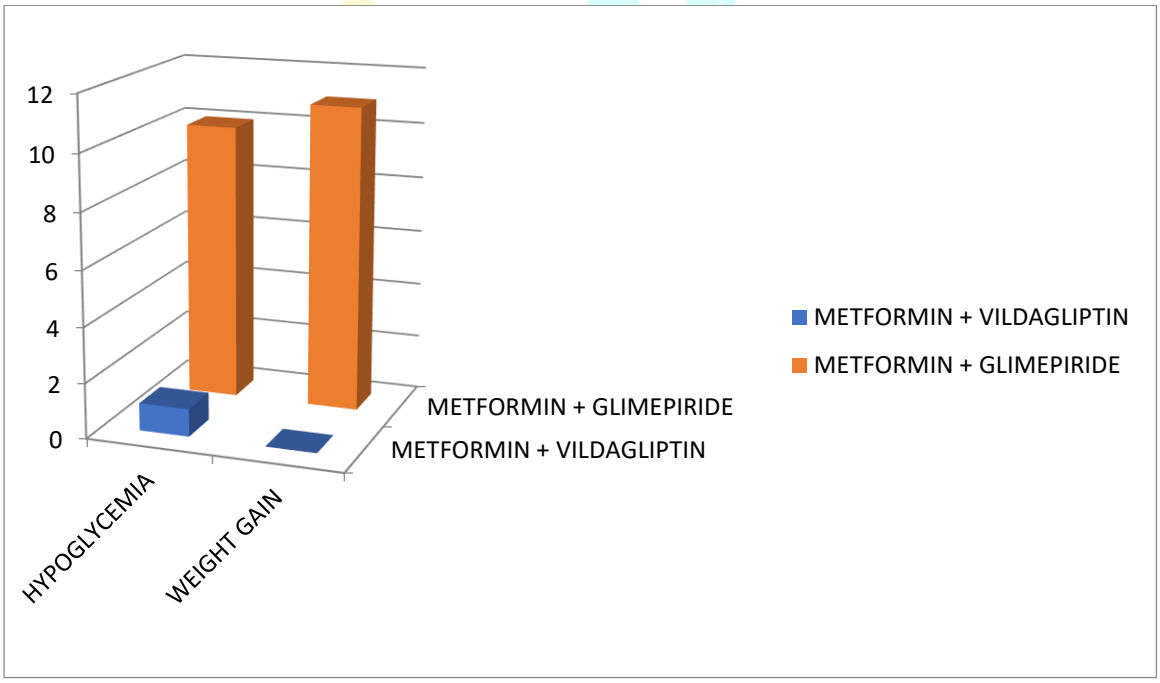


The above Table No 3 and Figure 3 shows the change from baseline in FPG and PPG. The reductions in FPG level were comparable between treatment groups (vildagliptin-metformin 1.54±2.41 mmol/L vs. glimepiride-metformin 2.16±2.51 mmol/L). Both treatments showed similar efficacy with regard to the 2hPPG level; the reduction was 3.53±4.11 mmol/L (from 13.67± 3.59 to 10.14±3.46) in the vildagliptin-metformin group and 3.72±4.17 mmol/L (from 14.44±2.22 to 10.72±3.36) in the glimepiride-metformin group. [7]

TABLE NO 4: SAFETY SUMMARY

VARIABLE	METFORMIN + VILDAGLIPTIN (n=51)	METFORMIN + GLIMEPIRIDE (n=51)
Hypoglycemia	1	10
Weight gain	0	11

FIGURE 4 : SAFETY SUMMARY



The above Table No 4 and Figure 4 shows the safety summary. Regarding safety, the vildagliptin-metformin treatment had a favorable hypoglycemic profile: a 10-fold lower incidence of hypoglycemia, with no severe hypoglycemia observed. Several papers have recently been published regarding the association between hypoglycemia and adverse clinical outcome [4,5]. In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, intensive blood glucose control did not produce any benefits with regard to CV events but did provoke unanticipated excess mortality: 19 of the 41 deaths were attributed to unexpected CV disease, which may have been related to severe hypoglycaemia. [5]

In terms of safety profiles, decreased weight gain and low incidence of hypoglycemia were also observed in the vildagliptin treatment group [7]. In the extended two-year observation period in the previous study, the vildagliptin-metformin combination treatment group still evidenced similar glucose control and better safety profiles. [8]

In the present study, changes in body weight differed between the treatment groups. Body weight was unchanged in the vildagliptin-metformin treatment group, whereas the patients treated with glimepiride-metformin evidenced increase in body weight. [9,10]

CONCULUSION

The results demonstrated that Vildagliptin-Metformin combination treatment offered comparable efficacy in terms of HbA1c reduction, no weight gain, and a lower risk of hypoglycemia in type 2 diabetic patients with unfavorable blood glucose control. [11,12] When safety is considered along with effectiveness, the Vildagliptin-Metformin combination treatment may constitute a better therapeutic option than does the Glimepiride-Metformin combination treatment. [13] Hence it was concluded that Vildagliptin-Metformin treatment provided blood glucose control efficacy comparable to that of Glimepiride-Metformin treatment and resulted in decreased adverse event profiles with lower risks of hypoglycemia and weight gain.

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