

# An Observational Study to Evaluate Effect of Vildagliptin in Combination with Metformin and Glimepiride on Glycaemic Control and lipid profile in T2DM Patients

Dipti Ranjan Darjee

Asst. Professor, Dept. of Medicine, SCB Medical College, Cuttack

## ABSTRACT

**Objective:** The study was conducted to evaluate the effect of addition of Vildagliptin in patients on glycaemic control (Plasma glucose and HbA1c) and Lipid Profile [Triglyceride (TG), Total cholesterol (TC), Low density lipoprotein cholesterol (LDL-C), High density lipoprotein cholesterol (HDL-C)] who were inadequately control with glimepiride and metformin therapy.

**Material and Method:** This was a prospective observational study and patients who were not adequately control with metformin and glimepiride were included in this study. Patients who were having HbA1c > 8% and comparably higher lipid profile were included in this study. All serological test were performed from NABL accelerated pathological laboratory. Efficacy was measured by the changes in glycemic parameters and in lipid profile from baseline to 12 weeks.

**Result:** At the end of 12 weeks there were statistical significant drop in glycemic parameters i.e., fasting plasma glucose ( $p < 0.05$ ), post prandial plasma glucose ( $p < 0.05$ ) and glycated haemoglobin (HbA1c%) ( $p < 0.05$ ). There also a significant change observed in lipid profile but there was not significant increase in High density lipoprotein cholesterol (HDL-C). Hypoglycaemic events were significantly low as compare to baseline.

**Conclusion:** Addition of Vildagliptin in uncontrolled T2DM patients will significantly bring down the glycemic level. Patients who were uncontrolled with metformin and glimepiride therapy will be benefited in both in terms go glycemic control and lipid control after addition of DPP4i like Vildagliptin.

**Keywords:** Vildagliptin, glimepiride, metformin, T2DM.

## INTRODUCTION

The prevalence of diabetes in India is on the rise and is related to changing characteristics of our population [1]. Although diabetes is traditionally considered a metabolic disorder, it is now viewed by many as a vascular disease as well [2]. This is based on the fact that most patients who have diabetes develop cardiovascular (CV) complications, which account for the majority of deaths in diabetic patients. CV complications of diabetes are especially concerning not only because of the emerging epidemic of diabetes but also because of the earlier onset of coronary artery disease in individual who have diabetes [3-5]. Furthermore, the progress of vascular disease in diabetes often begins several years before the clinical diagnosis of diabetes and usually remains silent for many years until it has reached an advanced stage or leads to irreversible damage such as myocardial infarction, stroke or heart failure [6,7].

There are several trials which established the efficacy to control glycemic parameters by the combination of metformin and glimepiride [8]. Metformin acts to improve insulin sensitivity whereas sulphonylureas enhance insulin secretion and this synergistic combination acts to suppress hepatic glucose output and to improve insulin sensitivity [9].

Vildagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor that enhances incretin hormone activity, sustains insulin levels, and reduces glycemia in type 2 diabetes mellitus (T2DM) [10,11]. Several previous clinical trials have shown that vildagliptin monotherapy and add-on therapy are tolerable and effective in patients with poor glycemic control [12-16].

The study was conducted to evaluate the effect of addition of Vildagliptin in patients on glycaemic control (Plasma glucose and HbA1c) and Lipid Profile [Triglyceride (TG), Total cholesterol (TC), Low density lipoprotein cholesterol (LDL-C), High density lipoprotein cholesterol (HDL-C)] who were inadequately control with glimepiride and metformin therapy.

## MATERIAL AND METHOD

This was a prospective observational study and patients who were not adequately control with metformin and glimepiride were included in this study. This was a single centred study.

Type 2 diabetes mellitus (T2DM) patients who were having HbA1c > 8% and comparably higher lipid profile were included in this study. Patients who were having any abnormalities like history of any cardiovascular events, history of any type of micro or macro vascular complication, vision disability or with any serious adverse events were excluded from the study.

Baseline parameters such as Glycosylated haemoglobin (HbA1c), Postprandial Blood Sugar (PPBS), Fasting Blood Sugar (FBS), Low Density Lipoprotein-Cholesterol (LDL-C), Triglycerides (TGs), Total-Cholesterol (TC), High Density Lipoprotein-Cholesterol (HDL-C) were assessed at the time of enrolment. All serological tests were

performed from NABL accelerated pathological laboratory. Efficacy was measured by the changes in glycemic parameters and in lipid profile from baseline to 12 weeks.

Unpaired 't' test for difference between two means were used to analyse continuous variables at baseline and 'z' test for difference between two proportions were used to analyse categorical characteristics at baseline. Statistical software was used to perform all statistical measurements. In analysis, 'p' value < 0.05 was considered statistically significant.

## RESULT

Total 100 patients were participated in this observational trial and the baseline characteristics of the study populations were listed in the following tables (Table 1). It was observed that participants were having long duration of diabetes ( $5.79 \pm 2.32$ ) and high BMI ( $25.82 \pm 3.51$ ) index. Glycemic parameters and lipid profiles were also listed in table 1.

**Table 1: Baseline characteristics of the study population**

Variables	Total Participants (N=100)
Age (Yrs.)	53.46 ± 7.10
Male (%)	58 (58%)
Duration of Diabetes (Yrs)	5.79 ± 2.32
Weight (kgs.)	71.78 ± 7.23
BMI (kg/m <sup>2</sup> )	25.82 ± 3.51
FBS (mg/dl)	172.6 ± 17.34
PPBS (mg/dl)	261 ± 24.26
HbA <sub>1c</sub> (%)	9.66 ± 0.96
Total cholesterol (mg/dl)	188.34 ± 23.54
TG (mg/dl)	171.95 ± 15.41
LDL-C (mg/dl)	121.93 ± 16.1
HDL-C (mg/dl)	41.21 ± 4.94

At the end of 12 weeks there were statistical significant drop in glycemic parameters i.e., fasting plasma glucose (p<0.05), post prandial plasma glucose (p>0.05) and glycated haemoglobin (HbA1c%) (p<0.05).

Variables	At Base line (Met +Glim)(N=100)	After 12 weeks (Met + Glim+Vilda) (N=100)	P value
Weight (kgs.)	71.78 ± 7.23	68.31 ± 5.14	<0.05
FBS (mg/dl)	172.6 ± 17.34	121.3 ± 11.22	<0.05
PPBS (mg/dl)	261 ± 24.26	179 ± 19.13	<0.05
HbA1c (%)	9.66 ± 0.96	8.56±0.75	<0.05
Total cholesterol (mg/dl)	188.34 ± 23.54	159.28 ± 21.36	<0.05
TG (mg/dl)	171.95 ± 15.41	152.57 ± 13.27	<0.05
LDL-C (mg/dl)	121.93 ± 16.1	109.87 ± 15.6	<0.05
HDL-C (mg/dl)	41.21 ± 4.94	41.84 ± 5.21	NS

There also a significant change observed in lipid profile but there was not significant increase in High density lipoprotein cholesterol (HDL-C). Hypoglycaemic events were significantly low as compare to baseline.

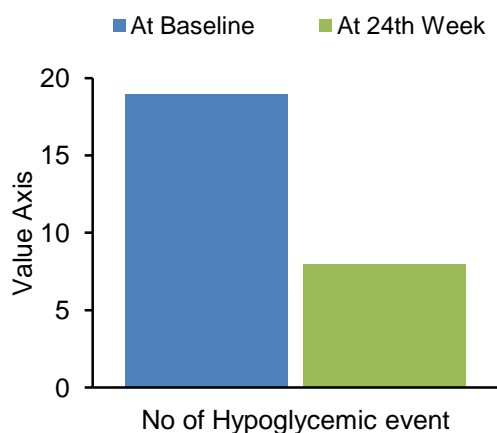


Figure 1: No of glycaemic events from baseline to 24th week

## DISCUSSION

In this present study the effect of addition of Vildagliptin was evaluated against the initial combination therapy of metformin and glimepiride therapy. Different mechanism of actions among biguanide with that of DPP4i and sulphonylureas are the rationales for combining these three different drugs.

Because of the increasing prevalence of overweight, obesity and metabolic syndrome in the population at large, it is quite likely that incidence of diabetes and its related CV complications will continue to rise and could potentially lead to a new epidemic of cardiovascular disease (CVD). Significant reductions in TC, TG, and LDL-C with the combination treatment of glimepiride and metformin were also observed by Shimpi et al<sup>[17]</sup>. Blood pressure and lipid profile are important determinants of cardiovascular risk in patients with type 2 diabetes mellitus (T2DM). Many studies was already demonstrated that vildagliptin add-on treatment may have beneficial effects on lipid profiles<sup>[18-20]</sup>.

Having diabetes is now considered the equivalent of having two or three major

risk factors for coronary atherosclerosis. The presence of diabetes in an individual increases the risk of any procedure and is associated with proper prognosis compared to those individuals who do not have diabetes.

The combination of hyperglycemia, hypertension, obesity, dyslipidemia and atherosclerosis that is seen commonly with diabetes mellitus increases the risk of systolic and diastolic left ventricular (LV) dysfunction and often leads to heart failure in diabetic patients; this explains the more common occurrence of the syndrome in diabetic patients<sup>[21-24]</sup>. In this study At the end of 12 weeks there were statistical significant drop in glycaemic parameters i.e., fasting plasma glucose ( $p < 0.05$ ), post prandial plasma glucose ( $p < 0.05$ ) and glycated haemoglobin (HbA1c%) ( $p < 0.05$ ). There also a significant change observed in lipid profile but there was not significant increase in High density lipoprotein cholesterol (HDL-C). Hypoglycaemic events were significantly low as compare to baseline.

In the United Kingdom Prospective Diabetic Study (UKPDS), the incidence of heart failure correlated with the extent of hypoglycemia; each 1% increases in haemoglobin A1c (HbA1c) levels was associated with a 12% increase in heart failure risk.<sup>[25]</sup>

Thus we can conclude that the patients who were inadequately controlled should opt for an aggressive treatment and triple drug combination like metformin plus glimepiride and Vildagliptin can be an ideal combination to bring down the glycaemic levels aggressively to prevent further macro and micro vascular complications.

## CONCLUSION

Addition of Vildagliptin in uncontrolled T2DM patients will significantly bring down the glycaemic level. Patients who were uncontrolled with metformin and glimepiride therapy will be benefited in both in terms go glycaemic control and lipid control after addition of

DPP4i like Vildagliptin.

## REFERENCE

1. Pradeepa R, Reema M, Vignesh J, Deepa M, Deepa R, Mohan V. Prevalence and risk factors for diabetic neuropathy in an urban south Indian population: the Chennai Urban Rural Epidemiology Study (CURES-55). *Diabet Med.* 2008;25(4):407-12.
2. Nathan DM, Genuth S, Lachin J, et al.; Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329:977–986
3. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998;352: 837–853
4. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet* 1998;352:854–865
5. Gerstein HC, Miller ME, Byington RP, et al.; Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* 2008;358:2545–2559
6. Duckworth W, Abraira C, Moritz T, et al.; VADT Investigators. Glucose control and vascular complications in veterans with type 2 diabetes. *N Engl J Med* 2009;360:129–139
7. Ray KK, Seshasai SR, Wijesuriya S, et al. Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials. *Lancet* 2009;373:1765–1772
8. Matthew C. Riddle. A Verdict for Glimepiride: Effective and Not Guilty of Cardiovascular Harm. *Diabetes Care* Dec 2019, 42 (12) 2161-2163
9. Charpentier G, Fleury F, Kabir M, Vaur L and Halimi S. Improved glycaemic control by addition of glimepiride to metformin monotherapy in Type 2 diabetic patients, *Diabetic Medicine.* 2001;18:828- 834.
10. AhrénB, Landin-OlssonM, JanssonPA, et al. Inhibition of dipeptidyl peptidase-4 reduces glycemia, sustains insulin levels, and reduces glucagon levels in type 2 diabetes. *J Clin Endocrinol Metab.* 2004;89:2078–2084.
11. UtzschneiderKM, TongJ, MontgomeryB, et al. The dipeptidyl peptidase-4 inhibitor vildagliptin improves beta-cell function and insulin sensitivity in subjects with impaired fasting glucose. *Diabetes Care.* 2008;31: 108–113.
12. BosiE, CamisascaRP, ColloberC, et al. Effects of vildagliptin on glucose control over 24 weeks in patients with type 2 diabetes inadequately controlled with metformin. *Diabetes Care.* 2007;30:890–895.
13. GarberAJ, SchweizerA, BaronMA, et al. Vildagliptin in combination with pioglitazone improves glycaemic control in patients with type 2 diabetes failing thiazolidinedione monotherapy: a randomized, placebo-controlled study. *Diabetes Obes Metab.* 2007;9:166–174.
14. GarberAJ, FoleyJE, BanerjiMA, et al. Effects of vildagliptin on glucose control in patients with type 2 diabetes inadequately controlled with a sulphonylurea. *Diabetes Obes Metab.* 2008;10:1047–1056.
15. FonsecaV, BaronM, ShaoQ, et al. Sustained efficacy and reduced hypoglycemia during one year of treatment with vildagliptin added to insulin in patients with type 2 diabetes mellitus. *Horm Metab Res.* 2008; 40:427–430.
16. KikuchiM, AbeN, KatoM, et al. Vildagliptin dose-dependently improves glycemic control in Japanese patients with type 2 diabetes mellitus. *Diabetes Res Clin Pract.* 2009;83:233–240.
17. Shimpi RD, Patil PH, Kuchake VG, Ingle PV, Surana SJ, dighore PN. Comparison of effect of metformin in combination with glimepiride and glibenclamide on glycaemic control in patients with type 2 diabetes mellitus. *International Journal of Pharmatech Research.* 2009;1:50-61.
18. Shimodaira M, Niwa T, Nakajima K, Kobayashi M. Beneficial Effects of Vildagliptin on Metabolic Parameters in Patients with Type 2 Diabetes. *Endocr Metab Immune Disord Drug Targets.* 2015; 15(3):223-8.

19. Nomoto H, Kimachi K, Miyoshi H, Kameda H, Cho KY, Nakamura A, Nagai S, Kondo T, Atsumi T. Effects of 50 mg vildagliptin twice daily vs. 50 mg sitagliptin once daily on blood glucose fluctuations evaluated by long-term self-monitoring of blood glucose. *Endocr J.* 2017 Apr 29;64(4):417-424.
20. Vianna AGD, Lacerda CS, Pechmann LM, Polesel MG, Marino EC, Faria-Neto JR. A randomized controlled trial to compare the effects of sulphonylurea gliclazide MR (modified release) and the DPP-4 inhibitor vildagliptin on glycemic variability and control measured by continuous glucose monitoring (CGM) in Brazilian women with type 2 diabetes. *Diabetes Res Clin Pract.* 2018 May;139:357-365.
21. Kannel WB, McGee DL. Diabetes and cardiovascular disease: the Framingham Study. *JAMA* 1979;241:2035-8.
22. Kirpichnikov D et al. Heart failure in diabetic patients: utility of beta blockade. *J Card Fail* 2003;9:333-44.
23. Massie BM. Obesity and heart failure-risk factor or mechanism? *N Engl J Med* 2002; 347:358-9.
24. Sowers JR, Epstein M, Frohlich ED. Diabetes, hypertension and cardiovascular disease: an update *Hypertension* 2001; 37(4):1053-9.
25. Stratton IM et al. Association of glycemia with microvascular and macrovascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000;321:405-12.

How to cite this article: Darjee DR. An observational study to evaluate effect of vildagliptin in combination with metformin and glimepiride on glycaemic control and lipid profile in T2DM patients. *International Journal of Research and Review.* 2021; 8(3): 321-325.

\*\*\*\*\*