ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 11 | November - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY TO ASSESS SAFETY AND EFFICACY OF GLIMEPIRIDE – METFORMIN WITH VILDAGLIPTIN - METFORMIN IN TYPE 2 DIABETES MELLITUS PATIENTS IN A TERTIARY MEDICAL INSTITUTE

Medicine

Dr Ankit kumar Tiwari Resident Doctor, Department Of Internal Medicine, Kothari Institute Of Medical Sciences, Bikaner, Rajasthan

Dr Anil Sobti Head of Department, Department of Internal medicine, Kothari Institute of medical sciences, Bikaner, Rajasthan

Dr Ujjwal Sourav* Department Of Community Medicine, Saraswathi Institute Of Medical Science, Hapur. *Corresponding Author

ABSTRACT

To compare the safety and efficacy of glimepiride – metformin with vildagliptin - metformin in type 2 diabetes mellitus patients in a tertiary care hospital

Introduction: Type 2 diabetes (T2DM) is a very complicated disease and it involves multiple local and systemic defects, including impaired islet function and insulin resistance, resulting in impaired glucose tolerance and inappropriately high fasting hepatic glucose production

Aim and Objective: To compare the safety and efficacy of Glimepiride – Metformin with Vildagliptin - Metformin in type 2 diabetes mellitus patients in a tertiary care hospital

Methodology: A Prospective observational study was conducted at Kothari medical institute, Bikaner. Study subjects was selected from Patients visiting the Medicine out-patient department at Kothari medical Institute, Bikaner with type 2 diabetes mellitus. Patients was randomly assigned in (1:1) ratio after randomization to either of two groups (35 in each group), one group prescribed glimepiride(1mg) +metformin (500mg) twice daily half an hour before meals and other group vildagliptin(50mg)+ metformin(500mg) twice half an hour before meals. Results: The HBA1C in Vidagliptine group at 0, 6 and 12 wk were 8.99±0.37, 7.69±0.38 and 6.48±0.44 mg/dl. For glimipride group at 0,6 and 12 wk were 8.94±0.59, 7.51±0.66 and 6.40±0.55. when we compare by applying t test we found P value 0.67, 0.16 and 0.50 with no significant difference

Conclusion: Vildagliptin- metformin and glimepiride-metformin were equally efficacious in reducing fasting plasma glucose levels when given in type 2 diabetes mellitus patients.

KEYWORDS

crumb rubber, utilization, compressive strength, low cost, sustainable

INTRODUCTION

Type 2 diabetes (T2DM) is one of the complicated disease and it involves both local and systemic defects, it also impair islet function and insulin resistance, and results in impaired glucose tolerance and inappropriately high fasting hepatic glucose production. Insulin resistance generally unchanged over time, but deficit in islet function is a progressive event with quantitative and qualitative abnormalities in insulin and glucagon. Type 2 diabetes is an islet pancreopathy in which the reciprocal relationship between the glucagon secreting alpha cell and the insulin-secreting beta cell is lost, leading to hypoinsulinemia and hyperglucagonemia.[1]

T2DM includes significant microvascular complications, as well as macrovascular complications.[2] American Diabetes Association (ADA) shows a reasonable glycosylated haemoglobin (HbA1c) for non-pregnant adults to be less than 7%. The common practice in todays era to give sulfonylurea like glimepiride or selective DPP-4 inhibitor like vildagliptin as add-on to metformin, when metformin alone is not working for managing hyperglycemia as many patients need two or more Oral Hypoglycaemic Agents (OHA) to be used as combination therapy.[3]

Many Research paper concluded that tight glycemic control to prevent diabetic complications is superior. But tight glycemic control is also related with multiple hypoglycemic attacks, and multiple study says that aggressive glucose control is not better for cardiovascular (CV) benefits but may induce severe hypoglycaemia and chances of increased mortality in type 2 DM patients.[4]

Glimipride belongs to sulfonylurea group. They are the drugs that activate insulin release in β-cells of pancreas and may also act via extra pancreatic mechanisms. Those patients who are not under control for glycaemia by diet and exercise may take glimipride, and if secondary failure is there we can combined it with insulin.[5]

DPP-4 inhibitors are considered as new generation of drugs for diabetes mellitus, providing better efficacy than current module of treatments. For the patients inadequately controlled with diet and exercise it is given alone but also used as add-on therapy in combination with metformin, thiazolidinediones, and insulin.[5]

Vildagliptin is DPP-4 inhibitor used for the treatment of patients with type 2 DM. It can be combined with Metformin and may expand GLP-1 levels by working through other different. "The combination of metformin and glimepiride is a well established treatment regimen for type 2 DM."

Hence, the present study was undertaken to compare the efficacy and safety of vildagliptin-metformin and glimepiride-metformin treatment in type 2 diabetic patients

AIM OF THE STUDY

To compare the safety and efficacy of Glimepiride – Metformin with Vildagliptin - Metformin in type 2 diabetes mellitus patients in a tertiary medical Institute

MATERIALS AND METHODS

A Prospective observational study was conducted at Kothari medical institute, Bikaner. Study subjects was selected from Patients visiting the Medicine out-patient department at Kothari medical Institute, Bikaner with type 2 diabetes mellitus.

Sample Size:

The sample size is estimated in consultation with a biostatistician based on previous year's case load and the sample size is 70 [35 in each arm]. Based on previous studies, in order to establish statistical significance for change in HbA1C and FBS/PPBS- it is required to study at least 35 patients in each arm at a probability α error of 5% and keeping power of study at 80%. 70 patients diagnosed with Type 2 diabetes mellitus attending medicine out-patient section was included in the study.

INCLUSION CRITERIA: -

1) Patients diagnosed with type 2 diabetes mellitus.
2) HbA1c levels between ≥ 7 and ≤10%.
3) Age ≥ 40 years and ≤ 80 years.

EXCLUSION CRITERIA:

1) Those with known adverse reactions to Vildagliptin.
2) Cardiovascular diseases:
3) Severe hypertension
4) Any untoward Cardiac or cerebrovascular emergencies, that had happened previously.

70 patients diagnosed with type 2 DM, attending outpatient clinic was recruited after obtaining clearance from Ethical Review Board and taking written informed consent. A baseline demographic data (age, sex, weight, blood pressure, associated diseases, habits, and drug history) was collected at the time of recruitment.

HbA1c, FBS and PPBS was done at the time of recruitment. Patients was randomly assigned in (1:1) ratio after randomization to either of two groups (35 in each group), one group prescribed glimepiride(1mg) +metformin (500mg) twice daily half an hour before meals and other group vildagliptin(50mg)+ metformin(500mg) twice half an hour before meals. HbA1c, FBS, PPBS was repeated at the end of 3rd month.

Group A: Patients on glimepiride(1mg) +metformin (500mg)
Group B: Patients on vildagliptin(50mg)+ metformin(500mg)

In case of any emergencies, infections or surgery- patient was switched over to insulin momentarily and shifted back to the regular treatment as per study protocol on complete recovery. However, those who develop complications or morbidity associated with hyperglycaemia was withdrawn from the study.

Also, patients with fasting sugars > 200 mg/dl and/or postprandial sugars > 300 mg/dl at the 6th week of study was also withdrawn from the study and treatment was given as per the American Diabetes Association [ADA] guidelines.

STATISTICALANALYSIS:

Quantitative data was summarized in terms of descriptive statistics like mean and standard deviation for patients who are treated for both the therapies. In order to test for statistical significance in mean values, appropriate T test was employed. Appropriate graph such as box plot and error plot was used wherever necessary.

RESULTS

Table 1: Basic demography of study subjects

Basic demography	GroupA(Vidagliptin)	GroupB (Glimipride)	P value
Age	60.03±8.69	58.49±9.06	0.47
Sex(Male)	18(51.4%)	19(54.3%)	
BMI	24.09±3.98	25.27±4.50	0.25
Duration of DM	2.49±1.12	2.31±1.21	0.52

Table 1 shows basic demography of study subjects in both group i.e Group A(Vidagliptine group) and Group B (Glimipride group) , There was no statistically significant difference in Age, BMI , Duration of Diabetes between study subjects of both groups with P value 0.47, 0.25 and 0.52.

Table 2: Distribution of subjects according to baseline blood sugar levels

Variable	Group A (Vidagliptine)	Group B (Glimipride)	P value
FBS	**174.71±19.05**	**178.83±28.77**	**0.48**
PPBS	**278.09±28.02**	**279.37±33.25**	**0.86**
HBA1C	**8.99±0.37**	**8.94±0.59**	**0.67**

Table 2 shows distribution of subjects according to baseline blood sugar levels. There was no statistically significant difference between baseline FBS, PPBS and HBA1C with P value 0.48, 0.86 and 0.67.

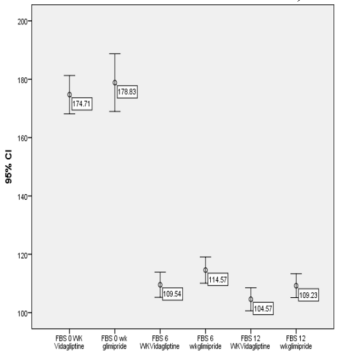

Fig 1: Effect of treatment on Fasting Blood Sugar levels in study groups

Fig 1 shows Error plot of FBS at baseline, at 6 wk and at 12 wk in both the group. The FBS in Vidagliptine group at 0, 6 and 12 wk were 174.71±19.05, 109.54±12.53 and 104.57±11.53 mg/dl. For glimipride group at 0,6 and 12 wk were 178.83±28.77, 114.57±13.09 and 109.23±11.90. when we compare by applying t test we found P value 0.48, 0.10 and 0.10 with no statistically significant difference.

Fig 2: Effect of treatment on Post prandial Blood Sugar levels in study groups

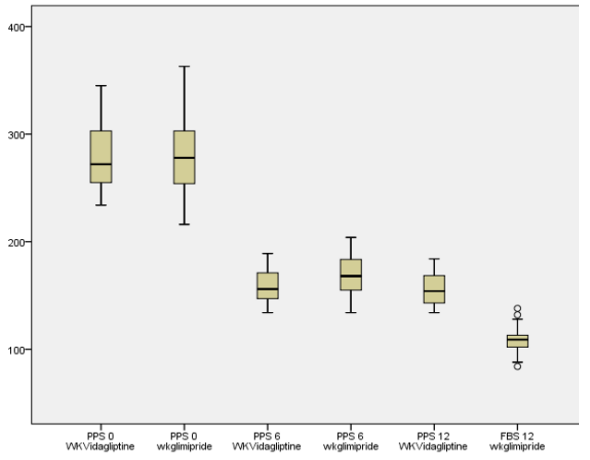

Fig 2 shows box plot of post prandial blood sugar at baseline, 6 wk and at 12 wk. The PPBS in vidagliptine group were 278.09±28.02, 158.83±15.77 and 154.46 ±13.91 whereas in Glimipride group it was 279.37±33.25, 167.57±18.07 and 158.20±16.25. when we compare both group statistically we found P value 0.86, 0.03 and 0.30 , showing there was statistically significant difference between two groups only at 6 wk.

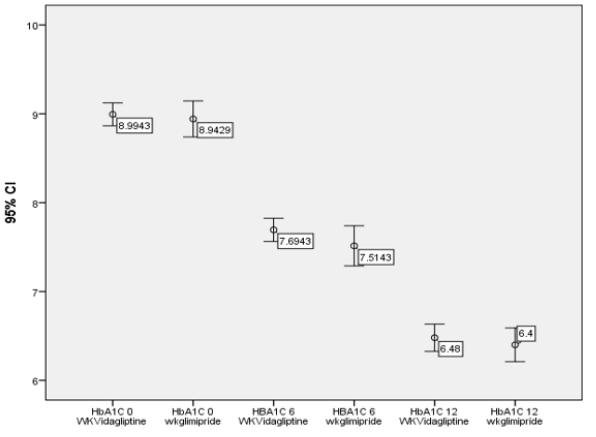

Fig 3: Effect of treatment on HbA1c levels in study groups

Fig 3 shows Error plot of HBA1C at baseline, at 6 wk and at 12 wk in both the group. The HBA1C in Vidagliptine group at 0, 6 and 12 wk were 8.99±0.37, 7.69±0.38 and 6.48±0.44 mg/dl. For glimipride group at 0,6 and 12 wk were 8.94±0.59, 7.51±0.66 and 6.40±0.55. when we compare by applying t test we found P value 0.67, 0.16 and 0.50 with no significant difference

The adverse effects in Glimipride group subjects was maximum with related to hypoglycemia. 5 subjects suffered symptomatic hypoglycemia in Group Glimipride as contrasted to 2 subjects in Group Vidagliptine. Elevated liver enzymes was seen more in group Vidagliptine subjects along with diarrhoea which shows statistical significance.

DISCUSSION

This study is prospective observational study conducted at tertiary medical centre at Bikaner. In present study two combination of therapy glimepiride-metformin and Vidagliptine-metformin was used and compared for 3 months.

In present study there was no statistically significant difference in Age,

BMI , Duration of Diabetes between study subjects of both groups with P value 0.47, 0.25 and 0.52. No statistically significant difference between two groups ensures matching group to compare. Other studies done on similar topics such as Sarkar BS et al3 shows that the age , sex composition and BMI of the two groups did not vary significantly (p>0.05).

In the present study there was no statistically significant difference between baseline FBS, PPBS and HBA1C with P value 0.48, 0.86 and 0.67.This is also important to make two group comparable. In the study by Sarkar BS et al3 also FBS,PPBS and HBA1C were comparable.

In the present study fasting blood sugar in Vidagliptine- metformin group were 174.71±19.05,at baseline which reduces to 109.54±12.53 at 6 wk and 104.57±11.53 mg/dl at the end of treatment i.e 12 wk. The improvement is highly significant. For this group PPBS were 278.09±28.02, at baseline which reduces to 158.83±15.77 at 6 wk and 154.46 ±13.91 at 12 wk. Improvement is significant. The HBA1C in Vidagliptine group at 0, 6 and 12 wk were 8.99±0.37, 7.69±0.38 and 6.48±0.44 mg/dl. Study by Dhanju AS et al1 shows Vildagliptin-metformin combination when administered to Type 2 diabetes mellitus patients, it reduced fasting blood glucose levels from a baseline mean value of 161±16.57 mg/dl to 110.96±14.22 mg/dl at the end of 24 weeks with a mean reduction of 50.04 mg/dl. This decrease in levels was statistically highly significant. With vildagliptin-metformin therapy, 2 hour post prandial blood glucose levels were reduced from 265.66±22.12 mg/dl to 154.80±13.50 mg/dl after 24 weeks with a mean reduction of 110.86 mg/dl. This change was statistically highly significant. Vildagliptin-metformin when given for 24 weeks in same group resulted in fall of HbA1c from 8.40±0.70% to 7.18±0.60% with a mean reduction of 1.22%. The decline in HbA1c levels after 24 weeks of treatment was statistically highly significant. Almost similar findings were observed by use of Vidagliptine-metformin combination in diabetic patients by L. Cai et al6, Ferrannini et al7, Jeon HJ4, Ahren et al8 , Matthews et al9, Derosa et al10 and Goke et al11

In another group on Glimepiride-metformin therapy given for 12 weeks in the resulted in fall in FBS at baseline 178.83±28.77, to 114.57±13.09 at 6 wk and 109.23±11.90 at 12 wk. PPBS at baseline 279.37±33.25, to 167.57±18.07 at 6 wk and 158.20±16.25 at 12 wk. and HBA1C is 8.94±0.59, 7.51±0.66 and 6.40±0.55 at baseline, 6 wk and 12 wk. these reduction by therapy is significant , similar type of significant reduction in FBS, PPBS and HBA1C was found in study by by Charpentier et al12 ,Ferrannini et al7, Jeon HJ4, Matthews et al9, Derosa et al10, Goke et al11 in their studies.

When we compare the reduction in FBS ,PPBS and HBA1C between 2 groups at 6 wk and 12 wk after treatment , we found no statistically difference in the reduction of these parameter between two groups except PPBS at 6 wk. Similar findings of no statistically difference was found in other studies such as by Jeon JH et al4, Dhanju AS1, Sarkar BS et al3.

In the present study Treatment with Vildagliptin emerge to be safe and well tolerated by most study subjects. Vildagliptin-metformin therapy appears unlikely to cause hypoglycemia and is generally weight-neutral. Other adverse effects noted to occur of nasopharyngitis, upper respiratory infection, and headache – these were not likely to be severe or result in discontinuation of the medication. Similar studies done on this topic such as study by Dhanju AS et al1, Jeon HJ et al4

CONCLUSION

On the basis of present study Vildagliptin- metformin and glimepiride-metformin were equally efficacious in reducing fasting plasma glucose levels when given in type 2 diabetes mellitus patients. Reduction in 2 hour post prandial glucose levels during the study was similar with both the therapies except at 6 wk post therapy. HbA1c control was also almost simiar in both the groups. So we can conclude that both therapy are equally efficacious. as far as adverse effects are concerned vidagliptin-metformin had less adverse effect than Glimipride-metformin combination.

Ethical permission: Instituitional ethical permission was taken
Funding: No
Conflict of Interest : No

REFERENCES

1. Dhanju AS, Chhabra A, A Comparative Study of Vildagliptin-Metformin Versus Glimepiride-Metformin Therapy in Type 2 Diabetes Mellitus At A Tertiary Hospital of North India.2016;6(5): 708-11.
2. Kousoulakou H, Hatzikou M, Baroutsou V, Yfantopoulos J, Cost effectiveness of vildagliptin versus glimepiride as add on treatment to metformin for the treatment of diabetes mellitus type 2 patients in Greec. Cost Eff Resour Alloc .2017; 15(19):1-7.
3. Sarkar BS, Mukherjee S, Maji M, Biswas S. A Prospective Observational Study to Compare the Efficacy and Adverse Effects of Glimepiride and Vildagliptin Added to Metformin in Type 2 Diabetes Mellitus, Journal of Clinical and Diagnostic Research. 2019;13(2): OC09-OC11
4. Jeon HJ, Oh TK, Comparison of Vildagliptin-Metformin and Glimepiride-Metformin Treatments in Type 2 Diabetic Patients. Diabetes Metab J 2011;35:529-535
5. Sharma S, Sharma P, Sharma M, Comparative study of efficacy and safety of sitagliptin in comparison with glimepiride in treatment of type 2 diabetes mellitus. International Journal of Medicine Research. 2018; 3(2): 56-60
6. Cai ML, Cai Y, Lu ZJ, Zhang Y and Liu P. The efficacy and safety of vildagliptin in patients with type 2 diabetes: a meta-analysis of randomized clinical trials. Journal of Clinical Pharmacy and Therapeutics, 2012; 37: 386–398.
7. Ferrannini E, Fonseca V, Zinman B, Matthews D, Ahrén B, Byiers S, Shao Q, Dejager S.;Fifty-two-week efficacy and safety of vildagliptin vs. glimepiride in patients with type 2 diabetes mellitus inadequately controlled on metformin monotherapy. Diabetes Obes Metab 2009;11: 157-66.
8. Ahren B, Foley JE, Ferrannini E, Matthews DR, Zinman B, Dejager S, Fonseca VA.;Changes in prandial glucagon levels after a 2-year treatment with vildagliptin or glimepiride in patients with type 2 diabetes inadequately controlled with metformin monotherapy. Diabetes Care 2010;33: 730-2.
9. Matthews DR, Dejager S, Ahren B, Fonseca V, Ferrannini E, et al.; Vildagliptin add-on to metformin produces similar efficacy and reduced hypoglycaemic risk compared with glimepiride, with no weight gain: results from a 2-year study. Diabetes Obes Metab 2010;12: 780-9.
10. Derosa G, Bonaventura A, Bianchi L, Romano D, Fogari E, D'Angelo A, et al. Vildagliptin compared to glimepiride on post-prandial lipemia and on insulin resistance in type 2 diabetic patients. Metabolism. 2014 ;63(7): 957-67.
11. Göke R, Gruenberger JB, Bader G, Dworak M. Real-life efficacy and safety of vildagliptin compared with sulfonylureas as add-on to metformin in patients with type 2 diabetes mellitus in Germany. Curr Med Res Opin. 2014 ;30(5): 785-9
12. Charpentier G, Fleury F, Kabir M, Vaur L, Halimi S. Improved glycaemic control by addition of glimepiride to metformin monotherapy in type 2 diabetic patients. Diabet Med. 2001 ;18(10): 828-34.