e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(5); 1285-1288

Original Research Article

Comparison Study on Efficacy and Safety of Metformin and Vildagliptin versus Metformin and Glimepiride in Patients with Type 2 Diabetes Mellitus

Rajashekar Katta[1], Anjum Jabeen[2]

[1]Senior Resident, Department of Pharmacology, ESIC Medical College & Hospital, Sanathnagar, Hyderabad, Telangana

[2]Assistant Professor, Department of Pharmacology, Father Colombo Institute of Medical Sciences, Warangal, Telangana

Received: 25-02-2024 / Revised: 23-03-2024 / Accepted: 26-04-2024

Corresponding Author: Dr. Anjum Jabeen

Conflict of interest: Nil

Abstract:

Introduction: Diabetes mellitus is a complex chronic metabolic condition defined by persistent hyperglycemia caused by abnormalities in insulin activity and/or secretion. Prolonged hyperglycemia and related metabolic abnormalities eventually cause tissue toxicity, which manifests as accelerated atherosclerosis, renoretinal microangiopathy, and neuropathy, resulting to a variety of vascular, neurological, and focal problems. The study aimed to examine the efficacy and safety of vildagliptin-metformin vs glimepiride metformin in patients with type 2 diabetes.

Materials and Methods: This comparative study was carried out over six months in a tertiary care Institution. A total of 100 participants participated in the study. These 100 patients were separated into two groups, each with 50 patients. Group A received glimepride 1mg and metformin 500mg in combination, while Group B received vildagliptin 50mg with metformin 500mg. The efficacy indicators such as fasting blood glucose, 2-hour postprandial glucose, and HbA1c were assessed, and any side effects were documented at 4-week intervals across the 24-week research period.

Results: Maximum number of patients belonged to the age group of 50–54 years. Of 100 patients, 62 patients were males and 38 patients were females. Average of FBS in Groups A and B before initiation of therapy was 166.24 ± 11.76 mg/dl and 162±12.42. At the end of 24 weeks of therapy, an average of FBS in Groups A and B was reduced to 112.21 ± 10.23 mg/dl and 107.65 ± 11.23 mg/dl which was significant. Average of FBS in Groups A and B before initiation of therapy was 166.24 ± 11.76 mg/dl and 162±12.42. At the end of 24 weeks of therapy, an average of FBS in Groups A and B was reduced to 112.21 ± 10.23 mg/dl and 107.65 ± 11.23 mg/dl which was significant. Baseline mean value of HbA1C in Group A before with glimepiride was 8.23±1.23, and mean value of HbA1C in Group B with vildagliptin before initiation of therapy was 8.28±0.70. Average of HbA1C at the end of 24 weeks in Groups A and B was 7.20 ±0.60 and 7.12±0.62

Conclusion: Vildagliptin in combination with metformin is a beneficial and significant new therapy option that can provide optimum glycemic control without causing weight gain or hypoglycemia. Vildagliptin is a more effective and well-tolerated medication for treating type 2 diabetes mellitus than glimepiride.

Keywords: Diabetes mellitus, type 2; Glimepiride; Metformin; Vildagliptin.

Introduction

Chronic and multifactorial, type 2 diabetes (T2DM) is characterized by a number of pathophysiological abnormalities, such as insulin resistance and decreased islet function, which lead to abnormally elevated fasting hepatic glucose production and poor glucose tolerance.

The deficiency in islet function is a gradual process with both quantitative and qualitative anomalies in insulin and glucagon secretion kinetics, whereas insulin resistance essentially stays unaltered over time.[1] The International Diabetes Federation (IDF) claims that In 2021, 537 million adults (20–79 years old) globally were estimated to have diabetes; by 2030, that number is predicted to rise to 643 million. Roughly 783 million people worldwide will have diabetes by 2045. [2]

Diabetes is predicted by the World Health Organization (WHO) to rank seventh among all causes of death by 2030.[3,4] Drug safety and efficacy are taken into consideration when selecting

antidiabetic drugs. For the first treatment of type 2 diabetes, metformin is the most often given monotherapy.[5-7] Ultimately, nevertheless, most patients have recommended combination therapy to maintain diabetic control. The combined regimens aim to lessen the negative effects and dosage of antihyperglycemic medications. In Indian clinical settings, the combination of glimepiride and metformin is often used due to its cost-effectiveness and efficacy in improving glycemic control.[8,9]

Glimepiride is typically the first-choice medication for non-obese diabetics, while metformin is recommended for obese diabetics. In India, the combination of metformin and sulfonylureas is most frequently used due to its low cost, and it can reduce hemoglobin A1c (HbA1c) more than either medication alone.[10] However, there is a risk of severe hypoglycemia and weight gain with this combined medication. Some Type 2 diabetic patients have poor glycemic control despite carefully designed dosing regimens utilizing oral hypoglycemic agents (OHAs), and many OHAs produce adverse drug reactions (ADRs) such weight gain and hypoglycemia. Vildagliptin is a potent, selective, and reversible inhibitor of DPP-4 that helps people with Type 2 diabetes (T2DM) better control their blood sugar levels.[11,12] Vildagliptin is an oral antidiabetic medication that has a low risk of edema, a lipid-neutral effect, weight neutrality, and moderate efficacy. It also has a favorable overall safety profile.[13]

The current study was undertaken to evaluate and compare the efficacy and adverse effects of combinations of metformin and vildagliptin and metformin and glimepiride in T2DM patients.

Materials and Methods:

This prospective, randomized, & comparative study was conducted at ESIC Medical College & Hospital, Sanathnagar, Hyderabad, Telangana for duration of 6 months after taking clearance from the Institutional ethics committee. Total 100 patients were enrolled in the study based on the inclusion criteria & exclusion criteria.

Inclusion Criteria

Males and females between 40 and 70 years with Type-2 diabetes already on treatment (on monotherapy with metformin or glimepiride) but with uncontrolled blood sugars, i.e., (fasting blood sugar [FBS] >126 mg/dl and postprandial blood sugar (PPBS) >200 mg/dl, having HbA1c >7.0%,

Exclusion criteria

Type-1 diabetes mellitus, diabetic ketoacidosis, renal failure, heart failure, pregnancy and breast feeding

After obtaining Written informed consent from all the participants, these 100 patients were divided into two groups of 50 patients each. Group A was given glimepride 1mg and metformin 500mg combination, Group B was given vildagliptin 50mg plus metformin 500mg combination. The total period of the study was 6 months. The efficacy variables like blood glucose, 2-hour postprandial glucose and HbA1c were measured and adverse effects if any were recorded at 4 weekly intervals for the total period of study of 24 weeks.

Statistical analysis: Data were analyzed using the Statistical Package for Social Sciences version 25. Mean ± standard deviations were calculated for quantitative variables for both the groups. Statistical significance between both groups was assessed using independent t-test and chi-square test. All p values less than 0.05 were regarded as statistically significant.

Results:

A total of 100 patients were enrolled in the study. Maximum number of patients belonged to the age group of 50–54 years. Of 100 patients, 62 patients were males and 38 patients were females.

Table 1: demographic characteristics of patients

characteristic	Group A (n=50)	Group B (n=50)
Age (Years)	53.51±10.41	55.38±10.98
Sex (m/f)	30/20	32/18

Average of FBS in Groups A and B before initiation of therapy was 166.24 ± 11.76 mg/dl and 162±12.42. At the end of 24 weeks of therapy, an average of FBS in Groups A and B was reduced to 112.21 ± 10.23 mg/dl and 107.65 ± 11.23 mg/dl which was significant as shown in Table 2

Table 2: Comparison of FBS levels between Group I (Metformin+ Glimepiride) and Group II (Metformin+ Vildagliptin)

FBS	Group A (n=50)	Group B (n=50)	p value
Before	166.24 ± 11.76	162±12.42	0.00*
After	112.21 ± 10.23	107.65 ± 11.23	0.03*

***significant**

Average of PPBS in Groups A and B before initiation of therapy was 268.60±20.12 mg/dl and 266.76±21.05 mg/dl. At the end of 24 weeks of therapy, average of PPBS in Groups A and B reduced to 158.34±10.65 mg/dl and 152.62±11.12 mg/dl which was significant as shown in Table 3

Table 3: comparison of PPBS levels between Group A (Metformin+ Glimepiride) and Group B (Metformin+ Vildagliptin)

PPBS	Group A (n=50)	Group B (n=50)	p value
Before	268.60±20.12	266.76±21.05	0.002*
After	158.34±10.65	152.62±11.12	0.001*

***significant**

Baseline mean value of HbA1C in Group A before with glimepiride was 8.23±1.23, and mean value of HbA1C in Group B with vildagliptin before initiation of therapy was 8.28±0.70. Average of HbA1C at the end of 24 weeks in Groups A and B was 7.20 ±0.60 and 7.12±0.62 as shown in Table 4

Table 4: comparison of HbA1c levels between Group I (Metformin+ Glimepiride) and Group II (Metformin+ Vildagliptin)

HbA1c	Group A (n=50)	Group B (n=50)	p value
Before	8.23±1.23	8.28±0.70	0.01*
After	7.20±0.62	7.12±0.60	0.02*

Hypoglycemic symptoms were observed in 18% of Group A patients and 2% of Group B patients. Weight gain was observed in 20% of patients on metformin and glimepiride combination as shown in table 5

Table 5: comparison of adverse effects between Group I (Metformin+ Glimepiride) and Group II (Metformin+ Vildagliptin)

variable	Group A (n=50)	Group B (n=50)	p value
Hypoglycemia	9	1	0.03*
Weight gain	10	0	0.003*

***significant**

Discussion

In the present study, the patients on metformin and vildagliptin combination showed a significant decline in mean FBS and PPBS to a maximum of 107.65 mg/dl and 152.62 mg/dl at 24 weeks.

The study's findings are similar to those of Bosi et al. [14], who found a significant decrease in FBS and PPBS levels, and Pan et al. [15], who found that combining metformin and vildagliptin significantly reduced fasting blood glucose (FBG) levels ($P < 0.001$) at 24 weeks compared to metformin placebo.

According to Chatterjee and Chatterjee [16], both once daily and twice daily regimens of metformin and vildagliptin resulted in significant reductions in FBS from baseline ($P < 0.0001$). Both groups showed a significant drop in PPBS levels ($P < 0.0001$).

Patients on metformin and glimepiride combination also showed a significant reduction in FBS and PPBS to a maximum of 112.21 mg/dl and 158.34mg/dl at 24 weeks, respectively A study by Charpentier et al., Wang et al., and Pareek et al. [17-19] found a significant reduction in FBS and PPBS ($P < 0.001$) from baseline compared to glimepiride or metformin alone. Baseline mean value of HbA1C in Patients on metformin and glimepiride & in Patients on metformin and vildagliptin before initiation of therapy was 8.23±1.23 & 8.28±0.70. Average of HbA1C at the end of 24 weeks, significantly reduced to 7.20 ±0.60 in Groups A and 7.12±0.62 in Group B. Matthewes et al.[20] shown that vildagliptin in combination with metformin is as effective as glimepiride in lowering mean HbA1C levels.

One episode of hypoglycemia occurred with vildagliptin compared with 10 episodes with glimepiride ($P < 0.01$) which was significant. Weight gain was observed in 10 patients on metformin and glimepiride combination compared with no weight gain in patients on metformin and vildagliptin combination. Previous studies by (Sarkar et al. and Jeon HJ et al.) revealed no weight gain with vildagliptin metformin therapy.[21,22]

Conclusion

In this study we found that both metformin + glimepiride and metformin + vildagliptin achieved optimal glycemic control almost equally. But in terms of adverse effects, the Vildagliptin-Metformin combination medication performed better than the Glimepiride-Metformin combination treatment.

As a result, vildagliptin plus metformin provides an advantage and represents an essential new

therapeutic option for excellent glycemic control while avoiding weight gain and hypoglycemia risk. Vildagliptin is more effective and well-tolerated than glimepiride for the treatment of type 2 diabetes mellitus.

References

1. Unger RH, Orci L. Paracrinology of islets and the paracrinopathy of diabetes. Proc Natl Acad Sci U S A. 2010; 107(37): 16009-12.
2. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: International Diabetes Federation, 2021.
3. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS medicine. 2006 Nov 28; 3(11): e442.
4. World Health Organization. World Health Organization Diabetes Fact Sheet. WHO: Geneva, Switzerland. 2011.
5. American Diabetes Association. 8. Pharmacologic approaches to glycemic treatment. Diabetes Care. 2017; 40(Suppl 1):S64–74.
6. International Diabetes Federation Guideline Development Group. Global guideline for type 2 diabetes. Diabetes Res Clin Pract. 2014; 104:1– 52.
7. McGuire H, Longson D, Adler A, Farmer A, Lewin I. Guideline Development Group. Management of type 2 diabetes in adults: Summary of updated NICE guidance? BMJ. 2016; 353:i1575.
8. Singh SK. Commentary on "Consensus recommendations on sulfonylurea and sulfonylurea combinations in the management of type 2 diabetes mellitus: International task force" Indian J Endocr Metab. 2018; 22:158–9.
9. Unnikrishnan AG, Pandit K, George J, Venkataraman S, Abhyankar MV. Clinical utilization pattern of multiple strengths of glimepiride and metformin fixed dose combinations in Indian type 2 diabetes patients. J Assoc Physicians India. 2020;68:57–61
10. Charbonnel B, Schernthaner G, Brunetti P, Matthews DR, Urquhart R, Tan MH, Hanefeld M. Long-term efficacy and tolerability of add-on pioglitazone therapy to failing monotherapy compared with addition of gliclazide or metformin in patients with type 2 diabetes. Diabetologia. 2005 Jun; 48(6):1093-104.
11. Winkler G. Incretin enhancers, incretin mimetics–from therapeutic concept to clinical application. Orvosi hetilap. 2007 Apr 1;148 (13):579-87
12. Holst JJ. Treatment of type 2 diabetes mellitus with agonists of the GLP-1 receptor or DPP-IV inhibitors. Expert opinion on emerging drugs. 2004 May 1; 9(1):155-66.
13. Mathieu C, Degrande E. A new oral treatment for type 2 diabetes mellitus. Vasc Health Risk Manag. 2008; 4:1349–60.
14. Bosi E, Camisasca RP, Collober C, Rochotte E, Garber AJ. Effects of vildagliptin on glucose control over 24 weeks in patients with Type 2 diabetes inadequately controlled with metformin. Diabetes Care 2007; 30:890-5.
15. Pan C, Xing X, Han P, Zheng S, Ma J, Liu J, et al. Efficacy and tolerability of vildagliptin as add-on therapy to metformin in Chinese patients with Type 2 diabetes mellitus. Diabetes Obes Metab. 2012; 14:737-44
16. Chatterjee S, Chatterjee S. Glycemic effects of vildagliptin and metformin combination therapy in Indian patients with Type 2 diabetes: An observational study. J Diabetes 2014; 6:237-42. .
17. 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; 18:828-34.
18. Wang M, Gao F, Xue YM, Han YJ, Fu XJ, He FY, et al. Effect of short-term intensive therapy with glimepiride and metformin in newly diagnosed Type 2 diabetic patients. Nan Fang Yi Ke Da Xue Xue Bao 2011; 31:564-6.
19. Pareek A, Chandurkar NB, Salkar HR, Borkar MS, Tiwari D. Evaluation of efficacy and tolerability of glimepiride and metformin combination: A multicentric study in patients with Type-2 diabetes mellitus, uncontrolled on monotherapy with sulfonylurea or metformin. Am J Ther 2013; 20:41-7.
20. Matthewes DR, Dejager S, Ahren B, GFonseca V, Ferrannini E, Cuturier A, et al. Vildagliptin add-on to metformin produces similar efficacy and reduced hypoglycaemic risk compared with glimeperide, with no weight gain: Results from a 2-year study. Horm Metab Res 2009; 41:368-73
21. Gillett MJ. International expect committee report on the role of the assay in the diagnosis care 2009; 32(7):1327-1334.
22. Diabetes Care "January 2010" Diabetes care. 33 S3. 2009. from the original on 13 January 2010. Retrieved 29 January 2010.