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Original Research Article

Assessment of Treatment Satisfaction and Efficacy of Vildagliptin Compared with Glimepiride as a Combination Therapy to Metformin in Patients with Type 2 Diabetes Mellitus Attending a Tertiary Care Hospital in India

Mondal M[1], Pramanik S[2], Sengupta M[3], Raychowdhuri P[4]

[1]Senior Resident, Department of Pharmacology, Calcutta National Medical College, Kolkata

[2]Associate Professor, Department of Pharmacology, Calcutta National Medical College, Kolkata

[3]Associate Professor, Department of Pharmacology, Calcutta National Medical College, Kolkata

[4]Professor, Department of Pharmacology, Calcutta National Medical College, Kolkata

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Corresponding author: Dr Sushobhan Pramanik

Conflict of interest: Nil

Abstract

Background: 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, glimepiride or vildagliptin can be added. Treatment satisfaction with these oral antidiabetic drugs can be measured by Diabetes Treatment Satisfaction Questionnaire (DTSQ) which can influence overall success and adherence to therapy.

Objective: To compare the treatment satisfaction level of patients between metformin-glimepiride and metformin-vildagliptin regimens using DTSQ and to also compare the efficacy between the two regimens.

Methods: An open-label, prospective, observational study was carried out in the Diabetology OPD and the Department of Pharmacology. Patients with T2DM not controlled on metformin monotherapy were divided in to groups: Group A with 58 subjects received metformin 1000 mg + glimepiride 2 mg twice daily and Group B with 62 subjects received metformin 1000 mg + vildagliptin 50 mg twice daily. Patients were assessed for DTSQ scores, FBS, PPBS, HbA1c and other clinical and biochemical indicators at baseline, 6 weeks and 12 weeks. The study parameters were compared between two groups statistically using unpaired t-test.

Results: Patients in Group B receiving metformin-vildagliptin combination achieved better control of FBS at 6 weeks ($p<0.01$) and 12 weeks ($p < 0.001$) compared to those in Group A receiving metformin-glimepiride combination. Similarly Group B patients had better reduction of HbA1c ($p < 0.001$) compared to Group A at the end of study. Group B patients also had better DTSQ score ($p <0.05$) and less perceived frequency of hypoglycemia ($p <0.001$) compared to Group A at 6 weeks and 12 weeks interval. Group B also showed significant reduction in body weight ($p <0.05$) and BMI ($p<0.01$) compared to group B at the end of study period.

Conclusions: Vildagliptin-metformin combination leads to better treatment satisfaction profile, better glycemic control, lower risk of weight gain and lower risk of hypoglycemia; and can be a better treatment alternative to glimepiride-metformin.

Keywords: Diabetes Treatment Satisfaction Questionnaire, Diabetes Mellitus, Vildagliptin

Introduction

Diabetes mellitus is a global health problem on a massive scale with 425 million people suffering from it worldwide. India is the 2nd most affected country with estimated 72 million diagnosed diabetic patients and another 80 million with pre-diabetes, of which around 95% patients are suffering from diabetes mellitus type 2 (T2DM) [1]. Type 2 diabetes is a chronic disease characterized by primarily hyperglycemia and varying degree of hypertension, dyslipidemia and other metabolic problems. It is associated with serious long-term complications like accelerated atherosclerosis, cardiovascular and cerebrovascular diseases and other end organ damages like nephropathy, neuropathy and retinopathy [2]. Hence adequate control of diabetes mellitus type 2 is extremely important to avoid its dangerous consequences, which can be achieved and maintained by lifestyle changes, drugs and regular monitoring.

There are a number of oral medications that are available for the management of T2DM, among which metformin is considered as the 1st line drug due to its efficacy, safety and affordability [3,4]. However, a large number of patients fail to achieve fair control with metformin alone, in in such cases the combination of metformin with other oral hypoglycemic agents is recommended [5].

One of the most commonly used combination in India in this regard is metformin with glimepiride [6,7]. Glimepiride is a sulfonylurea that acts mainly via increasing insulin secretion, and the combination with metformin is well established due to its cost effectiveness. However common adverse effects of this combination include weight gain and severe hypoglycemia [8].

Vildagliptin is an orally active dipeptidyl peptidase-4 (DPP-4) inhibitor that is another popular combination with metformin [9]. Vildagliptin as an add-on therapy to metformin has demonstrated good efficacy but fewer adverse effects and better tolerability [10,11].

Optimal management of hyperglycemia in type 2 diabetes mellitus mandates regular monitoring of blood glucose parameters, continuous use of prescribed drugs and high degree of self-motivation and engagement by the patient [12-14]. This can become very difficult to follow if the treatment is plagued by adverse reactions, poor tolerability and low treatment satisfaction, leading to an unfavorable impact on the quality of life. These issues often create poor treatment adherence and negatively affect glycemic control, which can usher in the serious complications of the disease in the long term [15].

In this context, The Diabetes Treatment Satisfaction Questionnaire (DTSQ) is internationally validated and WHO approved tool for assessment of treatment satisfaction in type 2 diabetes mellitus [16]. DTSQ is easy to answer and can be conveniently applied to investigate patients' wellbeing, self-efficacy and overall satisfaction regarding any particular therapeutic regimen [17].

While there are several Randomized Clinical Trials (RCTs) and interventional studies that have evaluated the comparative efficacy of glimepiride and vildagliptin as add-on therapy to metformin [18-21], there are very limited number of works that have considered the treatment satisfaction among type 2 diabetes mellitus patients receiving either of these combinations in Indian

context. The current study aims to address this gap by focusing on the assessment of treatment satisfaction level of patients between metformin-glimepiride and metformin-vildagliptin therapy in the management Type 2 Diabetes Mellitus in India. The results of this study may provide valuable insights that can predict better adherence to treatment regimens and help recommend the most suitable therapy for long term control of the disease.

Objectives

The objective of this study is to compare the treatment satisfaction level of patients between metformin-glimepiride and metformin-vildagliptin regimens using the Diabetes Treatment Satisfaction Questionnaire; and to also compare the efficacy between the two therapies.

Materials and Methods

This was a single center, open-label, prospective, observational study carried out in the Diabetology Out Patient Department and the Department of Pharmacology of Calcutta National Medical College and Hospital, Kolkata from February 2020 to July 2021. Recruitment of study subjects was for six months starting from the initiation of the study period. To calculate the sample size, the standard normal variate was taken as 1.96 (Z value); the estimated proportion of patients diagnosed and treated with Type 2 diabetes every year in Calcutta National Medical College, Kolkata was 9.5% (p) and precision of the study was considered to be 5% (d value). P value of 0.05 was considered to be significant. Following these criteria, a sample size of 120 was obtained, and considering an expected attrition rate of 20%, about 138 patients were enrolled for follow up, out of which total 120 patients completed the study.

Inclusion Criteria

- Patients more than 18 years of age from both the genders diagnosed with Type 2 diabetes mellitus that is not controlled by metformin monotherapy for at least last one month.
- Diabetes Mellitus Type II was diagnosed using the following criteria [22,23]:
  1. Fasting Plasma Glucose (FPG) ≥ 126 mg/dL (7.0 mmol/L); and/or
  2. Post Prandial Glucose (PPG) ≥ 200 mg/dL (11.1 mmol/L); and/or
  3. Glycated haemoglobin (HbA1c) ≥ 6.5% (48 mmol/mol).

Exclusion Criteria

- Pregnant and lactating patient.
- Patients taking insulin or other anti-diabetic medications.
- Patient with active serious heart, liver, respiratory and renal disease or patients who were critically ill during the study period.
- Previous history of allergy to the study medications.

Ethical considerations:

Ethical clearance was obtained from Institutional Ethics Committee of Calcutta National Medical College and Hospital, Kolkata prior to initiation of the study. Permission to use "Diabetes Treatment Satisfaction Questionnaire (DTSQ)" was obtained from Health Psychology Research Ltd., University of London (www. healthpsychologyresearch.com). Voluntary Informed Consent in writing was obtained from the all the study subjects before commencing the study proper. The study was conducted according to the principles of Declaration of Helsinki and good clinical practices.

Methodology

Patients selected were divided into two groups based on the clinician's assessment with respect to the patient's profile, with 58 patients were allotted in Group A and 62 patients in Group B.

Group A received metformin 1000 mg + glimepiride 2 mg twice daily (n=58). Group B received metformin 1000 mg + vildagliptin 50 mg twice daily (n = 62). Each patient recruited in the study underwent detailed clinical examination at baseline including thorough history taking, general survey with recording of BP and BMI; and laboratory investigations like FPG, PPG, HbA1c, Serum urea and creatinine, lipid profile, bilirubin and liver enzymes, and were followed up to 3 months from the date of initiation of treatment. They were re-evaluated at 6 week and 12 week interval, during which relevant clinical and laboratory investigations were repeated, and they were provided with the Diabetes Treatment Satisfaction Questionnaire to assess treatment satisfaction.

DTSQ contains eight questions: (1) satisfaction with ongoing treatment, (2) perceived frequency of hyperglycaemia, (3) perceived frequency of hypoglycaemia, (4) convenience of the treatment, (5) flexibility of the treatment, (6) understanding of diabetes mellitus, (7) likelihood to recommend the treatment to others, and (8) satisfaction to continue the treatment. Scores against items 1,4,5,6,7 and 8 were added to produce the treatment satisfaction scale total, and higher scores indicate better satisfaction with therapy. Items 2 (perceived frequency of hyperglycaemia) and 3 (perceived frequency of hypoglycaemia) were treated separately during data analysis, and lower scores in each of these two items indicate better control of blood glucose.

Data analysis

MS Excel software was used for tabulation and scoring the data, while SPSS version 22 was used for statistical analysis. Student's unpaired t-test was done to compare between the two study groups at baseline and follow up. $P < 0.05$ was considered as statistically significant.

Results & Analysis

Demographic details

Total 120 patients were included in this study. Among them 65 patients (54.17%) were male and 55 patients (45.83%) were female. Male to female ratio was 1.18:1.

In this study, majority of the patients were in the age group of 50-54 years, followed by the age group of 55-59 years. (Figure1).

Diabetes Treatment Satisfaction Questionnaire

The DTSQ Scores were compared among Group A and Group B patients at the end of 6 weeks and 12 weeks of initiation of therapy. Group B patients had a significantly higher overall DTSQ score ($P < 0.05$) and very highly significant DTSQ score for perception of hypoglycemia ($P < 0.001$) as compared to Group A. This indicates better treatment satisfaction and less perceived frequency of hypoglycemia in patients receiving vildagliptin with metformin. No significant difference was observed in DTSQ score for perception of hyperglycemia between Groups A and B ($P > 0.05$). These results were consistent for both the follow up observations (Table 1).

Efficacy measured by the control of FBS, PPG and HbA1c

The mean FPG in Groups A and B before initiation of therapy was 179.81±5.2 mg/dl and 181.47±4.86 mg/dl, while the mean PPG values were 262.72±6.12 mg/dl and 264.80±5.91 mg/dl respectively. Mean value of Hemoglobin A1c was 7.73±0.37 for Group A and 7.85±0.33 for Group B. All the blood glucose parameters were comparable at baseline ($P > 0.05$) (Table 2).

The fasting and post prandial plasma glucose levels were again obtained and compared after 6 weeks (Table 2). The mean FPG levels among the study subjects in Group A at the end of the study were 147.15±4.8 mg/dl as compared to 139.34±5.02 mg/dl among Group B study population. The difference was found to be highly statistically

significant ($p<0.01$). The mean PPG levels among the study subjects in Group A at the end of 6 weeks were 209.55±5.27 mg/dl as compared to 211.4±6.05 mg/dl among Group B study population but in this case the difference between the two groups was statistically insignificant ($p>0.05$).

At the end of 12 weeks of therapy, both the groups showed a saubstantial decrease in FPG (Table 2). The average of FPG in Groups A and Group B was reduced to 120.03 mg/dl and 117.64 mg/dl. There was a significant difference between the two groups in decreasing the FPG levels ($p < 0.001$). It indicated that the patients on vildagliptin and metformin had better control over FPG after 12 weeks as the serum FPG was lowered more in Group B compared to Group A. Though the mean PPG in Groups A and Group B was also reduced to 168.16 mg/dl and 170.02 mg/dl respectively; there was no significant difference between the two groups in as far as the PPG levels are concerned at the end of 12 weeks ($P >0.05$).

Average of HbA1c% at the end of 12 weeks in Group A and Group B was 6.35 and 6.01 respectively (Table 2). While both the groups showed a decrease in the mean HbA1c levels from the baseline, there was a significant difference between the HbA1c% levels of the two groups ($P < 0.001$), indicating that subjects on metformin and vildagliptin combination had superior control over HbA1c after 12 weeks in comparison to the patients receiving glimepiride and metformin combination. The proportion of patients who achieved optimal glycemic control at the end of study period was compared among the two groups. Group B had a significantly greater number of patients achieving recommended HbA1c% target of <6.5% at the of 12 weeks as compared to Group A ($P <0.05$).

Both the drug combinations were found to be well tolerated during the study period; no adverse drug reactions requiring any alteration or discontinuation of study drugs were observed. To monitor the safety of the study medications, assessment of relevant clinical and biochemical parameters was done at the beginning of the study and also at the end of study period.

The mean body weight as well as BMI was slightly increased in the patients receiving glimepiride with metformin by the end of study duration, while at the same interval, the body weight and BMI was found to be decreased in the vildagliptin-metformin group (Table 4). The difference in both body weight ($p = 0.028$) and BMI ($p = 0.008$) between the two groups at the end of 12 weeks was observed to be statistically significant, indicating that Group B achieved greater reduction in both weight and BMI. However, the blood pressure measurements in both the groups remained relatively unchanged across the study duration (Table 4).

Regarding the biochemical parameters like serum urea and creatinine, they were observed to be within normal limits at both the baseline and 12 weeks, with no significant differences when compared between the two groups at any of the time intervals (Table 4). Similarly, bilirubin, hepatic SGOT and SGPT and lipid profile values remained relatively unchanged and normal across the study duration in both the study arms (Table 4), without any significant differences among Group A and B at any point of time.

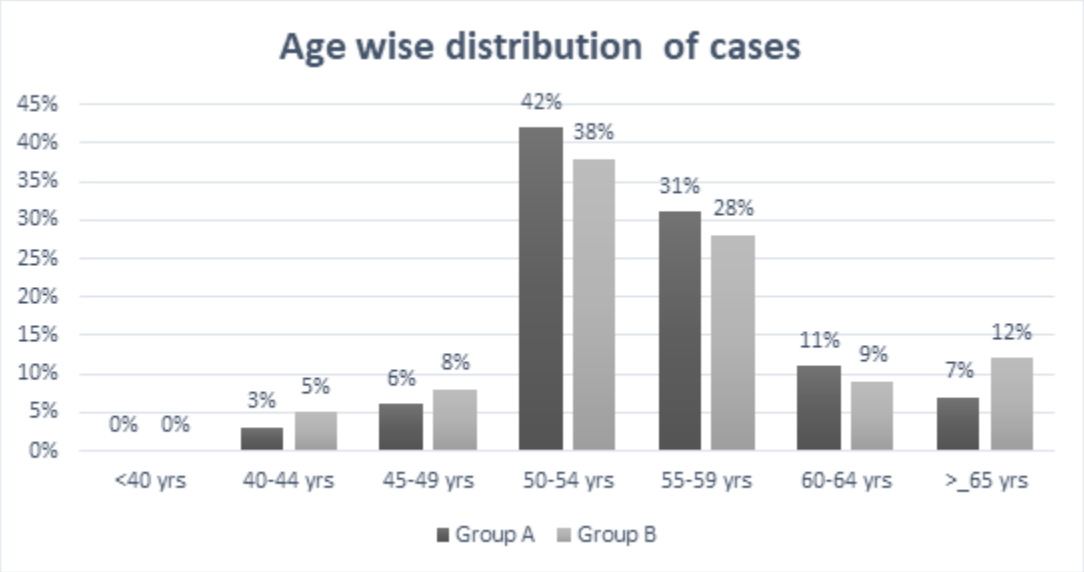

Figure 1: Age wise distribution of cases

Table 1: Difference in Diabetes Treatment Satisfaction Questionnaire (DTSQ) Scores among Group A and Group B patients during follow up visits.

Parameters	1st follow up (6 weeks)			2nd follow up (12 weeks)		
	Group A (N=58)	Group B (N=62)	p value (unpaired t-test)	Group A (N=58)	Group B (N=62)	p value (unpaired t-test)
DTSQ (mean±SD)	18.92±4.08	20.68±3.95	0.018	19.04±4.35	21.01±4.29	0.014
DTSQ for perception of hyperglycemia (mean±SD)	2.94±0.53	2.85±0.6	0.386	2.86±0.36	2.77±0.31	0.145
DTSQ for perception of hypoglycemia (mean±SD)	2.82±0.57	2.37±0.4	<0.001	2.88±0.4	2.21±0.51	<0.001

Test applied: Unpaired t-test for comparison of DTSQ Scores between Group A and B

Table 2: Comparative analysis of different plasma glucose indicators between Group A and Group B.

Parameters	Group A (N=58)	Group B (N=62)	p value (Unpaired t- test)
Baseline			
FPG (mg/dl)	179.81±5.2	181.47±4.86	0.0682
PPG (mg/dl)	262.72±6.12	264.80±5.91	0.0607
HbA1c (%)	7.73±0.37	7.85±0.33	0.0633
6 weeks			
FPG (mg/dl)	147.15±4.8	139.34±5.02	0.001
PPG (mg/dl)	209.55±5.27	211.4±6.05	0.076
12 weeks			

FPG (mg/dl)	120.03±4.05	117.64±4.17	0.002
PPG (mg/dl)	168.16±5.03	170.02±5.84	0.065
HbA1c (%)	6.35±0.53	6.01±0.37	<0.0001

Test applied: Unpaired t-test for comparison of Plasma glucose parameters between Group A and B

Table 3: Percentage of patients who achieved HbA1c <6.5% at the end of 12 weeks (2nd follow up)

Parameter	Group A (N=58)	Group B (N=62)	p value (Chi-square-test)
Percentage of patients who achieved HbA1c <6.5%, n (%)	33 (56.89%)	46 (74.19%)	0.044

Test applied: Chi-square-test for comparison of subjects achieving HbA1c target between Group A and B

Table 4: Comparison of clinical and laboratory parameters between Group A and Group B Test applied: Unpaired t-test for comparison of clinical and biochemical parameters between Group A and B

Parameters	Group A	Group B	p value	Group A	Group B	p value
At Baseline				After 12 weeks		
Weight (Kg)	67.28±2.97	68.03±2.88	0.163	67.55±2.18	66.45±2.08	0.028
BMI (Kg/m^2)	27.84±2.56	28.02±2.48	0.696	28.01±1.95	27.01±2.07	0.008
SBP (mm/Hg)	129.32±5.12	127.86±5.62	0.139	128.86±6.28	129.45±6.65	0.619
DBP (mm/Hg)	84.02±7.88	82.25±6.94	0.194	82.84±7.35	82.14±7.3	0.602
Serum Urea	33.81±1.24	33.53±1.3	0.229	33.79±1.33	33.43±1.57	0.178
Serum creatinine	0.88±0.06	0.89±0.07	0.403	0.87±±0.09	0.88±0.05	0.453
Total cholesterol	189.08±8.93	190.21±9.41	0.501	188.76±9.78	189.65±8.26	0.591
Triglyceride	175.18±11.26	179.05±10.87	0.758	174.87±12.08	177.81±11.52	0.175
LDL-C	118.63±6.76	118.04±6.62	0.63	119.46±6.35	120.23±7.08	0.531
HDL-C	37.65±1.08	36.84±1.11	0.344	37.78±1.37	37.94±1.34	0.519
Total Serum Bilirubin	0.72±0.04	0.7±0.08	0.085	0.71±0.07	0.7±0.06	0.403
SGPT	25.58±1.64	26.01±1.53	0.319	25.74±1.2	25.88±1.61	0.192
SGOT	22.67±2.06	23.02±1.95	0.341	22.8±1.72	23.1±2.14	0.399

Discussion

Type 2 diabetes mellitus has become a common and massive health problem in India, where the prevalence of the disease in adult population has increased from 5.5% in 1990 to 7.7% in 2016 [1,24]. The treatment of T2DM has evolved rapidly in last few decades with a great emphasis on oral antidiabetic agents; consequently, vast majority of the patients are dependent on the oral medications for the control of blood

sugar. In patients who fail to achieve fair control of the disease with the 1st line metformin monotherapy alone, glimepiride is hailed as one of the most popular drugs to add on with metformin. But glimepiride being an insulin secretagogue, comes with the inherent problem of high incidence of hypoglycemia which can be often dangerous and intolerable [25,26]. Hypoglycemic episodes can negatively affect the quality of life of the patients, with other problems of glimepiride like weight gain only adversely contributing to the same. Among the other alternatives to glimepiride, DPP-4 inhibitors like vildagliptin act as insulin sensitizer, hence chances of hypoglycemia are far less likely. The current study was designed on this rationale that that vildagliptin as an add on therapy to metformin may have better acceptability among the target populations while maintaining similar efficacy, hence contributing to a better quality of life and treatment satisfaction among the patients.

However, studies comparing the DTSQ scores in patients receiving glimepiride or vildagliptin are rare, particularly in the Indian context. In one study conducted by Singh *et al*. [27] the authors observed the effects of different regimens containing DPP4 inhibitors (one of sitagliptin, vildagliptin, or teneligliptin) against those taking other regimens, on the DTSQ scores of the elderly patients. They concluded that in general DPP4 inhibitors may be associated with better treatment satisfaction and better efficacy outcomes in geriatric patients; however, they admitted that the sample size was small and a smaller number of patients taking DPP4 inhibitor-based therapies (only 14 patients on vildagliptin based regimen) participated in the study. Also, the study participants were exclusively from geriatric age group and the results may not be extrapolated to general population. In another study Otowa-Suematsu *et al*. [28] observed that vildagliptin added to basal insulin in diabetic patients achieved good DTSQ scores and glycaemic control in Japanese patients. In the present study it was found that patients on vildagliptin and metformin regimen had a significantly better overall DTSQ score ($p<0.05$) and DTSQ score for perception of hypoglycemia ($p<0.001$) as compared to patients receiving combination of glimepiride and metformin, thus supporting the previous observations.

In earlier studies, Redekop *et al*. [29] and Marra [30] had found significantly better quality of life scores among patients having lower HbA1c levels as compared to those having higher HbA1c levels. These results indicate that the diabetes treatment satisfaction score to some extent can provide valuable information regarding glycaemic as well as metabolic parameters, and resonates well with findings of the current study.

In the present study, it was observed that vildagliptin-metformin regimen was associated with significantly better reduction of FPG at 6 weeks ($p<0.01$) and 12 weeks ($p<0.001$) compared to the glimepiride-metformin regimen. While the reduction of PPG was similar in both the groups across the study period, patients in Group B achieved far superior control of HbA1c at the end of study period ($p<0.001$) compared to Group B.

These results are comparable with studies done by Bosi *et al*. [31] and Pan *et al*. [32] who demonstrated that metformin and vildagliptin combination significantly improved glycaemic control when compared with metformin alone. Similar findings were echoed in a retrospective observation by Chatterjee and Chatterjee,[33] where vildagliptin-metformin combination regimen significantly reduced FPG level from the baseline ($P<0.001$). The authors of a study in Karnataka conducted by Gullapalli *et al*. [34] found that both the glimepiride and vildagliptin containing regimens significantly decreased mean FPG, PPG and HbA1c % at the end of 12 weeks. The same

study also showed that the decrement in mean FPG was significantly more in the vildagliptin group than in the glimepiride group, which coincides with the findings of current study.

The present study found that vildagliptin-metformin group represents a significantly ($p<0.05$) greater number of patients who achieved recommended target HbA1c % of less than 6.5% compared to glimepiride-metformin group. This is consistent with the results of a study conducted by Mokta JK *et al*. [35] where the vildagliptin-metformin regimen represents a more effective combination in terms of better glycemic control and number of patients achieving target level of HbA1c % with a lower risk of hypoglycemia.

In the present study, vildagliptin-metformin regimen showed a significant reduction in mean body weight ($p = 0.028$) and BMI ($p = 0.008$) compared to glimepiride-metformin group, where actually a slight increase in body weight and BMI observed. This is consistent with the findings of previous works that have well documented the risk of weight gain and hypoglycemia with glimepiride-metformin combination [8,25,26].

Study Limitations

Due to limitations of available resources, no blinding at any stage of the study period was attempted, hence there were some chances of certain bias. Also, this study was conducted in a single tertiary care hospital for a limited time duration. Future works addressing these limitations undertaken in a more heterogenous population can validate the results of present observations in a more decisive manner.

Conclusion

To conclude, patients taking vildagliptin-metformin regimen had significantly better Diabetes Treatment Satisfaction Questionnaire (DTSQ) score and lower perception of hypoglycaemia as compared to patients taking glimepiride-metformin regimen. In addition, better glycaemic control was associated with higher treatment satisfaction as indicated by significantly better control of FBS and HbA1c among patients taking vildagliptin-metformin regimen. Owing to better glycaemic control, better treatment satisfaction profile, lower risk of weight gain and lower risk of hypoglycaemia, the present study would like to recommend that, vildagliptin-metformin combination can be a better alternative to glimepiride-metformin combination in treatment of T2DM that is not adequately controlled by metformin monotherapy.

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References

1. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, *et al*. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR–INDIAB population-based cross-sectional study. The Lancet Diabetes & Endocrinology [Internet]. 2017 Aug [cited 2022 Sep 17];5(8):585–96. Available from: https://www.thelancet.com/journals/landia/article/PIIS2213-8587(17)30174-2/fulltext
2. Gorst C, Kwok CS, Aslam S, Buchan I, Kontopantelis E, Myint PK, *et al*. Long-term glycemic variability and risk of adverse outcomes: A systematic review and meta-analysis. Diabetes Care.2015 Dec;38(12):2354-69
3. IDF Clinical Guidelines Task Force. Global Guideline for Type 2 Diabetes: recommendations for standard, comprehensive, and minimal care.

Diabetic Medicine. 2006 Jun;23(6):579-93.
4. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, *et al*. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2009 Jan;32(1):193–203.
5. Rodbard H, Jellinger P, Davidson J, Einhorn D, Garber A, Grunberger G, *et al*. Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology Consensus Panel on Type 2 Diabetes Mellitus: An Algorithm for Glycemic Control. Endocrine Practice. 2009 Sep;15(6):540–59.
6. Ag U, K P, J G, S V, Mv A. Clinical Utilization Pattern of Multiple Strengths of Glimepiride and Metformin Fixed Dose Combinations in Indian Type 2 Diabetes Patients. The Journal of the Association of Physicians of India. 2020 Jul 1; 68(7):57–61.
7. Sahay RK, Mittal V, Gopal GR, Kota S, Goyal G, Abhyankar M, *et al*. Glimepiride and Metformin Combinations in Diabetes Comorbidities and Complications: Real-World Evidence. Cureus. 2020 Sep 28 [cited 2022 Sept 29];12(9):e10700. Available from: https://www.cureus.com/articles/37779-glimepiride-and-metformin-combinations-in-diabetes-comorbidities-and-complications-real-world-evidence
8. Basit A, Riaz M, Fawwad A. Glimepiride: evidence-based facts, trends, and observations. Vascular Health and Risk Management [Internet]. 2012 Aug 15 [cited 2020 May 21]; 8:463–72. Availablefrom:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3448454/
9. Mathieu C, Degrande E. Vildagliptin: a new oral treatment for type 2 diabetes mellitus. Vascular Health and Risk Management [Internet]. 2008 Dec [cited 2022 Nov 21];4(6):1349–60. Available from: https://www.dovepress.com/vildagliptin-a-new-oral-treatment-for-type-2-diabetes-mellitus-peer-reviewed-fulltext-article-VHRM.
10. Pan CY, Wang. Profile of vildagliptin in type 2 diabetes: efficacy, safety, and patient acceptability. Therapeutics and Clinical Risk Management [Internet]. 2013 May [cited 2022 Nov 21]; 9:247. Available from: https://pubmed.ncbi.nlm.nih.gov/23818788/
11. Van Gaal L, Hermans MP, Daci E, Denhaerynck K, De Meester L, MacDonald K, *et al*. Effectiveness and Tolerability of Vildagliptin and the Single Pill Combination of Vildagliptin and Metformin in "Real-World" Management of Type 2 Diabetes Mellitus: The G-FORCE Study. Diabetes Therapy. 2019 Mar 27;10(3):965–79.
12. Krapek K, King K, Warren SS, George KG, Caputo DA, Mihelich K, *et al*. Medication Adherence and Associated Hemoglobin A1c in Type 2 Diabetes. Annals of Pharmacotherapy. 2004 Sep;38(9):1357–62.
13. Schectman JM, Nadkarni MM, Voss JD. The Association Between Diabetes Metabolic Control and Drug Adherence in an Indigent Population. Diabetes Care. 2002 Jun 1;25(6):1015–21.
14. Holt RIG, Nicolucci A, Kovacs Burns K, Escalante M, Forbes A, Hermanns N, *et al*. Diabetes Attitudes, Wishes and Needs second study (DAWN2TM): Cross-national comparisons on barriers and resources for optimal care-healthcare professional perspective. Diabetic Medicine. 2013 Jun 23;30(7):789–98.
15. Anderson RT, Balkrishnan R, Camacho F, Bell R, Duren-Winfield V, Goff D.

Patient-centered outcomes of diabetes self-care. Associations with satisfaction and general health in a community clinic setting. North Carolina Medical Journal [Internet]. 2003 Mar-Apr[cited 2022 Sept. 29];64(2):58–65. Available from: https://pubmed.ncbi.nlm.nih.gov/12774734/

16. Saisho Y. Use of Diabetes Treatment Satisfaction Questionnaire in Diabetes Care: Importance of Patient-Reported Outcomes. International Journal of Environmental Research and Public Health. 2018 May 9;15(5):947.
17. Bradley C, Gamsu DS. Guidelines for Encouraging Psychological Well-being. Diabetic Medicine. 1994 Jun;11(5):510–6.
18. Werida R, Kabel M, Omran G, Shokry A, Mostafa T. Comparative clinical study evaluating the effect of adding Vildagliptin versus Glimepiride to ongoing Metformin therapy on diabetic patients with symptomatic coronary artery disease. Diabetes Research and Clinical Practice. 2020 Dec; 170:108473.
19. Ferrannini E, Fonseca V, Zinman B, Matthews D, Ahrén B, Byiers S, *et al*. Fifty-two-week efficacy and safety of vildagliptin vs. glimepiride in patients with type 2 diabetes mellitus inadequately controlled on metformin monotherapy. Diabetes, Obesity and Metabolism. 2009 Feb;11(2):157–66.
20. Matthews DR, Dejager S, Ahren B, Fonseca V, Ferrannini E, Couturier A, *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, Obesity and Metabolism. 2010 Apr 19;12(9):780–9.
21. He YL, Foteinos G, Neelakantham S, Mattapalli D, Kulmatycki K, Forst T, *et al*. Differential effects of vildagliptin and glimepiride on glucose fluctuations in patients with type 2 diabetes mellitus assessed using continuous glucose monitoring. Diabetes, Obesity and Metabolism. 2013 Jul 14;15(12):1111–9.
22. American Diabetes Association. Classification and diagnosis of diabetes: Standards of medical care in diabetes—2021. Diabetes Care [Internet]. 2021 Dec 9 [cited 2022 Sept. 29];44(Supplement 1):S15–33. Available from: https://care.diabetesjournals.org/content/diacare/44/Supplement_1/S15.full.pdf
23. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2010 Dec 30;34(Supplement_1): S62–9.
24. Pradeepa R, Mohan V. Prevalence of type 2 diabetes and its complications in India and economic costs to the nation. European Journal of Clinical Nutrition. 2017 Apr 19;71(7):816–24.
25. Ahrén B, Foley JE, Dejager S, Akacha M, Shao Q, Heimann G, *et al*. Higher Risk of Hypoglycemia with Glimepiride Versus Vildagliptin in Patients with Type 2 Diabetes is not Driven by High Doses of Glimepiride: Divergent Patient Susceptibilities? Diabetes Therapy. 2014 Sep 18;5(2):459–69.
26. Cryer PE. Glycemic goals in diabetes: trade-off between glycemic control and iatrogenic hypoglycemia. Diabetes [Internet]. 2014 Jul [cited 2022 Sept. 7];63(7):2188–95. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24962915
27. Singh H, Chakrawarti A, Singh H, Guruprasad P, Gupta YK. Evaluation of treatment satisfaction, efficacy and safety of dipeptidyl peptidase-4 inhibitors in geriatric patients with type 2 diabetes mellitus: A cross-sectional comparative study. Journal of Family Medicine and Primary Care [Internet]. 2018 Jan-Feb [cited 2022 Sept. 29];7(1):70–6. Available from:https://pubmed.ncbi.nlm.nih.gov/29915736/

28. Otowa-Suematsu N, Sakaguchi K, Nakamura T, Hara K, Kishi M, Hashimoto N, *et al*. Comprehensive Evaluation of Combination Therapy with Basal Insulin and Either Lixisenatide or Vildagliptin in Japanese Patients with Type 2 Diabetes: A Randomized, Open-Label, Parallel-Group, Multicenter Study. Diabetes Therapy. 2018 Sep 11; 9(5): 2067–79.
29. Redekop WK, Koopmanschap MA, Stolk RP, Rutten GEHM, Wolffenbuttel BHR, Niessen LW. Health-Related Quality of Life and Treatment Satisfaction in Dutch Patients With Type 2 Diabetes. Diabetes Care [Internet]. 2002 Mar 1;25(3):458–63. Available from: https://diabetesjournals.org/care/article/25/3/458/21940/Health-Related-Quality-of-Life-and-Treatment
30. Marra G, DIAB. & TE.S Project Study Group. The DIAB.&TE.S Project: how patients perceive diabetes and diabetes therapy. Acta Bio-Medica: Atenei Parmensis [Internet]. 2004 Dec 1 [cited 2022 Sept. 29];75(3):164–70. Available from:https://pubmed.ncbi.nlm.nih.gov/15796090/
31. 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 Feb 2; 30(4):890–5.
32. 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, Obesity & Metabolism [Internet]. 2012 Aug 1 [cited 2022 Sept. 29];14(8):737–44. Available from: https://pubmed.ncbi.nlm.nih.gov/22369287/
33. Chatterjee S, Chatterjee S. Glycemic effects of vildagliptin and metformin combination therapy in Indian patients with type 2 diabetes: An observational study. Journal of Diabetes. 2013 Aug 27;6(3):237–42.
34. Gullapalli H, Desai S. Comparison of efficacy and safety of metformin and vildagliptin versus metformin and glimepiride in patients of Type 2 diabetes mellitus. National Journal of Physiology, Pharmacy and Pharmacology. 2018; 8(4):521-525
35. Mokta JK, Ramesh, Sahai AK, Kaundal PK, Mokta K. Comparison of Safety and Efficacy of Glimepiride-Metformin and Vildagliptin- Metformin Treatment in Newly Diagnosed Type 2 Diabetic Patients. The Journal of the Association of Physicians of India [Internet]. 2018 Aug 1 [cited 2022 Sept. 29];66(8):30–5. Availablefrom:https://pubmed.ncbi.nlm.nih.gov/31324081/