https://doi.org/10.33472/AFJBS.6.5.2024.3954-3962

African Journal of Biological Sciences

Effectiveness and Safety Evaluation of Teneligliptin along with Metformin plus Glimepiride Combination inType-2 Diabetes Mellitus

Mohd Ajmal[1], Badruddeen[2]*, Mukhtar Ahmad[3],Juber Akhtar[4], Md Nematullah[5], Md Sohel Akhter[6], Mohammad Irfan Khan[7]

[1, 2,4, 5, 6, 7]Faculty of Pharmacy, Integral University, Lucknow, Uttar Pradesh, India-226026
[3]Integral Institute of Medical Science and Research Integral University, Lucknow, Uttar Pradesh, India-226026

*Corresponding Author: Badruddeen
*Professor, Faculty of Pharmacy Integral University, Lucknow-206026, Uttar Pradesh, India, Email: badarmiracle@gmail.com

Article History
Volume 6, Issue 5, May 2024
Received: 30 Apr 2023
Accepted: 20 May 2024
Doi: 10.33472/AFJBS.6.5.2024.3954-3962

Abstract

Background: The rising global prevalence of type 2 diabetes mellitus necessitates effective and safe treatment approaches. This study explores the real world effectiveness and safety of the Teneligliptin along with Metformin plus Glimepiride combination in the management of type-2 Diabetes Mellitus, addressing the critical need for individualized therapeutic options in diabetes care.

Material and methods: This observational study was approved by Institutional Ethics Committee (Approval number: IEC/IIMS&R/2022/77) and was conducted at the Integral Institute of Medical and Research Hospital, Lucknow, India, from September 2022 to January 2023, The study goal was to investigate the effectiveness and safety of the Teneligliptin along with Metformin plus Glimepiride combination in poorly controlled Type-2 Diabetes Mellitus. In this study, 68 participants were enrolled on the basis of inclusion criteria/exclusion criteria, and oral/written consent. The outcomes were assessed as reduction in glycated hemoglobin (HbA1c), fasting blood sugar (FBS), and postprandial blood sugar (PPBS) at baseline, 12 weeks, and 24 weeks during treatment.

Result: The results indicated significant improvements in glycemic control, including reductions in HbA1c, FBS, and PPBS levels. The study also highlighted the occurrence of adverse events among the participants, revealing a higher incidence of gastrointestinal disorders and other minor complications such as upper respiratory tract infection, weakness, dizziness, and liver dysfunction.

Conclusion: The findings support the effectiveness of the Teneligliptin along with Metformin plus Glimepiride combination as a well-tolerated therapeutic option for individuals with T2DM. This lays the groundwork for future comparative studies and enhances the understanding of individualized treatment approaches in diabetes management.

Keywords: Type-2 Diabetes Mellitus; Hyperglycemia; Hypoglycemia; Teneligliptin; Metformin

Introduction

Type 2 diabetes (T2DM) is a chronic metabolic condition characterized by insulin resistance and impaired activity of the pancreatic beta cells [1, 2], leading to a gradual illness with several pathophysiological defects [3]. This results in serious multi-organ problems that lower survival and quality of life [4]. Over the past 30 years, the number of individuals with diabetes mellitus has doubled worldwide, posing a significant concern to global health due to the continuous diabetes mellitus epidemic and its repercussions [5].According to estimates from the International Federation of Diabetes, 9.3% of people worldwide between the ages of 20 and 79 have diabetes. By 2045, that number is expected to rise by 51%, or 700 million individuals, with 7% of cases coming from Central and South America [6]. Consequently, type 2 diabetes mellitus (T2D) has a significant negative impact on healthcare expenses and public health [7]. India ranks as the second most affected country behind China (109.6 million), with approximately 69.2 million people living with diabetes, according to a 2015 survey conducted by the International Diabetes Federation (IDF). In India, DM was identified in almost 73 million cases in 2017 [8].According to the IDF's health prediction study from 2015, 123.5 million people in India would develop diabetes by 2040 if the current trend in the disease continues [9]. The incidence of diabetes mellitus (DM) has suddenly increased in India for a number of causes, but type 2 diabetes (T2DM) is associated with a greater death rate, a worse quality of life, and various vascular complications. Although most studies have not been able to show that reducing glycated hemoglobin (HbA1c) levels can lower the risk of cardiovascular events, doing so does successfully reduce microvascular events [10]. When treating type 2 diabetes, the standard approach is to begin with metformin monotherapy and gradually add other anti-diabetic drugs when glycaemic control declines. The majority of individuals eventually need to take two or more medications to address their condition and meet their glycaemic objectives. Since sulphonylureas are inexpensive and have a strong anti-hyperglycemic impact, they are frequently used as a second-line treatment for type 2 diabetes. However, its disadvantages include weight gain, a shortened half-life of therapeutic efficacy, and an increased risk of hypoglycemia. SGLT-2 inhibitors and DPP-4 inhibitors are two of the more recent groups of oral ant-diabetic drugs that are effective second-line therapies to sulphonylureas [11]. The management of diabetes and the prevention of its complications have been demonstrated by pharmacological anti-diabetic therapies, which also improve insulin secretion or resistance or supplement the insulin. However, side effects like weight gain and hypoglycemia have been documented and remain unresolved [12]. A number of novel glucose-lowering drugs, including DPP-4 inhibitors, GLP-1 receptor agonists, and SGLT-2 inhibitors, have been developed in response to the demand for new drugs that effectively decrease blood sugar levels, safely, and without inducing weight gain [13]. SGLT2 inhibitors and DPP-4 inhibitors are two classes of oral glucose-lowering drugs increasingly prescribed to treat type 2 diabetes mellitus. If lifestyle changes combined with metformin monotherapy prove unsuccessful, the treatment regimen may be expanded to include an SGLT2i or DPP-4i. However, the mechanisms by which these two glucose-lowering drugs function are very dissimilar [14]. When addressing inadequate insulin production, Asian individuals respond better to DPP4 inhibitors than Caucasians who also have insulin resistance. Studies have shown that using teneligliptin 20 mg/day can lower HbA1C by 0.7% [15]. This study aims to systematically investigate the real-world safety and efficacy of Teneligliptin along with Metformin plus glimepiride combination in managing Type 2 diabetes mellitus (T2DM). By addressing the critical need for individualized therapeutic options in diabetes care, the study endeavors to provide valuable insights that contribute to the enhancement of glycemic control and establish this combination as a well-tolerated therapeutic choice. The

findings are anticipated to lay the foundation for future comparative studies, enriching our comprehension of personalized treatment approaches in diabetes management

Material and methods

This study, which took place between September 2022 to January 2023, was a prospective observational study done on T2DM patients who were routinely attending the Integral Institute of Medical and Research (IIMSR) Hospital, Lucknow, India. The study protocol was approved by Institutional Ethics Committee (Approval number: IEC/IIMS&R/2022/77). The Helsinki Declaration's ethical guidelines, good clinical practices, and the research protocol were all followed in the conduct of the investigation. The study goal was to investigate the effectiveness and safety of the Teneligliptin along with Metformin plus Glimepiride combination in poorly controlled Type-2 Diabetes Mellitus. In this study, participants were enrolled on the basis of inclusion criteria/exclusion criteria, and oral/written consent.

Inclusion Criteria

- Males and Females (age more than 30 years)
- Patients who had poor glycemic control (PPBS≥ 180 mg/dl,FBS≥130 mg/dl, HbA1c >7.0)
- Patientswho wished to delay starting insulin.
- Patients already on Metformin monotherapy.
- Diabetic patient with co-morbidities

Exclusion Criteria:

- Type-1 Diabetic patient
- Patients who were or have been using insulin.
- Patients on SGLT2 inhibitor therapy
- Acute illness, pregnancy/lactating, liver disease, were excluded from the study.

Study procedure

This study was designed to assess the efficacy and safety of Teneligliptin and Metformin plus Glimepiride. A total 68 participants were received teneligliptin 20 mg/day, metformin 1000 mg/day, and glimepiride 2 mg/day.

Assessment

The assessments began on the week zero (baseline), followed by subsequent evaluations at 12 and 24 weeks. The study recorded the effects of the Teneligliptin along with Metformin plus Glimepiride, on variables including sex, age, glycated hemoglobin (HbA1c), fasting blood sugar (FBS) and postprandial blood sugar (PPBS). Adverse events were tracked in order to evaluate safety.

Statistical analysis:

The statistical software package SPSS version 23.0 together with Microsoft Excel was utilized for data analysis. Based on the p value, which was deemed statistically significant at $p<0.05$, the statistical significance was stated.

Results

68 subjects were taken Teneligliptin along with metformin plus glimepiride therapy. In Table 1, demonstrated demographic representation such as mean age of participants having 51.29±8..23, gender distribution in which 44.12% male and 55.88% female. Age distribution exhibited that 5.88% were age group in between the 30-40 years, 52.94% between 41-50 years 25% between 51-60 years and 12.17% between more than 60 years of age. The 61.76% of the participants reported a history of diabetes from 0-5 years, while 20.58% had a history of 6-10 years, and 17.64% reported more than 10 years. The mean body weight was reported as 69.48±9.55 kg, and the mean BMI was reported as 25.57±2.26 kg/m². Comorbidities like Hypertension, Cardiovascular disease, Dyslipidemia, Diabetic neuropathy and Diabetic retinopathy were found to be associated with the participants. Among all, Dyslipidemia was found to be the most common Comorbidity comprising 44.11% of total patients. 29.41% were found to have hypertension, 14.70% have diabetic neuropathy and 11.76% was comorbid with other cardiovascular disease.

Table1. Demographic distribution of study participants taking Teneligliptin + Metformin + glimepiride.

Variable	Number of participants (n=68)
Age (year) Mean ±SD	51.26 ±8.23
Gender, n (%)	
Male	30 (44.12%)
Female	38(55.88%)
Age group, n (%)	
30-40	4(5.88%)
41-50	36(52.94%)
51-60	17 (25%)
> 60	11(12.17%)
History of MD (year), n (%)	
0-5	42(61.76%)
6-10	14 (20.58%)
>10	12(17.64%)
Body weight (kg) Mean ±SD	69.48±9.55
BMI Mean ±SD	25.57±2.26
FBG	198.94±22.64
PPBG	304.22±26.43
HbA1c	9.58± 0.86
Comorbidity	
Hypertension	20 (29.41%)
Cardiovascular Disease	8 (11.76%)
Dyslipidemia	30(44.11%)
Diabetic Neuropathy	10 (14.70%)

Data are mean (±SD); HbA1c: glycated hemoglobin; FBS: fasting blood sugar; PPBS: postprandial blood sugar; BMI: body mass index

Table 2; explain the impact of Teneligliptin along with Metformin plus Glimepiride combination therapy on HbA1C, FBS and PPBS levels at 12 and 24 weeks after treatment. On day first prior to

treatment the HbA1C (%) was found to be 9.58 ±0.86 %. Followed by 12 weeks of treatment, a notable significant reduction ($p<0.0001$) to 8.7±087 % was observed, this positive trend further augmented at the 24-week, demonstrating a mark significant reduction ($p<0.0001$) to 8.08±0.92 %. Similarly the fasting blood sugar (FBS) was found to be decreased from day first prior to treatment 198.94±22.64 mg/dl to 135.56 ±21.61 mg/dl and 133.03±17.87 mg/dl at 12 weeks and 24 weeks respectively, with both changes being significant ($p < 0.0001$). Likewise, postprandial blood sugar (PPBS) exhibit significant decrease from 3.4.22±26.43 mg/dl on the day first to 240.96±24.05 mg/dl at 12 weeks and 232.07±22.74 mg/dl at 24 weeks. Demonstrating a PPBS significant reduction ($p<0.0001$).

Table2. Impact of Teneligliptin along with Metformin plus Glimepiride combination on HbA1c, FBS and PPBS.

Parameters	Before treatment/ Mean±SD	12 week treatment/ Mean±SD	Mean reduction 12 week from baseline	24 week treatment /Mean±SD	Mean reduction 24 week from baseline
HbA1c	9.58± 0.86	8.77± 0.87	0.81*	8.08 ±0.92	1.5*
FBS	198.94±22.64	135.56±21.61	63.38#	133.03 ±17.87	65.91#
PPBS	304.22±26.43	240.96 ±24.05	63.26$	232.07 ±22.74	72.15$

HbA1c: glycated hemoglobin; FBS: fasting blood sugar, PPBS: postprandial blood sugar.
All values were expressed as mean ±SD; HbA1c significant (*$p<0.0001$) when compared to the base line; FBS significant (#$p<0.0001$) when compared to the base line; PPBS significant ($p<0.0001$) when compared to the base line

In Table 2.3/Fig. 2.6 we comprehensively detail the adverse events observed during the study period among participants receiving the DPP-4 (Teneligliptin 20mg) and Metformin 500mg combination. Particularly the incidence of hepatic function impairment was minimal, with only 1.73% of participants reporting such events. Other adverse events included viral upper respiratory tract infection (2.60%), dizziness (2.60%) and gastrointestinal disorders (3.47%).

Table3. Reported adverse events during Teneligliptin along with Metformin plus Glimepiride combination therapy.

Adverse Event	Number of subject (Percentage) (N-68)
Viral upper respiratory tract infection	4 (5.88%)
Dizziness	2(2.94%)
Hepatic function impairment	1(1.47%)
Gastrointestinal disorders	7(10.29%)
Weakness	2 (2.94%)

In Table 3, we comprehensively detail the adverse events observed during the study period among participants receiving the Teneligliptin along with Metformin plus Glimepiride. Notably,

the incidence of hepatic function impairment was minimal, with only 1.47% of participants reporting such events. Other adverse events included gastrointestinal disorders (10.29%), viral upper respiratory tract infection (5.88%), dizziness (2.94%), and Weakness (2.94%) were reported.

Discussion

The present study was grounded in a carefully designed prospective observational study conducted at the Integral Institute of Medical and Research Hospital in Lucknow, India. The global prevalence of T2DM has surged in recent decades, presenting a significant health threat. In type 2 diabetes mellitus, the present observational study was conducted to assess the safety and effectiveness of Teneligliptin along with Metformin plus Glimepiride combination therapy in type 2 diabetic patients. A total number of subjects, accounting for 68 participated were enrolled in present study. Participants are in accordance with demographic patterns 44.12% male and 55.88% female.The majority of people (52.94%) were between the 41-50 year of age, thereafter (25%) between age 51-60 year, followed by 30-40 year age and more than 60 year age with (5.88%) and (12.17%) respectively this present study result are similar with study [16,17]. When evaluating the history of Type 2 diabetes (DMT2), the significant percentage of patients (61.76%) who fall into the 0-5 years category. baseline, the mean body weight of 69.48±9.55 kg and BMI of 25.57±2.26 kg/m^2,indicate a profile that is consistent with being overweight or obese, which is frequently linked to people with Type 2 diabetes agree with the study [18]. The assessments of glycemic change were analyzed by mean change in the reading of, FBS and PPBS. The safety and efficacy of Teneligliptin along with Metformin plus Glimepiride therapy, after 12 and 24 weeks showed significant improvement in glycemic control such as HbA1c, FBS and PPBS were observed,

In addition to present work an observational studies conducted by Vinendra (2020), 61 patient received metformin /glimepiride plus additional teneligliptin 20 mg for six months showed significant reduction in glycemic parameters (HbA1c, fasting, and postprandial blood glucose) [19]. Additionally, Patil (2020) conducted a cross sectional study involving 20 patients treated with a combination of Metformin, Glimepiride, Pioglitazone therapy for 12 weeks, showed significant reduction in glycemic parameters, such as HbA1c, fasting plasma glucose (FPG), and postprandial plasma glucose (PPG) [20]. Moreover Mitra *et al.,* (2020) conducted a retrospective study involving 100 patients undergoing treatment with teneligliptin and metformin over a three-month periods, showed significant reductions in glycemic markers [9]. In the present study, 68 patients were administered teneligliptin along with metformin plus glimepiride for duration of 24 weeks showed significant improvements in glycemic parameters such as HbA1c, FBS, and PPBS. The study comprehensive evaluation of adverse events further strengthened its reliability. Adverse events, including hypoglycemia, viral upper respiratory tract infection, dizziness, hepatic function impairment and gastrointestinal disorders, were systematically monitored. The present study demonstrated that a low incidence of adverse events, consistent with earlier research findings [21, 22]. This indicates a favorable safety profile associated with the use of DPP-4 inhibitors in combination along with other antidiabetic medications, emphasizing the importance of such combination therapies in effectively managing type -2 diabetes mellitus while minimizing adverse effects. Despite the strengths of the study, certain limitations and challenges were acknowledged. The absence of a control group and randomization could introduce selection bias, limiting the ability to establish causal relationships definitively. The single center nature of the study and the specific patient population in Lucknow, India, raised questions about the generalizability of findings to broader populations. These limitations underscored the need for cautious interpretation and highlighted areas for improvement in future research. The study findings

contributed valuable insights, positioning the teneligliptin along with metformin plus glimepiride combination as a potential therapeutic option.

Conclusion

In conclusion, present study successfully addressed its objectives by evaluating the safety and efficacy of the Teneligliptin along with metformin plus glimepiride combination in a real-world setting. The results underscore the substantial efficacy of the Teneligliptin along with metformin plus glimepiride combination in improving glycemic control, as evidenced by the statistically significant reductions in HbA1C, FBS, and PPBS at both 12 and 24 weeks. The low incidence of adverse events highlights the favorable safety profile of this combination, supporting its viability as a well-tolerated therapeutic option for individuals with Type 2 diabetes mellitus.

Acknowledgement

The authors express their gratitude to Integral University for its facilities, the research community for giving a manuscript communication number for additional communication, and critical suggestions on the work's development – (IU/R&D/2023-MCN0002296).

Conflict of Interest

There is no conflict of interest.

Reference

1. Haque E, Kamil M, Irfan S, Hasan A, Sheikh S, Ssm M. Protein aggregation: A new challenge in type-II diabetes. Adv Biotech & Micro. 2017.
2. Sayana SB, Shareef SM, Muralidhar C, Rao R, Burli K. Renal function and hypoglycemic events with teneligliptin versus vildagliptin in diabetic patients : prospective. 2023;4:1246–9.
3. Ajmal Mohd, Badruddeen, Ahmad M, Sohel Akhter Md, Khushtar M, Akhtar J, Khan MI, Parveen S, Ahmad A. An update on fixed-dose combination of SGLT-2 and DPP 4 inhibitors in the management of TYPE-2 diabetes. Eur Chem Bull. 2023;12(10):707–16.
4. Longato E, Bonora BM, Di Camillo B, Sparacino G, Tramontan L, Avogaro A, et al. Outcomes of patients with type 2 diabetes treated with SGLT-2 inhibitors versus DPP-4 inhibitors. An Italian real-world study in the context of other observational studies. Diabetes Res Clin Pract [Internet]. 2021;179:109024. Available from: https://doi.org/10.1016/j.diabres.2021.109024.
5. Mishra M, Tiwari D, Khan MM. A study on serum total bilirubin and uric acid in newly diagnosed type 2 diabetes mellitus.IJPSR, 2020; Vol. 11(11): 5884-5889
6. Joaqui VB, Gómez NB, Ortiz RC, Toro LM, Lombo JP, Cifuentes CA, García MA, Lomba AA. Effectiveness of triple therapy with dapagliflozin add-on to dual therapy over 52 weeks in patients with uncontrolled type 2 diabetes mellitus in a centre of high complexity, Cali-Colombia. Archives of Endocrinology and Metabolism. 2021 Jan 18;65:49-59.
7. Van Hulten V, Driessen JHM, Starup-Linde JK, Al-Mashhadi ZK, Viggers R, Klungel OH, et al. The associations of sodium-glucose cotransporter-2 inhibitors versus dipeptidyl peptidase-4 inhibitors as add-on to metformin with fracture risk in patients with type 2 diabetes mellitus. Diabetes Obes Metab [Internet]. 2023;(May).
8. Khan MD, Alam R, Ahsan H, Khan MM, Khan S. Evaluation of serum alkaline phosphatase and calcium in type 2 diabetes mellitus patients at Lucknow, India. Journal of Current Biomedical Reports jcbior. com. 2022 Sep 30;3(3).

9. Mitra A, Ray S. Evaluation of the Safety and Efficacy of Teneligliptin at a Higher Dose in Indian Type 2 Diabetes Patients: A Retrospective Analysis. Cureus. 2020;12(1):1–9.
10. Son C, Makino H, Kasahara M, Tanaka T, Nishimura K, Taneda S, et al. Comparison of efficacy between dipeptidyl peptidase-4 inhibitor and sodium-glucose cotransporter 2 inhibitor on metabolic risk factors in Japanese patients with type 2 diabetes mellitus: Results from the CANTABILE study. Diabetes Res Clin Pract [Internet]. 2021;180:109037. Available from: https://doi.org/10.1016/j.diabres.2021.109037.
11. Gonzalez-galvez G, Johnsson E, Maaske J, Testa MA, Simonson DC. Efficacy and safety of dual add-on therapy with dapagliflozin plus saxagliptin versus glimepiride in patients with poorly controlled type 2 diabetes on a stable dose of metformin : Results from a 52-week , randomized , active-controlled trial. 2020;(September 2019):1083–93.
12. Roth GA, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1736–88.
13. Cahn A, Cernea S, Raz I. An update on DPP-4 inhibitors in the management of type 2 diabetes. Expert Opin Emerg Drugs [Internet]. 2016;21(4):409–19. Available from: http://dx.doi.org/10.1080/14728214.2016.1257608.
14. Scheen AJ. Reduction in HbA1c with SGLT2 inhibitors vs. DPP-4 inhibitors as add-ons to metformin monotherapy according to baseline HbA1c: A systematic review of randomized controlled trials. Diabetes Metab [Internet]. 2020;46(3):186–96. Available from: https://doi.org/10.1016/j.diabet.2020.01.002.
15. Poornima R, Brigida S, Elizabeth AA, Soujania G, Lella T. A Comparative Study of Safety and Efficacy of Metformin Monotherapy Against Teneligliptin and Metformin in Type 2 Diabetes Mellitus. J Pharm Negat Results. 2022;13(2):7–12.
16. Bommineni sr, shravani p, shyam j, alekhya m, srikanth b. A comparative study of efficacy on glycemic control by glimepiride versus teneligliptin as an add on to metformin therapy in type 2 diabetes mellitus patients. Int j curr pharm res. 2022;14(2):26–30.
17. Nishanth T, Maheswari CU, Lakshmi RS, Sri D, Goud P, Tabassum K. A study to compare efficacy of metformin-glimepiride versus metformin-teneligliptin in type II diabetic patients. Int J Pharm Sci Res. 2018 Dec 1;9(12):5258–64.
18. Raghuveer B, Netaji N. Efficacy of teneligliptin with metformin in Type 2 diabetes mellitus patients. National Journal of Physiology, Pharmacy and Pharmacology. 2020 Jul 31;10(8):663.
19. Vinendra MP, Sunita SG. Efficacy and Safety of Teneligliptin as Add on Therapy in Indian Type 2 Diabetes Mellitus Patients having Dyslipidemia. J Diabetes Metab. 2020;10:844.
20. Patil DP. A study of effectiveness of addition of drug teneligliptin to metformin, glimepiride, pioglitazone combination in type II diabetic patients. Int J Res Med Sci. 2020 Feb;8(2):692-695
21. Kim HJ, Kim YS, Lee CB, Choi MG, Chang HJ, Kim SK, Yu JM, Kim TH, Lee JH, Ahn KJ, Min KW. Efficacy and safety of switching to teneligliptin in patients with type 2 diabetes inadequately controlled with dipeptidyl peptidase-4 inhibitors: 52-week results from a prospective observational study. Diabetes Therapy. 2021 Nov;12:2907-20.
22. Ji L, Li L, Ma J, Li X, Li D, Meng B, Lu W, Sun J, Liu Y, Takayanagi G, Wang Y. Efficacy and safety of teneligliptin added to metformin in Chinese patients with type 2 diabetes mellitus inadequately controlled with metformin: a Phase 3, randomized, double-blind, placebo-controlled study. Endocrinology, Diabetes & Metabolism. 2021 Apr;4(2):e00222.

Cite this article as: Mohd Ajmal, Effectiveness and Safety Evaluation of Teneligliptin and Metformin plus Glimepiride Combination in Type-2 Diabetes Mellitus, African Journal of Biological Sciences (South Africa). 6(5), 1-09.

DOI:xyz