Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 3, 2024

Beneficial Effect of Triple-Drug Combination of Teneligliptin with Metformin and Glimepiride in Patients with Type 2 Diabetes Mellitus

[1]Rahat Khan Warsi, [2]Dr. Prashant Wadagbalkar, [3]Ragini Bhardwaj

[1,3]Research Scholar, Department of Pharmacology, Index Medical College, Hospital & Research Centre, Malwanchal University, Indore, India

[2]Research Supervisor & Professor, Department of Pharmacology, Index Medical College, Hospital & Research Centre, Malwanchal University, Indore, India

Corresponding Author

Rahat Khan Warsi

rahatwarsi23@gmail.com

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a progressive metabolic disorder characterized by insulin resistance and progressive β-cell dysfunction. Although metformin remains the preferred first-line therapy, a substantial proportion of patients fail to achieve adequate glycemic control with dual-drug regimens, necessitating the addition of a third antidiabetic agent. Teneligliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, has demonstrated favorable glycemic efficacy and safety when used as add-on therapy.

Objective: To evaluate the effectiveness of triple-drug combination therapy comprising teneligliptin, metformin, and glimepiride in patients with inadequately controlled Type 2 diabetes mellitus.

Materials and Methods: A prospective observational study was conducted among 72 patients with Type 2 diabetes mellitus inadequately controlled on metformin and glimepiride therapy. Teneligliptin 20 mg once daily was added to the existing treatment regimen, and patients were followed for 24 weeks. Fasting blood glucose (FBG), postprandial blood glucose (PPBG), glycated hemoglobin (HbA1c), body mass index (BMI), and adverse events were assessed at baseline and study completion.

Results: The mean age of participants was 54.7 ± 8.6 years. After 24 weeks of treatment, significant reductions were observed in FBG (168.3 ± 24.7 mg/dL to 126.8 ± 18.9 mg/dL), PPBG (256.7 ± 35.8 mg/dL to 182.5 ± 27.3 mg/dL), and HbA1c (8.9 ± 0.8% to 7.2 ± 0.6%) ($p < 0.001$). A modest reduction in BMI was also noted. The therapy was generally well tolerated, with only mild adverse events reported.

Conclusion: Addition of teneligliptin to metformin and glimepiride significantly improved glycemic control and was well tolerated in patients with inadequately controlled Type 2 diabetes

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 3, 2024

mellitus. Triple-drug therapy may represent an effective treatment strategy for achieving target glycemic goals.

Keywords: Type 2 diabetes mellitus; Teneligliptin; Metformin; Glimepiride; Triple-drug therapy; Glycemic control; HbA1c.Introduction

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most prevalent chronic metabolic disorders worldwide and continues to impose a substantial burden on healthcare systems. The disease is characterized by insulin resistance, progressive pancreatic β-cell dysfunction, and chronic hyperglycemia, leading to microvascular and macrovascular complications if left inadequately controlled. The global prevalence of diabetes has increased steadily over the past decade, highlighting the need for effective and sustainable therapeutic strategies [1].

Metformin remains the cornerstone of pharmacological management in T2DM because of its proven efficacy, favorable safety profile, and cardiovascular benefits. However, owing to the progressive nature of the disease, many patients eventually fail to maintain optimal glycemic control with metformin alone and require additional therapeutic agents. Sulfonylureas such as glimepiride are frequently used as second-line drugs because of their potent glucose-lowering action and affordability [2].

Despite dual therapy with metformin and glimepiride, a considerable proportion of patients continue to exhibit elevated glycated hemoglobin (HbA1c) levels. In such situations, treatment intensification through the addition of a third oral antidiabetic agent is often required. Dipeptidyl peptidase-4 (DPP-4) inhibitors have emerged as valuable treatment options because they enhance endogenous incretin activity, improve insulin secretion in a glucose-dependent manner, and reduce glucagon secretion with a relatively low risk of hypoglycemia [3].

Teneligliptin is a newer DPP-4 inhibitor that has gained widespread clinical acceptance, particularly in Asian countries, due to its potent glycemic efficacy, convenient once-daily dosing, and favorable safety profile. Several clinical studies have demonstrated significant reductions in fasting plasma glucose, postprandial glucose, and HbA1c levels following teneligliptin therapy in patients with inadequately controlled T2DM [4,5].

Recent systematic reviews and meta-analyses have further confirmed the efficacy and tolerability of teneligliptin both as monotherapy and as add-on therapy to existing antidiabetic regimens. In

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 3, 2024

addition, teneligliptin has shown beneficial effects across diverse patient populations without causing substantial weight gain or severe hypoglycemia [6,7].

Although evidence supporting the effectiveness of teneligliptin is increasing, data evaluating its role as part of a triple-drug combination with metformin and glimepiride in routine clinical practice remain relatively limited. Therefore, the present study was undertaken to assess the beneficial effect of triple-drug combination therapy comprising teneligliptin, metformin, and glimepiride in patients with Type 2 diabetes mellitus.

MATERIALS AND METHODS

A prospective observational study was conducted in the Department of General Medicine at a tertiary care teaching hospital over a period of 12 months. A total of 72 patients diagnosed with Type 2 diabetes mellitus and inadequately controlled on dual therapy with metformin and glimepiride were enrolled in the study.

Inclusion Criteria

- Patients aged 30–70 years.
- Confirmed diagnosis of Type 2 diabetes mellitus.
- HbA1c between 7.5% and 10.5%.
- Patients receiving stable doses of metformin and glimepiride for at least 3 months.
- Patients willing to provide written informed consent.

Exclusion Criteria

- Type 1 diabetes mellitus.
- Pregnant or lactating women.
- Severe hepatic impairment.
- Severe renal dysfunction (eGFR <30 mL/min/1.73 m^2).
- History of diabetic ketoacidosis.
- Acute cardiovascular events within the previous three months.
- Patients receiving insulin therapy.
- Known hypersensitivity to teneligliptin.

Study Procedure

Baseline demographic and clinical data were recorded. Teneligliptin 20 mg once daily was added to the existing metformin and glimepiride regimen. Patients were followed for 24 weeks.

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 3, 2024

The following parameters were assessed at baseline and at 24 weeks:

- Fasting blood glucose (FBG)
- Postprandial blood glucose (PPBG)
- Glycated hemoglobin (HbA1c)
- Body mass index (BMI)
- Adverse drug reactions

Outcome Measures

Primary Outcome:

Reduction in HbA1c after 24 weeks of therapy.

Secondary Outcomes:

Reduction in FBG and PPBG, change in BMI, and assessment of safety and tolerability.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Comparison between baseline and post-treatment values was performed using the paired Student's t-test. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 72 patients with inadequately controlled Type 2 diabetes mellitus completed the study. The mean age of participants was 54.7 ± 8.6 years. Males constituted 58.3% of the study population, while females accounted for 41.7%.

Table 1: Baseline Demographic Characteristics of the Study Population (n=72)

Characteristic		Number	Percentage
Age in Years	30-40	10	13.9%
	41-50	20	27.8%
	51-60	28	38.9%
	>60	14	19.4%
Gender	Male	42	58.3%
	Female	30	41.7%
Duration of	<5 years	18	25.0%

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 3, 2024

Diabetes	5–10 years	36	50.0%
	>10 years	18	25.0%

Most patients belonged to the 51–60-year age group. Half of the participants had a diabetes duration of 5–10 years, indicating a predominantly middle-aged population with established disease.

Table 2: Comparison of Glycemic Parameters before and After 24 Weeks of Therapy

Parameter	Baseline (Mean ± SD)	24 Weeks (Mean ± SD)	p-value
FBG (mg/dL)	168.3 ± 24.7	126.8 ± 18.9	<0.001
PPBG (mg/dL)	256.7 ± 35.8	182.5 ± 27.3	<0.001
HbA1c (%)	8.9 ± 0.8	7.2 ± 0.6	<0.001

A statistically significant reduction was observed in all glycemic parameters following addition of teneligliptin. HbA1c decreased by 1.7%, demonstrating substantial improvement in long-term glycemic control.

Table 3: Change in Body Mass Index Following Treatment

Parameter	Baseline	24 Weeks	p-value
BMI (kg/m²)	27.8 ± 3.2	27.1 ± 3.0	0.012

A modest but statistically significant reduction in BMI was observed over the study period, suggesting that the therapy did not contribute to weight gain.

Table 4: Achievement of Glycemic Targets after 24 Weeks

HbA1c Category	Number	Percentage
<7.0%	28	38.9%
7.0–7.5%	24	33.3%
>7.5%	20	27.8%

More than seventy percent of patients achieved an HbA1c value of 7.5% or less, indicating effective glycemic management with triple-drug therapy.

Table 5: Adverse Events Observed During the Study

Adverse Event	Number	Percentage
Mild Hypoglycemia	4	5.6%

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 3, 2024

Headache	3	4.2%
Gastric Discomfort	2	2.8%
Dizziness	2	2.8%
No Adverse Event	61	84.7%

The treatment was generally well tolerated. Most participants did not report any adverse event, and no serious drug-related complications were observed.

DISCUSSION

The present study evaluated the effectiveness of teneligliptin as an add-on to metformin and glimepiride in patients with inadequately controlled Type 2 diabetes mellitus. The findings demonstrated significant improvements in fasting blood glucose, postprandial blood glucose, and HbA1c levels after 24 weeks of therapy. These results suggest that triple-drug combination therapy can provide substantial glycemic benefits in patients who fail to achieve adequate control with conventional dual-drug treatment alone [8].

In the current study, mean HbA1c decreased from 8.9 ± 0.8% to 7.2 ± 0.6%, representing a clinically meaningful reduction of 1.7%. Similar findings have been reported in previous investigations evaluating the efficacy of teneligliptin as an add-on therapy. Gupta et al. demonstrated significant improvement in glycemic parameters when teneligliptin was used as an add-on third-line therapy in patients with inadequately controlled Type 2 diabetes mellitus [9].

A significant reduction in fasting and postprandial blood glucose levels was also observed in the present study. These findings are consistent with observations from real-world clinical studies conducted in Asian populations, where teneligliptin effectively improved both fasting and postprandial glycemic parameters while maintaining a favorable safety profile [10]. The glucose-dependent mechanism of DPP-4 inhibition contributes to improved insulin secretion and suppression of glucagon release, thereby facilitating better glycemic control.

The achievement of glycemic targets is an important objective in diabetes management. In the present study, 72.2% of patients achieved HbA1c values ≤7.5% after treatment. Comparable outcomes have been documented in observational studies from India, which demonstrated that teneligliptin serves as an effective third-line oral antidiabetic agent in patients inadequately controlled on existing therapies [11]. These findings support the utility of teneligliptin-based triple therapy in routine clinical practice.

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 3, 2024

Another noteworthy observation was the modest reduction in body mass index following treatment. Unlike several conventional antidiabetic agents that may contribute to weight gain, teneligliptin has generally been associated with weight neutrality. Previous reviews have highlighted the favorable pharmacological profile of teneligliptin, including sustained glycemic efficacy without significant adverse effects on body weight [12].

The safety analysis in the present study revealed a low incidence of adverse events. Mild hypoglycemia was observed in a small proportion of participants, while no severe hypoglycemic episodes or serious drug-related complications were reported. Similar safety outcomes have been reported in post-marketing surveillance studies and clinical trials, which demonstrated good tolerability of teneligliptin when administered either alone or in combination with other antidiabetic medications [10,13].

The study has certain limitations. The observational design and relatively short follow-up period may limit the generalizability of the findings. In addition, the absence of a control group prevented direct comparison with alternative treatment strategies. Nevertheless, the study reflects real-world clinical practice and provides useful evidence regarding the effectiveness of teneligliptin-based triple-drug therapy in patients with Type 2 diabetes mellitus.

CONCLUSION

The addition of teneligliptin to metformin and glimepiride therapy resulted in significant improvements in glycemic control, including reductions in fasting blood glucose, postprandial blood glucose, and HbA1c levels. The treatment was well tolerated, with only a small number of mild adverse events reported. A substantial proportion of patients achieved recommended glycemic targets following therapy. These findings indicate that teneligliptin-based triple-drug combination therapy represents an effective, safe, and practical treatment option for patients with inadequately controlled Type 2 diabetes mellitus and may contribute to improved long-term diabetes management outcomes.

REFERENCES

1. Sharma SK, Panneerselvam A, Singh KP, Parmar G, Gadge P, Swami OC. Teneligliptin in management of type 2 diabetes mellitus. Diabetes Metab Syndr Obes. 2016 Aug 16;9:251-60. doi: 10.2147/DMSO.S106133.

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 3, 2024

2. Hong S, Park CY, Han KA, Chung CH, Ku BJ, Jang HC, Ahn CW, Lee MK, Moon MK, Son HS, Lee CB, Cho YW, Park SW. Efficacy and safety of teneligliptin, a novel dipeptidyl peptidase-4 inhibitor, in Korean patients with type 2 diabetes mellitus: a 24-week multicentre, randomized, double-blind, placebo-controlled phase III trial. Diabetes Obes Metab. 2016 May;18(5):528-32. doi: 10.1111/dom.12631.
3. Agarwal P, Jindal C, Sapakal V. Efficacy and Safety of Teneligliptin in Indian Patients with Inadequately Controlled Type 2 Diabetes Mellitus: A Randomized, Double-blind Study. Indian J Endocrinol Metab. 2018 Jan-Feb;22(1):41-46. doi: 10.4103/ijem.IJEM_97_16.
4. Li X, Huang X, Bai C, Qin D, Cao S, Mei Q, Ye Y, Wu J. Efficacy and Safety of Teneligliptin in Patients With Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Front Pharmacol. 2018 May 4;9:449. doi: 10.3389/fphar.2018.00449.
5. Ceriello A, De Nigris V, Iijima H, Matsui T, Gouda M. The Unique Pharmacological and Pharmacokinetic Profile of Teneligliptin: Implications for Clinical Practice. Drugs. 2019 May;79(7):733-750. doi: 10.1007/s40265-019-01086-0.
6. Ghosh S, Trivedi S, Sanyal D, Modi KD, Kharb S. Teneligliptin real-world efficacy assessment of type 2 diabetes mellitus patients in India (TREAT-INDIA study). Diabetes Metab Syndr Obes. 2016 Nov 8;9:347-353. doi: 10.2147/DMSO.S121770.
7. Ghosh S, Tiwaskar M, Chawla R, Jaggi S, Asirvatham A, Panikar V. Teneligliptin Real-World Effectiveness Assessment in Patients with Type 2 Diabetes Mellitus in India: A Retrospective Analysis (TREAT-INDIA 2). Diabetes Ther. 2020 Oct;11(10):2257-2268. doi: 10.1007/s13300-020-00880-4.
8. 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 Jan 29;12(1):e6812. doi: 10.7759/cureus.6812.
9. Gupta CN, Raghavan V, Sen S, Kothari S. Role of teneligliptin in rural India as add-on third drug in patients with type 2 diabetes mellitus. Int J Adv Med. 2017;4(2):401-405. doi:10.18203/2349-3933.ijam20170966

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 3, 2024

10. Haneda M, Kadowaki T, Ito H, Sasaki K, Hiraide S, Ishii M, Matsukawa M, Ueno M. Safety and Efficacy of Teneligliptin in Patients with Type 2 Diabetes Mellitus and Impaired Renal Function: Interim Report from Post-marketing Surveillance. Diabetes Ther. 2018 Jun;9(3):1083-1097. doi: 10.1007/s13300-018-0416-2.
11. Kim Y, Kang ES, Jang HC, Kim DJ, Oh T, Kim ES, Kim NH, Choi KM, Kim SR, You J, Kim SJ, Lee MK. Teneligliptin versus sitagliptin in Korean patients with type 2 diabetes inadequately controlled with metformin and glimepiride: A randomized, double-blind, non-inferiority trial. Diabetes Obes Metab. 2019 Mar;21(3):631-639. doi: 10.1111/dom.13566.
12. Bryson A, Jennings PE, Deak L, Paveliu FS, Lawson M. The efficacy and safety of teneligliptin added to ongoing metformin monotherapy in patients with type 2 diabetes: a randomized study with open label extension. Expert Opin Pharmacother. 2016 Jul;17(10):1309-16. doi: 10.1080/14656566.2016.1190334.
13. Mohan V, Ramu M, Poongothai S, Kasthuri S. A ProspectIve, OpeN-Label, Randomized Study Comparing EffIcacy and Safety of Teneligliptin VErsus Sitagliptin in Indian Patients with Inadequately Controlled Type 2 Diabetes Mellitus: INSITES Study. J Assoc Physicians India. 2019 Oct;67(10):14-19.