International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 03 Issue 03 March 2023

Page No: 546-550

DOI: https://doi.org/10.47191/ijmscrs/v3-i3-40, Impact Factor: 6.597

Study to Determine the Safety and Efficacy of Teneligliptin (20 Mg) in Naive Type 2 Diabetes Mellitus

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ABSTRACT

Background: Teneligliptin is a novel, highly selective DPP-4 inhibitor with long half-life, approved in Japan (2012) and in Korea (2014) to treat patients of type 2 DM. It is characterized by a considerably rigid structure formed by five consecutive rings. Teneligliptin, 20mg/day as monotherapy and combination therapy in type 2 DM was shown to be effective in reducing HbA1c and fasting plasma glucose levels without any significant adverse events. Present study was conducted to determine the safety and efficacy of Teneligliptin (20 mg) in naive type 2 diabetes mellitus.

Materials and methods: The present study was a hospital based prospective study undertaken to study the safety and efficacy of teneligliptin (20 mg) in naïve type 2 diabetes mellitus. Newly diagnosed type 2 diabetes mellitus patients within age group 18-70 years were studied. All patients were assessed for Blood sugar levels (Fasting and Postprandial HbA1C, Serum urea, Serum Creatinine, Serum uric acid, Lipid profile and ECG.

Results: The mean age of total patients was 52.86 ±9.24 years. The mean HbA1c among patients with DM was 7.76 ±1.61. The mean serum urea was 29.12±6.58mg/dl while Serum creatinine was 1.08±0.18 mg/dl. The mean fasting Blood sugar of the patients before treatment was 123.55 ±10.72 and 103.12 ±8.63 mg/dl after treatment with statistical significant difference ($p<0.05$). The mean blood urea of the patients before treatment was 29.12 ±6.58 and 20.86 ±5.04 mg/dl after treatment with no statistical significant difference. ($p >0.05$) The mean QT interval of the patients before treatment was 0.37±0.03 and 0.38±0.03 seconds after treatment with statistical non-significant difference ($p <0.05$).

Conclusion: The present study concludes that, Teneligliptin, a novel DPP-4I, when prescribed as a monotherapy antidiabetic agent in a dose of 20 mg daily, significantly improved glycemic parameters. The results of this study suggest that teneligliptin can be considered to be an effective antidiabetic agent in the management of Indian patients with type naive 2 Diabetes Mellitus.

KEYWORDS: diabetes mellitus, diabetic HbA1c, teneligliptin, Blood sugar fasting

ARTICLE DETAILS

Published On:
28 March 2023

Available on:
https://ijmscr.org/

INTRODUCTION

Diabetes is a complex, chronic illness requiring continuous medical care with multifactorial risk-reduction strategies beyond glycemic control.[1] Depending on the etiology of diabetes, factors contributing to hyperglycemia comprise reduced insulin secretion, decreased glucose utilization and increased glucose production.[2] Globally, 425 million people are affected with diabetes and Type 2 diabetes (type 2 DM) is also increasingly seen in younger adults nowadays. Epidemic of diabetes and by the year 2040, incidence of diabetes mellitus will increase.[3] The treatment goal for diabetes is usually individualized based on patient preferences and disease factors.[4] With the use of anti-diabetic agents in current therapeutic options, only 37% of the patients achieved a glycosylated hemoglobin (HbA1c) ≤7.0%. Gliptins or dipeptidyl peptidase-4 (DPP-4) inhibitors are a relatively new class of orally administered glucose lowering agents for Type 2 DM. These drugs can augment the effect of incretin hormones, glucose dependent insulinotropic polypeptide and Glucagon like peptide-1. Compared to the other oral

hypoglycemic agents, gliptins possess several clinical advantages like a negligible risk of hypoglycemia and weight neutrality.[5] Teneligliptin is a novel, highly selective DPP-4 inhibitor with long half-life, approved in Japan (2012) and in Korea (2014) to treat patients of type 2 DM. It is characterized by a considerably rigid structure formed by five consecutive rings. [6,7] Teneligliptin, 20mg/day as monotherapy and combination therapy in type 2 DM was shown to be effective in reducing HbA1c and fasting plasma glucose levels without any significant adverse events.[8,9] However the efficacy and safety of teneligliptin demonstrated so far is based on researches done over a short time period. Teneligliptin is currently marketed in India with limited number of available clinical studies and data comparing the efficacy and safety of the various DPP-4 inhibitors are very few. Present study was conducted to determine the safety and efficacy of Teneligliptin (20 mg) in naïve type 2 diabetes mellitus.

MATERIALS AND METHODS

The present study was a hospital based prospective study undertaken to study the safety and efficacy of teneligliptin (20 mg) in naïve type 2 diabetes mellitus. The present study was conducted in Department of Medicine, S.N. Medical College, Agra from January 2019 to June 2020. The study population was patients with newly diagnosed type 2 diabetes mellitus attending Medicine and Diabetic OPD and admitted in hospital. Approval from Ethical committee was taken prior to study and informed consent was obtained from patients participating in the study.

Sample Size

- Total 100 patients attending OPD and admitted in hospital during study period considering the inclusion and exclusion criteria were included in the study.

Inclusion Criteria

- Newly diagnosed type 2 diabetes mellitus patients within age group 18-70 years, willing to take participation and giving consent for study.
- Criteria for diagnosis of Diabetes Mellitus : Symptoms of Diabetes Mellitus plus random blood glucose concentration >200 g/dl, Fasting plasma glucose > 126 mg/dl, Two-hour plasma glucose > 200 g/dl during oral glucose tolerance test, HbA1C>6.5. All newly diagnosed type 2 diabetic patients attending Medicine outdoor, diabetic clinic and patients admitted in Department of Medicine are included in the study.

Exclusion criteria

- Previously diagnosed diabetes mellitus
- Age group <18 years and >70 years.
- Patient taking any other oral anti-hyperglycemic agent
- Patient not willing to take part in study
- Pregnant female and lactating women.
- Patient having any complication of previously undiagnosed diabetes mellitus

Parameters for assessment

- Blood sugar levels (Fasting and Postprandial)
- HbA1C
- Serum urea
- Serum Creatinine and Serum uric acid
- Lipid profile
- ECG

Data collection

Informed consent was taken from the patients before enrolment in the study. A detailed medical history and clinical examination of the patient was done. After obtaining detailed medical history and clinical examination of the patient blood sample was taken for laboratory investigations. The investigations include blood sugar, serum urea, serum creatinine, serum uric acid. The serial ECG of the patient was done. BCollected samples were sent to the standard laboratory and tests were conducted under investigator supervision. The result of the test was entered to the proforma and computer for analysis

Data Entry, Management and Analysis

Data were double entered using Microsoft excel 2010, cleaned and analyzed using STATA version 11.Data were summarized in frequency tables, pie chart and histogram. Categorical variables were reported as proportion. Continuous data were described as means (standard deviation) or medians (interquartile range) depending on the distribution of data.

Statistical Methods

The observed clinical outcome was analyzed by Chi square test, paired t test and other tests. P value of less than 0.05 was taken as statistically significant.

RESULTS

The majority of patients were in age group 41-50 years (33%) followed by age group >60 years (29%). The mean age of total patients was 52.86 ±9.24 years. The mean age of males and females were 52.26 ±8.78 and 54.55 ±10.23 years respectively. Out of 100 patients 63% were males and 37% females. The male to female ratio was 1.70:1. 15 (15%) patients were having hypertension and 17 (17%) patients were having IHD. There were 23 (23%) patients who had history of dyslipidemia (multiple responses present). 21 (21%) patients had addiction of smoking/ tobacco chewing. The addiction of alcohol was among 14 (14%) patients while 64 (64%) patients had no addiction (multiple responses present)

Table 1. Distribution of Patients according to investigation findings

Investigations	Mean± SD
Hemoglobin (gm/dl)	12.59 ±1.08
Fasting Blood sugar (mg/dl)	103.55 ±10.72
Postprandial Blood Sugar (mg/dl)	163.56 ±16.99
HbA1c	7.76±1.61
Serum urea (mg/dl)	29.12 ±6.58
Serum creatinine (mg/dl)	1.08 ±0.18
Serum uric acid (mg/dl)	4.69 ± 1.41
HDL (mg/dl)	38.60 ±5.06
LDL (mg/dl)	99.92±12.72
VLDL (mg/dl)	15.55 ±5.81
Total cholesterol (mg/dl)	231.39 ±16.59
Triglycerides (mg/dl)	157.87 ±14.48

Table 1 shows distribution of patients according to investigation findings. The mean Hb level was 12.59±1.08 while mean FBS and mean PBS was 103.55±10.72 and 163.56±16.99 respectively. The mean HbA1c among patients with DM was 7.76 ±1.61. The mean serum urea was 29.12±6.58mg/dl while Serum Creatinine was 1.08±0.18 mg/dl. Mean HDL was 38.60±5.06 while mean LDL was 99.92±12.72. Total cholesterol level was 231.39±16.59 while triglycerides level was 157.87±14.48.

Table 2. Comparison of blood sugar levels before and after treatment

Investigations	Before Treatment	After Treatment	P value
Fasting Blood sugar (mg/dl)	123.55 ±10.72	103.12±8.63	0.003 (S)
Postprandial Blood Sugar (mg/dl)	163.56±16.99	128.48±11.31	0.02 (S)
HbA1c	7.76±1.61	6.03±1.05	0.001

The above table shows distribution of patients according to blood sugar levels before and after treatment. The mean fasting Blood sugar of the patients before treatment was 123.55 ±10.72 and 103.12 ±8.63 mg/dl after treatment with statistical significant difference ($p < 0.05$). Similarly, postprandial blood sugar levels and HbA1c shows statistical significant difference before and after treatment. ($P<0.05$)

Table 3. Comparison of BUN investigations before and after treatment

Investigations	Before Treatment	After Treatment	P value
Serum urea (mg/dl)	29.12 ±6.58	20.86 ±5.04	0.14
Serum Creatinine (mg/dl)	1.08 ±0.18	0.92 ±0.14	0.09
Serum uric acid (mg/dl)	3.69 ± 1.41	3.15 ± 1.23	0.13

The above table shows distribution of patients according to BUN before and after treatment. The mean blood urea of the patients before treatment was 29.12 ±6.58 and 20.86 ±5.04 mg/dl after treatment with no statistical significant difference ($p > 0.05$). It was observed that Serum creatinine decreased after treatment with no statistical significant difference before and after treatment. ($P>0.05$)

Table 4. Comparison of QT interval before and after treatment

QT interval	Before Treatment	After Treatment	P value
QT interval (seconds)	0.37±0.03	0.38 ±0.03	0.41 (NS)

The above table shows distribution of patients according to QT interval before and after treatment. The mean QT interval of the patients before treatment was 0.37±0.03 and 0.38 ±0.03 seconds after treatment with statistical non-significant difference. ($p < 0.05$)

DISCUSSION

The present prospective study was undertaken to study the safety and efficacy of teneligliptin in naïve type 2 diabetes mellitus. A total of 100 patients presenting to Medical College and Hospital during study period of January 2019 to June 2020 were included in the study. In study done by Takashi Kadowaki et al[10] on efficacy and safety of teneligliptin in patients of type 2 diabetes mellitus observed of 204 patients, 108 (52.9%) showed a response to teneligliptin 40 mg (change in HbA1c of (0.1% from week 28 to 52) and 96 patients (47.1%) did not respond (change in HbA1c of (0.1% from week 28 to week 52). Among the 108 patients who showed a response to teneligliptin 40 mg, 20.4% achieved HbA1c\7% at week 52. The mean (± SD) change in HbA1c during weeks 28–52 in the patients responding to teneligliptin 40 mg was 0.50 ± 0.44%. Sujoy Ghosh et al [11] assessed the effectiveness of teneligliptin in improving glycemic control amongst Indian patients with T_2DM observed mean HbA1c dropped from 8.66 ± 1.15% at baseline to 7.67 ± 1.28% at 12 weeks (71 ± 12.6 to 60 ± 14 mmol/mol), with a difference of - 0.99% (95% confidence interval [CI] 0.96–1.02) or - 10.8 (95% CI 10.5–11.1) mmol/mol (p\0.0001). The mean reductions in FPG and PPG were 43.12mg/dL (2.39 mmol/L) and 87.73 mg/dL (4.87 mmol/L) (both p\0.0001) respectively.

The mean blood urea of the patients before treatment was 29.12 ±6.58 and 20.86 ±5.04 mg/dl after treatment with no statistical significant difference. (p>0.05) It was observed that Serum creatinine decreased after treatment with no statistical significant difference before and after treatment (P>0.05). Mathew George et al[12] in a study on safety and effectiveness of teneligliptin in type 2 diabetic patients observed decrease in serum creatinine with no statistical significant difference. (p >0.05)

In the present study, the mean QT interval of the patients before treatment was 0.37±0.03 and 0.38±0.03 seconds after treatment with no statistical significant difference. (p >0.05) Kishimoto M. et al [13] observed no QT prolongations were detected with 40 mg daily of teneligliptin, which is the maximal dose in usual clinical practice. Anyway, a mild QTc transient prolongation was documented while using supraclinical dosages. Therefore, caution is needed if the drug is used for a long period or in co administration with medications known to cause QT prolongation on their own. On the other hand, teneligliptin treatment was associated with improvements in left ventricular function— particularly diastolic—and endothelial functions, as well as with an increase in serum adiponectin levels. [14]

The limitations of this study are that the number of the subjects is small and the study duration is short. However one can assume that the observed changes were caused exclusively by teneligliptin based on the design of the study (monotherapy with drug naive patients). Further randomized, double-blind, placebo-controlled longer period study with increased number of subjects will be necessary to strengthen the finding in this study.

CONCLUSION

The present study concludes that, Teneligliptin, a novel DPP-4I, when prescribed as a monotherapy antidiabetic agent in a dose of 20 mg daily, significantly improved glycemic parameters. The results of this study suggest that teneligliptin can be considered to be an effective antidiabetic agent in the management of Indian patients with type naive 2 Diabetes Mellitus.

CONFLICT OF INTEREST

None to declare.

SOURCE OF FUNDING

Nil

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