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Original Article

Evaluation of Safety and Effectiveness of Teneligliptin when Shifted from other Gliptins Uncontrolled with Type 2 Diabetes Mellitus

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Abstract

Aim: This study aims to evaluate the effectiveness and safety of teneligliptin when switched from other gliptins in patients not controlled on oral antidiabetic drugs in Type 2 diabetes mellitus (T2DM).

Methodology: Data of T2DM patients who were switched from other gliptins to teneligliptin uncontrolled by dual or triple drug therapy. Data of at least 3 months were collected from hospital records and analyzed. Efficacy was evaluated by the changes in fasting blood sugar (FBS), postprandial blood sugar (PPBS), and hemoglobin A1c (HbA1c) from the baseline.

Results: A total of 97 patients' data were collected and were analyzed. The mean age of the patients was 59.9 years and mean duration of diabetes was 16 years. Hypertension (61.9%) was the common comorbid condition with diabetes. Sitagliptin was most prescribed dipeptidyl peptidase-4 (DPP-4) inhibitors with 65 (67%) patients with a mean dose of 88.5 mg, followed by vildagliptin with 10 (10.3%) patients was prescribed with a mean dose of 95 mg. Metformin and glimepiride were the most common combination used with these DPP-4 inhibitors 91 (93.8%) patients and 69 patients (71.1%) were prescribed, respectively. There was a significant reduction in FBS, PPBS, and HbA1c from the baseline with a difference of 45 mg/dL, 102 mg/dL, and 1.6%, respectively, after switching to teneligliptin from other gliptins. Teneligliptin was well tolerated and no serious adverse events were reported.

Conclusion: Teneligliptin was effective in significantly reducing FBS, PPBS, and HbA1c when switching from other gliptins in T2DM patients not controlled with other antidiabetic agents. The drug was well tolerated and no serious adverse events were reported.

Key words: Diabetes mellitus, Gliptins, Glycated hemoglobin, Teneligliptin

INTRODUCTION

Diabetes mellitus is one of the leading global health issues of the 21st century. There has been a drastic increase in the global prevalence of diabetes mellitus in the past few decades reaching worldwide epidemic. The latest diabetes atlas of the International Diabetes Federation (IDF) reports over 415 million individuals with Type 2 diabetes mellitus (T2DM) globally.[1,2] India ranks second in the world after China for the highest number of diabetes cases. The IDF reported 69.2 million diabetic individuals in India and has anticipated this number to reach 123.5 million by 2040.[1]

Adequate glycemic control in T2DM is associated with the reduction of mortality and morbidity.[3] Most therapeutic agents available for the treatment of T2DM reduce the macrovascular complications; however, these may lead to progressive beta-cell damage and deterioration of health due to T2DM.[4] In patients with T2DM, beta-cell function is reduced to 60% as compared with non-diabetic patients. Beta-cell damage with antidiabetic medications has prompted researchers to hypothesize that long-term use of these medications may be harmful to the remaining beta-cells.[5] While some drugs such as sulfonylureas are associated with progressive beta-cell loss,[6] gliptins

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(also known as dipeptidyl peptidase-4 [DPP-4] inhibitors) improve insulin secretion from the beta-cells of the pancreas in response to increased blood glucose levels. The insulin secretion is stimulated by secretion of higher levels of glucagon-like peptide-1 and glucose-dependent insulinotropic peptide that are enzymes released from the intestine and are responsible for regulation of blood glucose levels.[7] In addition, the use of gliptins is associated with fewer hypoglycemic events.[8]

DPP-4 inhibitors offer effective, but expensive choice especially for a country like India where the financial burden of a disease and its treatment is born by patient's themselves. DPP-4 inhibitors are being used for nearly a decade for the management of T2DM.[3] In India, there are six types of DPP-4 inhibitors, namely vildagliptin, sitagliptin, linagliptin, saxagliptin, gemigliptin, and teneligliptin, which are being used for the management of T2DM.[7] Teneligliptin provides $1/4^{th}$–$1/5^{th}$ low-cost treatment in comparison to another agent of the same class. Teneligliptin is a third-generation gliptin, which offers a pharmacodynamic and pharmacokinetic advantage.[7] Due to its effects on vascular function, teneligliptin shows benefits in improvement of endothelial function, left the ventricular function, lipid levels, and least chances of hypoglycemia and neutral effect to body weight.[7]

This study was designed with an aim to evaluate the effectiveness and safety of teneligliptin when switched from other gliptins in patients not controlled on oral antidiabetic drugs in T2DM.

METHODOLOGY

The present study was an observational retrospective study carried out in patients who were taking gliptins (vildagliptin, sitagliptin, linagliptin, and saxagliptin) along with the conventional antihyperglycemic agents such as metformin, sulfonylurea, pioglitazone, and voglibose and whose level blood sugar was not controlled. These patients were then started on teneligliptin therapy with conventional dose of 20 mg once daily (OD). Data of at least 3 months were collected from hospital records and analyzed. Efficacy was evaluated by the changes in fasting blood sugar (FBS), postprandial blood sugar (PPBS), and hemoglobin A1c (HbA1c) from the baseline. The subjects enrolled for the study were properly instructed not to change or add any new drug and not to take any Ayurvedic, Homeopathic, or Unani medicines during this phase. Patients were also advised not to change lifestyle or dietary pattern. All statistical analyses were done using the SPSS version 20 (SPSS Inc., Chicago, USA). Independent Student's *t*-test was applied to compare the averages. Average standard deviation was calculated for quantitative data. All *P* values were two-tailed and values ($P < 0.05$) were considered statistically significant.

RESULTS

A total of 97 patients' data were collected and were analyzed. The average age of the patients was 59.9 ± 16 years with average duration of diabetes as 16 years. Almost, similar numbers of males and females were enrolled in the study; the male-to-female ratio in our study was 0.9:1. Hypertension (61.9%) was the common comorbid condition followed by dyslipidemia (17.5%). Sitagliptin was most commonly prescribed DPP-4 inhibitors, 65 (67%) patients, with an average dose of 88.5 mg followed by linagliptin in 22 (22.7%), with average dose 5 mg and vildagliptin in 10 (10.3%) patients, with average dose of 95 mg. Metformin and glimepiride were the most common coprescribed medication along with these DPP-4 inhibitors in 91 (93.8%) and 69 (71.1%) patients, respectively. There was significant reduction in FBS ($P < 0.0001$), PPG ($P < 0.0001$), and HbA1c ($P < 0.0001$) from the baseline with a differences of 45 mg/dL, 102 mg/dL, and 1.6%, respectively, at the end of 3 months and 75 mg/dL, 142.9 mg/dL, and 2.7%, respectively, at the end of 6 months after switching to teneligliptin from other gliptins. No side effect or SAEs were reported with teneligliptin during the study period and were well tolerated [Table 1-6].

DISCUSSION

The present study evaluated the effect of teneligliptin treatment in patients with uncontrolled hyperglycemia who were treated with gliptins such as vildagliptin, sitagliptin, linagliptin, and saxagliptin with other oral hypoglycemic agents. The baseline characteristics of the study participants showed average age as 59.9 ± 16 years with almost similar numbers of males and females. The average duration of diabetes was 16 years with hypertension and dyslipidemia as the common comorbid condition along with diabetes.

Significant reduction in FBS, PPG, and HbA1c from the baseline was seen at the end of 3 months and 6 months after switching to teneligliptin from other gliptins. Agrawal *et al.*[9] in his study evaluated patients who shifted to teneligliptin based on economical aspect of gliptins and reported no significant difference in the levels of blood sugar or glycosylated HbA1c before and after the treatment of teneligliptin. The average HbA1c before the start of teneligliptin therapy was 6.928 ± 0.02923 (%) and 6.878 ± 0.03539 (%) after teneligliptin therapy for 3 months, with no statistical difference ($P = 0.22$). Otsuki *et al.*[10] evaluated

Table 1: Gender-wise distribution

Gender	Number of patients (%)
Male	48 (49.5)
Female	49 (50.5)

Table 2: Gliptins prescription among study participants

Previous gliptin	Number of patients (%)	Mean dose (mg)
Sitagliptin	65 (67.0)	88.5
Vildagliptin	10 (10.3)	95
Linagliptin	22 (22.7)	5

Table 3: Antidiabetic medication

Concurrent antidiabetic medication	Number of patients (%)	Mean dose (mg)
Metformin	91 (93.8)	1368.1
Glimepiride	69 (71.1)	3.5
Gliclazide	4 (4.1)	90
Glipizide	2 (2.1)	10
Pioglitazone	12 (12.4)	14.4
Canagliflozin	1 (1.0)	10
Dapagliflozin	8 (8.2)	8.8
Voglibose	12 (12.4)	0.5

Table 4: Comorbid condition

Comorbidities	Number of patients (%)
Hypertension	60 (61.9)
Dyslipidemia	17 (17.5)
Stroke/TIA	11 (11.3)
CAD/ACS/IHD	27 (27.8)
CKD	4 (4.1)
Chronic diarrhea	1 (1.0)
COPD	3 (3.1)
Massive fluid overload	1 (1.0)
Morbid obesity	1 (1.0)
PSVT	1 (1.0)
Recurrent UTI	1 (1.0)
Severe anemia	1 (1.0)

COPD: Chronic obstructive pulmonary disease, UTI: Urinary tract infections, CAD: Coronary artery disease, ACS: Acute coronary syndrome, TIA: Transient ischemic attack, IHD: Ischemic heart disease

Table 5: Change in glycemic parameters at the end of the 3rd week

	FBS (*n*=59)	PPBS (*n*=96)	HbA1c (*n*=95)
	Mean±SD	Mean±SD	Mean±SD
Baseline visit	177.1±51.3	306.3±77.1	9.4±1.6
Follow-up visit (3 months)	131.1±22.9	203.6±43.3	7.8±1.1
Changes from baseline	46.0±28.4	102.7±33.8	1.6±0.5
P value	<0.0001	<0.0001	<0.0001

FBS: Fasting blood sugar, PPBS: Postprandial blood sugar, HbA1c: Hemoglobin A1c, SD: Standard deviation

Table 6: Change in glycemic parameters at the end of the 6th week

	FBS (*n*=41)	PPBS (*n*=89)	HbA1c (*n*=87)
	Mean±SD	Mean±SD	Mean±SD
Baseline visit	185.6±51.5	305.5±76.1	9.4±1.6
Follow-up visit (6 months)	110.9±18.1	162.6±26.6	6.9±0.7
Changes from baseline	74.7±33.4	142.9±49.5	2.5±0.9
P value	<0.0001	<0.0001	<0.0001

FBS: Fasting blood sugar, PPBS: Postprandial blood sugar, HbA1c: Hemoglobin A1c (HbA1c), SD: Standard deviation

the efficacy and safety in 45 patients, which included 16 patients enrolled in the teneligliptin group (seven therapy-naïve and nine switched from other medications) and 29 in the control group. 14 patients in the teneligliptin group (seven each as therapy-naïve and switched from other medications) and 29 in the control group completed 28-week study period. In patients who were switched to teneligliptin, reduction in HbA1C was noted in patients who were switched to teneligliptin from voglibose 0.2 mg 3 times in a day (TID) or vildagliptin 50 mg once per day (QD). The study also reported that teneligliptin 20 mg daily was more potent than voglibose 0.2 mg TID or vildagliptin 50 mg QD. Agarwal *et al.*[7] evaluated efficacy teneligliptin in inadequate glycemic control (glycosylated HbA1c: >7.0–≤8.5%). Treatment with teneligliptin led to statistically significant and clinically meaningful reductions in HbA1c levels ($P = 0.0002$) and PPBS ($P = 0.01$).

Agrawal *et al.*[9] in his study also reported that teneligliptin provides more economic choice of treatment than other gliptins, the average cost per day for DPP-4 inhibitors before teneligliptin was INR 47.75, whereas it was reduced to INR 9/day after switching to teneligliptin. Thus, the average price was reduced by INR 38.75 (39) for DPP4 inhibitors. There is a substantial economic impact of diabetes on individuals, society, health-care system, employer, and even the country in terms of loss of productivity; there is a strong and direct economic impact of T2DM on the lives of people in lower-income settings. In developing countries, where health-care expenditure is many times out of pocket, an economic impact of T2DM is huge and may affect the long-term outcome of T2DM.

Teneligliptin was also safe and well tolerated in our study with no SAE or hypoglycemia reported, which was similar to other reported studies.[9,10]

CONCLUSION

Teneligliptin was effective in significantly reducing FBS, PPBS, and HbA1c when switched from other gliptins in T2DM patients inadequately controlled with other antidiabetic agents. Furthermore, teneligliptin was well

tolerated with no serious adverse events or hypoglycemia reported.

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