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Original Research Article

Patients characteristics associated with better glycemic response to teneligliptin and metformin therapy in type 2 diabetes: a retrospective study

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ABSTRACT

Background: Teneligliptin was recently approved for type 2 diabetes (T2D) management in India and is used as monotherapy or in combination with different antidiabetic drugs. The aim of this study was to identify patients' characteristics associated with better glycemic response to teneligliptin and metformin.
Methods: A retrospective analysis of data was performed in patients of T2D with HbA1c above 7% who were treated with teneligliptin 20 mg/d as add on to metformin (500-100 mg/d) and whose follow-up data at 12-weeks was available. Fasting blood sugar (FBS) and post-prandial blood sugar (PPBS) changes were analysed.
Results: Among 66 patients included in analysis, mean age was 61.0±9.8 years and 53% were females. Median duration of diabetes was 2 years. At 12-weeks, a significant reduction PPBS was observed (mean change: -14.3 mg/dL, p=0.009) but not in FBS (mean change: -2.4 mg/dL, p=0.353). Among different patients' characteristics, age ≤60 years (p=0.006), duration of ≤1 year (p=0.023), body-mass index ≥25 kg/m2 (p=0.009), presence of dyslipidemia (p=0.05) and absence of complications (p=0.012) were associated with significant reduction in PPBS but not in FBS.
Conclusions: A younger, newly-diagnosed, obese T2D patients with dyslipidemia without any complications of diabetes can derive better therapeutic effectiveness from teneligliptin added to metformin. These findings need to be confirmed in large, prospective, long duration study.

Keywords: DPP4 inhibitors, FBS, India, PPBS, Teneligliptin; Type 2 diabetes

INTRODUCTION

Type 2 diabetes (T2D) is the rapidly growing epidemic in India. Epidemiological estimates suggest that currently 69.2 million people have diabetes, 36.5 million have impaired glucose tolerance (IGT), and 3.6 million are probably undiagnosed with T2D.[1] This colossal prevalence of diabetes stresses on appropriate management of T2D. Uncontrolled diabetes due to undertreatment or non-adherence to medication leads to serious complications and adverse clinical outcomes.[2] Amidst availability of multiple treatments, glycemia control to target levels is seen in 50% of the patients.[3] Targeting disease pathophysiology is essential for glycemic control in T2D. Dipeptidyl peptidase 4 inhibitors (DPP4i) are a new class of drugs which inhibit DPP4 enzyme leading to increased levels of glucagon-like peptide-1 (GLP-1), enhanced action of insulin and reduced release of glucagon. Rise in new beta-cells and inhibition of their apoptosis is seen with DPP4i which can potentially improve the disease pathogenesis.[4] The American Diabetes Association (ADA) guidelines

recommend DPP4i as second-line therapy after metformin.[5] Therefore, DPP4i can be the choice of drugs in every T2D patient.

Teneligliptin, a DPP4i approved recently (2015) in India is being used clinically either as monotherapy or as add on to metformin.[6] Teneligliptin as a monotherapy is effective in reducing glycemia without hypoglycemia and weight gain and is also efficacious and safe as add-on to metformin, glimepiride, pioglitazone and insulin.[7-13] However, it remains unclear as in what patient population teneligliptin offer best efficacy. T2D in Indians has a typical phenotype characterized by higher level of insulin resistance, more abdominal fat, lower levels of adiponectin and characteristic dyslipidemia.[14] Therefore, it is essential to look for patient characteristics in which teneligliptin can provide optimal efficacy in Indian with T2D. With this objective, we performed a retrospective study.

METHODS

This retrospective, observational study was conducted at a private, diabetes clinic in Mumbai, Maharashtra. Database was searched to identify patients who were first initiated with teneligliptin as add on to metformin treatment. Patients treated in eight months period between October 2016 to May 2017 were identified for inclusion in the study. Inclusion criteria was patients of T2D prescribed with teneligliptin (20 mg/d) add-on to metformin (500 – 1000 mg/d) who had HbA1c above 7% and the follow up data at 12 weeks on clinical and laboratory parameters was available. Patients receiving any other additional antidiabetic drug including insulin were excluded. Fasting blood sugar (FBS) and post-prandial blood sugar (PPBS) changes were assessed from baseline to 12 weeks which was considered as primary outcome measure and changes in body weight, body mass index (BMI), systolic blood pressure (SBP), and diastolic BP (DBP) were considered as secondary outcome measures.

Patients characteristics to determine the better glycemic response with use of teneligliptin and metformin were assessed. These were age of the patients (≤60 years – young/middle age and >60 years - elderly), gender (male and female), duration of diabetes (≤1 year – newly diagnosed and >1 year – known diabetes), BMI (<25 kg/m2 and ≥25 kg/m2), dyslipidemia (presence or absence) and presence or absence of complications of diabetes. Based on these characteristics, we assessed changes in FBS and PPBS from baseline to 12 weeks.

Statistical analysis

Data was entered in Microsoft excel spreadsheet and was analyzed using SPSS software version.[15] Categorical data was presented as frequency and percentages whereas continuous data as mean and standard deviation (SD). Changes in primary and secondary outcome measure from baseline to 12 weeks were assessed using paired t-test and presented as mean change and 95% confidence interval (CI). P-value less than 0.05 was considered significant for all the comparisons.

RESULTS

In this study, we included 66 patients who were treated with teneligliptin and metformin. Table 1 demonstrates the baseline characteristics of study participants. Mean age was 61 years with 43.9% and 56.1% being aged ≤60 and >60 years respectively. 53% patients were females. Mean BMI was 29.1±5.5 kg/m2. Among co-morbidities, dyslipidemia (59.1%) and hypertension (48.5%) were common.

Table 1: Baseline characteristics of study population.

Characteristics	Observation (n=66)
Age (years)	
Mean±SD	61.0±9.8
Age groups	
≤60	29 (43.9)
>60	37 (56.1)
Sex (%)	
Male	31 (47.0)
Female	35 (53.0)
Median duration of diabetes (IQR25-75, years)	2 (1.0-7.5)
Anthropometry	
Mean Weight (Kg)	72.5±13.6
Mean BMI (Kg/m^2)	29.1±5.5
Comorbidities and complications (%)	
Dyslipidemia	39 (59.1)
Hypertension	32 (48.5)
Peripheral neuropathy	7 (10.6)
Ischemic heart disease	7 (10.6)
Nephropathy	4 (6.1)
Retinopathy	2 (3.0)
Blood pressure (mmHg)	
Systolic	138.2±12.5
Diastolic	78.0±7.2
Laboratory parameters	
Fasting blood sugar (mg/dL)	107.3±18.9
Post-prandial blood sugar (mg/dL)	149.4±40.9
HbA1c (%)	7.6±0.7
Serum creatinine (mg/dL)	1.0±0.2
eGFR (mL/min/1.73m^2)	79.2±24.9
Metformin dose (mg/day)	
500	34 (51.5)
1000	32 (48.5)

BMI: Body mass index, IQR: inter-quartile range, eGFR: estimated glomerular filtration rate

Among different complications, peripheral neuropathy and ischemic heart disease (IHD) were noted in 10.6% patients each. Mean SBP and DBP were 138.2±12.5 and

78.0±7.2 mmHg respectively. Though mean HbA1c at baseline was 7.6±0.7%, mean levels of fasting and post-prandial blood sugar were 107.3±18.9 and 149.4±40.9 mg/dL respectively. Mean estimated glomerular filtration rate was 79.2±24.9 mL/min/1.73m2. Metformin dose of 500 and 1000 mg was prescribed in 51.5% and 48.5% patients respectively.

Table 2: Changes in primary and secondary outcome measures from baseline to 12 weeks

Parameter	Baseline	12 weeks	Mean change (95% CI)	P value
Primary outcome measures				
FBS (mg/dL)	107.3±18.9	104.9±15.6	-2.4 (2.64, -7.31)	0.353
PPBS (mg/dL)	149.4±40.9	135.1±26.5	-14.3 (-3.76, -24.74)	0.009
Secondary outcome measures				
Weight (Kg)	72.5±13.6	71.5±13.7	-1.0 (-0.46, -1.41)	<0.001
BMI (kg/m^2)	29.1±5.5	28.7±5.7	-0.4 (-0.10, 0.70)	0.009
SBP (mmHg)	138.2±12.5	134.5±12.9	-3.7 (-0.66, -6.79)	0.018
DBP (mmHg)	78.0±7.2	74.7±6.24	-3.3 (-1.60, -4.94)	<0.001

FBS: Fasting blood sugar, PPBS: post-prandial blood sugar, BMI: Body mass index, SBP: systolic blood pressure, DBP: Diastolic blood pressure, CI: confidence interval

Table 3: Comparative effect on blood sugar levels according different groups.

Parameter	n	FBS (mg/dL)		P value	PPBS (mg/dL)		P value
		Baseline	12 weeks		Baseline	12 weeks	
Age (years)							
≤60	29	112.2±15.9	105.8±15.2	0.054	163.9±44.2	137.2±24.8	0.006
>60	37	103.4±20.3	104.3±16.2	0.813	137.9±34.6	133.6±28.1	0.457
Gender (%)							
Male	31	108.9±20.9	103.4±14.2	0.133	155.1±51.0	136.6±27.1	0.053
Female	35	105.9±17.1	106.4±17.0	0.889	144.6±30.0	134.0±26.4	0.079
T2D duration (years)							
≤1	27	113.4±15.0	107.0±14.5	0.072	157.4±42.1	137.1±20.0	0.023
>1	39	103.0±20.3	103.5±16.4	0.895	143.8±39.7	135.0±30.0	0.156
BMI (Kg/m^2)							
<25	13	102.4±24.3	102.3±14.2	0.991	138.9±42.2	131.4±29.9	0.460
≥25	53	108.9±17.2	106.2±15.0	0.308	153.2±39.5	136.6±25.7	0.009
Dyslipidemia (%)							
Present	39	103.5±19.3	101.5±15.6	0.542	145.7±41.2	132.5±28.1	0.05
Absent	27	112.7±17.2	109.9±16.1	0.481	155.4±40.8	139.5±23.8	0.086
Complications (%)							
Present	16	100.9±22.3	98.8±17.2	0.724	137.0±39.5	131.8±35.9	0.450
Absent	50	109.3±17.4	106.9±14.8	0.386	153.7±41.0	136.3±22.9	0.012

FBS: Fasting blood sugar, PPBS: post-prandial blood sugar

Table 2 depicts the changes in different parameters from baseline to 12 weeks in study population. There was significant reduction in weight (Δ: -1.0, 95% CI -0.46, -1.41; p<0.001), BMI (Δ: -0.40, 95% CI -0.10, 0.70; p=0.009), SBP (Δ: -3.7, 95% CI -0.66, -6.79; p=0.018), DBP (Δ: -3.3 95% CI -1.60, -4.94; p<0.001) and post-prandial blood sugar (Δ: -14.25, 95% CI -3.76, -24.74; p=0.009). Fasting blood sugar did not change significantly (p=0.353). We assessed changes in FBS and PPBS based on different patient characteristics which are presented in Table 3. As observed with overall population, FBS did not change significantly in any of the patients' characteristics. However, reduction in FBS from baseline to 12 weeks was near significant level in patients who had diabetes duration of less than one year (113.4±15.0 to 107.0±14.5 mg/dL, p=0.072). Significant reduction in PPBS was noted in patients aged below 60 years (163.9±44.2 to 137.2±24.8 mg/dL, p=0.006), those with duration of diabetes less than 1 year (157.4±42.1 to 137.1±20.0 mg/dL, p=0.023), being overweight/obese (153.2±39.5 to 136.6±25.7 mg/dL, p=0.009), having dyslipidemia (145.7±41.2 to 132.5±28.1 mg/dL, p=0.05) and in those with absence of any diabetic complications (153.7±41.0 to 136.3±22.9 mg/dL, p=0.012). PPBS reduction was near significant in males (p=0.053).

DISCUSSION

Teneligliptin is a novel and potent DPP4 inhibitor approved for T2D management.[15] Studies evaluating teneligliptin have shown efficacy either monotherapy or in combination with other antidiabetics drugs. Additionally, teneligliptin has been shown to improve endothelial function and lower the oxidative stress.[16] However, patient characteristics that can determine better efficacy of teneligliptin remain unclear. In this study, we observed no significant reduction in FBS (p=0.353). This contrasts to finding of Kim et al who reported significant reduction of HbA1c and FBS as early as 4 weeks when teneligliptin was added to metformin.[10] Non-significant reduction in FBS in our study was because of lower mean (107.3±18.9 mg/dL) at the baseline. Kim et al study had mean FBS level of 150.3±27.6 mg/dL whereas HbA1c values were comparable. 10 Interestingly, there was significant reduction in PPBS (-14.3 mg/dL, p=0.009) in our study. Not many studies have reported PPBS reduction with teneligliptin. In a study from Kadowaki and Kondo, PPBS reduction was −43.1 mg/dL after 12 weeks of treatment with teneligliptin added to glimepiride therapy.[11] However, we did not assess teneligliptin added to glimepiride therapy but to metformin therapy which explains the difference in magnitude of PPBS reduction in two studies. Significant reduction in weight, BMI, SBP and DBP observed in our study could be due to improved glycemic control after addition of teneligliptin.

Among different patient characteristics, FBS reduction was non-significantly different. PPBS reduction was significant in patients aged below 60 years, those who had duration of diabetes <1 year, with BMI above 25 Kg/m2, in presence of dyslipidemia and absence of diabetes related complications. Also, PPBS reduction of near significant level in males (p=0.053) than females (p=0.079). These findings suggest teneligliptin should be considered in patients with obese, newly-diagnosed, young patient with T2D who have dyslipidemia and do not have any complications. In patients with these characteristics, teneligliptin probably offers best efficacy advantage. However, findings should not detriment using teneligliptin in other patients. The findings from Kim et al showing better glucose-lowering efficacy of DPP4-inhibitors in Asians than non-Asian ethnicity strongly support our observation.[17] In their metanalysis, Kim et al observed that BMI differences in ethnic groups may contribute to glucose lowering efficacy of DPP4-inhibitors.[17] This purports our study findings.

The strength of our study is that it is probably first observation which reported patients factors that could help derive maximal therapeutic efficacy with teneligliptin when used as add-on to metformin. There are certainly major limitations in our study. Retrospective design, small sample, and relatively short duration of follow-up of patients assessed have potential to affect study results. We did not assess HbA1c reduction from baseline to 12 weeks as data was not recorded for many patients. This could be due to our practice of repeating HbA1c test usually after six-month duration. Mean levels of FBS and PPBS at baseline were lower compared to previous studies which also could affect the results.

CONCLUSION

Thus, teneligliptin add-on to metformin is associated with improvement of glycemia. Young patients aged below 60 years who are obese and have dyslipidemia without any complications of diabetes probably can derive optimal therapeutic efficacy with teneligliptin-metformin combination. This finding need confirmation in a large, prospective, longer duration study.

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REFERENCES

1. International Diabetes Federation Diabetes Atlas. 7th Edition 2015. 144 p. Available from http://www.diabetesatlas.org/resources/2015-atlas.html Accessed 12 Jan 2018.
2. Simpson SH, Lin M, Eurich DT. Medication Adherence Affects Risk of New Diabetes Complications: A Cohort Study. Ann Pharmacother 2016;50:741-46.
3. Giugliano D, Maiorino MI, Bellastella G, Esposito K. Glycemic control in type 2 diabetes: from medication nonadherence to residual vascular risk. Endocrine. 2018;10:1-5.
4. Langley AK, Suffoletta TJ, Jennings HR. Dipeptidyl peptidase IV inhibitors and the incretin system in type 2 diabetes mellitus. Pharmacotherapy: J Human Pharmacol Drug Ther. 2007;1:27(8):1163-80..
5. American Diabetes Association. Standards of Medical Care in Diabetes. Diabetes Care. 2017; 40:S64-S74.
6. List of approved drug from 01-01-2015 to 31-01-2015. Last updated on 24/01/2018. Available from http://www.cdsco.nic.in/forms/list.aspx?lid=2034&Id=11&printPrevi Accessed 27 January 2018.
7. Eto T, Inoue S, Kadowaki T. Effects of once-daily teneligliptin on 24-h blood glucose control and safety in Japanese patients with type 2 diabetes mellitus: A 4-week, randomized, double-blind, placebo-controlled trial. Diabetes Obes. Metab. 2012;14:1040–6.
8. Kadowaki T, Kondo K. Efficacy, safety and dose-response relationship of teneligliptin, a dipeptidyl peptidase-4 inhibitor, in Japanese patients with type 2 diabetes mellitus. Diabetes Obes. Metab 2013;15:810–8.
9. Kutoh E, Hirate M, Ikeno Y. Teneligliptin As an Initial Therapy for Newly Diagnosed, Drug Naive Subjects With Type 2 Diabetes. J Clin Med Res 2014;6:287–94.

10. Kim MK, Rhee E-J, Han KA, Woo AC, Lee M-K, Ku BJ, et al. Efficacy and safety of teneligliptin , a dipeptidyl peptidase-4 inhibitor , combined with metformin in Korean patients with type 2 diabetes mellitus : a 16-week , randomized , double-blind , placebo-controlled phase III trial. Diabetes, Obes. Metab 2015;17:309-12.
11. Kadowaki T, Kondo K. Efficacy and safety of teneligliptin added to glimepiride in Japanese patients with type 2 diabetes mellitus: a randomized, double-blind, placebo-controlled study with an open-label, long-term extension. Diabetes, Obes. Metab 2010;21(2):262–8.
12. Kadowaki T, Kondo K. Efficacy and safety of teneligliptin in combination with pioglitazone in Japanese patients with type 2 diabetes mellitus. J Diabetes Investig 2013;4:576–84.
13. Tanaka S, Suzuki K, Aoki C, Niitani M, Kato K, Tomotsune T, et al. Add-on treatment with teneligliptin ameliorates glucose fluctuations and improves glycemic control index in Japanese patients with type 2 diabetes on insulin therapy. Diabetes Technol Ther 2014;16:1–6.
14. Unnikrishnan R, Anjana RM, Mohan V. Diabetes in South Asians: Is the phenotype different? Diabetes 2014;63:53-5.
15. Goda M, Kadowaki T. Teneligliptin for the treatment of type 2 diabetes. Drugs of Today 2013;49:615-29.
16. Sagara M, Suzuki K, Aoki C, Tanaka S, Taguchi I, Inoue T, et al. Impact of teneligliptin on oxidative stress and endothelial function in type 2 diabetes patients with chronic kidney disease: a case-control study. Cardiovasc Diabetol 2016;15:76.
17. Kim YG, Hahn S, Oh TJ, Kwak SH, Park KS, Cho YM. Differences in the glucose-lowering efficacy of dipeptidyl peptidase-4 inhibitors between Asians and non-Asians: A systematic review and meta-analysis. Diabetologia 2013;56:696-708.

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