

# Teneligliptin, An Economic and Effective DPP-4 Inhibitor for the Management of Type-2 Diabetes Mellitus: A Comparative Study

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## Abstract

**Context:** Increasing diabetic burden worldwide is creating an alarming situation for the management and development of economic resources for its treatment. Progressive nature of the disease requires allocation of a higher proportion of expenditure on health care initiative of any country.

**Aim:** Present study is designed with an aim to determine the effectiveness of cost-effective DPP-4 inhibitor, Teneligliptin, over the other agent of the same class.

**Material and Method:** The study was carried out in Postgraduate Department of Medicine, S.N. Medical College, Agra and 112 patients were selected as subjects with a selected inclusion criterion.

**Statistical Analysis used:** Independent student's t-test was applied to compare the means. Mean standard deviation was calculated for quantitative data. All p values were two-tailed and values  $p < 0.05$  were considered statistically significant

**Result:** There was no significant difference in the levels of blood sugar or glycosylated hemoglobin (HbA1c) before and after the treatment of Teneligliptin.

**Conclusion:** Teneligliptin offered an efficient second line treatment for the management of type-2 Diabetes Mellitus at a reduced average price of INR 39 per day, when compared to other DPP-4 inhibitors.

portion of expenditure on medical care and other economic resources.<sup>2</sup> 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 (Dipeptidyl peptidase-4) inhibitors are being used for nearly a decade for the management of Type 2 DM.<sup>3</sup> In India there are six types of DPP-4 inhibitors viz, Vildagliptin, Sitagliptin, Linagliptin, Saxagliptin, Gemigliptin, and Teneligliptin, which are being used for the management of Type 2 DM. Teneligliptin provides 1/4<sup>th</sup> to 1/5<sup>th</sup> low-cost treatment in comparison to another agents of the same class. DPP-4 inhibitors are classified as class 1, class 2 and class 3 based on their interaction at DPP-4 subsites. Class 1 inhibitors (Vildagliptin and Saxagliptin) bind

## Introduction

Global Diabetes has risen by 45% worldwide from 1990 to 2013 as per a study funded by the Bill

and Melinda Gates Foundation. The prevalence of Type 2 Diabetes Mellitus has been increased over recent decades, reaching worldwide epidemic.<sup>1</sup> Hence, for any country, it requires a higher

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**Table 1: Data for comparison of Tenueligliptin and other DPP-4 inhibitors (Vildagliptin, Sitagliptin, Linagliptin, Saxagliptin)**

Comparison parameters		Sitagliptin vs Tenueligliptin	Vildagliptin vs Tenueligliptin	Linagliptin vs Tenueligliptin	Saxagliptin vs Tenueligliptin
% HbA1c Level	Before Tenueligliptin	6.797 ± 0.07251	6.961 ± 0.06705	6.963 ± 0.04085	6.996 ± 0.04783
	After Tenueligliptin	6.79 ± 0.07646	6.952 ± 0.07382	6.853 ± 0.07282	6.936 ± 0.05569
p Value		0.8792	0.8753	0.0505	0.4118
Sample size (N)		n1= 29	n2= 23	n3= 32	n4= 28

N = 112, Data were expressed as Mean ± SD, P<0.05 was considered significant

to S1 and S2 and are considered as fundamental/ basic inhibitors. Class 2 (Alogliptin and Linagliptin) bind to the additional site of S1, S2 and S1' and may produce more DPP-4 inhibition than class 1, Linagliptin additionally binds to the S2' subsite. Class 3 inhibitors (Sitagliptin and Tenueligliptin) binds to S1, S2 and additional site of S2 extensive and produce more extensive DPP-4 inhibition.<sup>4,5</sup>

Tenueligliptin is a third-generation gliptin, which offers a pharmacodynamic advantage with unique "J-shaped anchor-lock domain" which signifies for its potent and long duration of action. It also offers a pharmacokinetic advantage with a long half-life of 26.9 hours and a convenient once-daily administration as an oral unit dosage form. It has a dual mode of elimination via renal and hepatic which sheds the burden of its clearance and can be preferred choice for the treatment of the patient with renal and mild to moderate hepatic impairment. Owing to its effects on vascular function, Tenueligliptin shows benefits in improvement of endothelial function, left the ventricular function, lipid levels, and least chances of hypoglycemia and neutral effect to body weight. Tenueligliptin has been approved in Japan, Korea, Argentina, India and currently undergoing phase

1 trials in the USA and phase 2 trials in Europe.<sup>6,7</sup>

This study is designed with an aim to evaluate the efficacy of the use of Tenueligliptin in comparison to other agents like Vildagliptin, Sitagliptin, Linagliptin, Saxagliptin as the second line agent with conventional oral hypoglycemic and to review the economic aspect of the treatment.<sup>8</sup>

### Materials and Method

The present study was carried out in the Postgraduate Department of Medicine, S.N. Medical College, Agra, India from September 2016 to March 2017. This study was approved by the institutional ethical review board.

Subjects were selected from the out-patient department of medicine and diabetic outdoor of S.N. Medical College, Agra, India, a tertiary care center.

Patients who were taking Gliptins (Vildagliptin, Sitagliptin, Linagliptin, Saxagliptin) along with the conventional antihyperglycemic agents like Metformin, Sulphonylurea, Pioglitazone, Voglibose and Insulin whose level blood sugar was controlled or nearly controlled; were selected as the subjects for the study. An informed consent was signed from all the patients before participating in the study.

**Table 2: Data of mean comparison between Tenueligliptin and other DPP-4 inhibitors on individual sample size (Vildagliptin, Sitagliptin, Linagliptin, Saxagliptin)**

% HbA1c	Before Tenueligliptin	6.928 ± 0.02923	P Value
	After Tenueligliptin	6.878 ± 0.03539	0.2773

N = 112, Data were expressed as Mean ± SD, P<0.05 was considered significant

Subjects were chosen so as to shift from expensive Gliptin (Vildagliptin, Sitagliptin, Linagliptin, Saxagliptin) to low cost (Tenueligliptin) because of their own affordability issue.<sup>9</sup> Inclusion and exclusion criteria were laid.

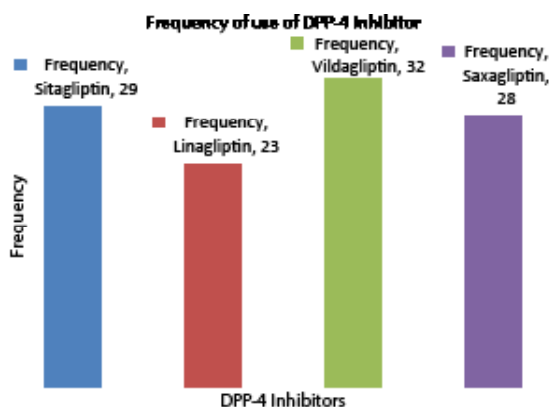
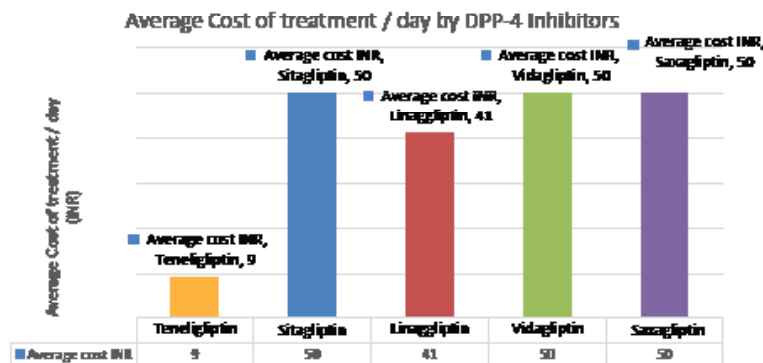
### Inclusion criteria

1. Diagnosed cases of Type 2 Diabetes Mellitus.
2. Patients between 25 to 80 years of both sexes.
3. Blood sugar level or glycosylated hemoglobin (HbA1C) is nearly controlled or controlled i.e., less than 7.

### Exclusion criteria

1. Patients who were taking conventional oral antihyperglycemic agents and had controlled blood sugar i.e., HbA1C more than 7.
2. Patients with a comorbid history of cerebrovascular accident, ischaemic heart disease or other debilitating conditions.
3. Patients with complications of diabetes.
4. Patients with hepatic or renal dysfunction.

Study subjects included 41, Females and 71 males. The average age of subjects was 44.13 ± 8.7 years. Sex distribution of BMI among subjects were females 25.3 ± 3.3 whereas, males 24.6 ± 3.2. An average duration of

**Fig. 1: Frequency of DPP4 inhibitor use****Fig. 2: Comparison of average daily cost of different DPP-4 inhibitors**

diabetes was since 8.4±4.2 years and the subjects taking DPP-4 inhibitor for diabetes was since 20±7 months.

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.

Glycosylated hemoglobin (HbA1C) was measured for all the subjects before and after starting the use of Teleniglipitin; spectrophotometrically by turbidimetric immune-inhibition (Olympus AU60, Beckman-Coulter, USA).

### Statistical Analysis

All statistical analysis was done by using SPSS version 20 (SPSS Inc., Chicago, USA). Independent student's t-test was applied to compare the means. Mean standard deviation was calculated for quantitative data. All p values were two-tailed and values  $p < 0.05$  were considered statistically significant.

### Results

Total 132 subjects were screened for this study after which 112 were selected after adequate consent. Twelve subjects were excluded due to their variable grades of abnormal renal function tests, 8 subjects didn't give consent to include in the study.

Statistically, there was no significant difference between the previous DPP-4 inhibitors (Sitagliptin, Linagliptin, Vildagliptin, Saxagliptin) and Teleniglipitin with respect to the level of HbA1c at a confidence interval of 95%. Teleniglipitin was equally potent to any other available DPP-4 inhibitor in terms of efficacy in maintaining HbA1c (Table 1).

Among the 112 subjects the frequency of choice of DPP-4 inhibitors, 29 were using Sitagliptin, 23 were using Vildagliptin, 32 were using Linagliptin and 28 were using Saxagliptin to

control blood glucose (Figure 1). It was ensured that each subject was taking same DPP-4 inhibitor for last 3 months (Figure 1).

There was no significant difference in the levels of % HbA1c when other DPP-4 inhibitors were changed to Teleniglipitin, when evaluated on total 112 sample size (Table 2). The average cost per day for DPP-4 inhibitors before Teleniglipitin was INR 47.75, whereas it was reduced to INR 9 per day after switching to Teleniglipitin. Thus, the average price was reduced by INR 38.75 (39) for DPP4 inhibitors (Figure 2).

### Discussion

Teleniglipitin has proved potential DPP-4 inhibitor promise in stabilizing glycemic fluctuations throughout the day and consequently suppressing the progression of diabetic complications.<sup>10</sup>

A head to head trial published by Tushar B. Chudiwal on 116 patients comparing effects of teleniglipitin to vildagliptin. Results show a 17.9% reduction in HbA1c with vildagliptin as compared to teleniglipitin which shows 18.9% reduction in DPP4i naïve patients at the end of three months.<sup>11</sup> Similar results were observed in our study where difference in HbA1c reduction between them is insignificant. In another study it was reported that gliptins (DPP-4 inhibitor) have slight lesser HbA1c lowering potential when compared to active glucose lowering agent like metformin. Though the former was reported of having better gastrointestinal tolerability.<sup>4</sup> In a study by Gupta CN et al, concluded that Teleniglipitin significantly improves glycemic control in Indian patients with T2DM when prescribed as an add-on to one or more other commonly prescribed antidiabetic drugs, even in patients of rural India.<sup>12</sup> In the present study it is evident that teleniglipitin shows insignificant difference between in glucose lowering potential when compared to other DPP-4 inhibitors the difference lies in the economic burden.

Teleniglipitin provides more economic choice of treatment than other gliptins.

### Conclusion

The study presents Teleniglipitin, a DPP-4 inhibitor as an effective, antihyperglycemic second line agent with the use of other conventional antidiabetic agents. Along with it, Teleniglipitin also offers low-cost treatment at an average reduced daily price of INR 39, when compared to other DPP-4 inhibitors. Since it is a hospital-based study which involves convenient sampling, and also the sample size is small, precaution needs to be taken before generalizing this finding to the general population.

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