Evaluation of treatment satisfaction, efficacy and safety of dipeptidyl peptidase-4 inhibitors in geriatric patients with type 2 diabetes mellitus: A cross-sectionalcomparative study

Harmanjit Singh¹, Avinash Chakrawarti², Harjit Singh², P. Guruprasad³, Yogendra Kumar Gupta³

¹Department of Pharmacology, GMCH, Chandigarh, Departments of ²Geriatric Medicine and ³Pharmacology, All India Institute of Medical Sciences, New Delhi, India

Abstract

Introduction: Dipeptidyl peptidase 4 (DPP4) inhibitors are attractive agents to be used in the elderly patients with Type 2 diabetes mellitus (T2DM) because of their beneficial effects. Methods: In this cross-sectional, observational study, we evaluated and compared the treatment satisfaction using Diabetes Treatment Satisfaction Questionnaire (DTSQ) in two groups (i.e., regimens containing DPP4 inhibitors vs. other regimens). Efficacy was evaluated by assessing and comparing the glycosylated hemoglobin (HbA1c) values and the percentage of patients who achieved the glycemic control (HbA1c <7%). The adverse drug reactions (ADRs) were also recorded and compared among two groups. Results: A total of 115 patients participated in the study (42 in Group 1 and 73 in Group 2). Significantly better DTSQ scores were observed among Group 1 patients in terms of DTSQ score total (P = 0.01) and DTSQ score for perception of hyperglycemia (P = 0.008) as compared to Group 2 patients. Significant difference was observed in HbA1c values among two groups (P = 0.02, 95% confidence interval [CI], 0.06–1.14). Also, significantly higher proportion of patients had achieved glycemic control, i.e., HbA1c <7% in Group 1 as compared to Group 2 (P = 0.002, 95% CI, 11.8%–48.1%). Significantly higher number of ADRs were observed among Group 1 patients as compared to Group 2 (P = 0.003). Conclusion: DPP4 inhibitors seem to offer better treatment satisfaction and efficacy in geriatric T2DM patients but at the expense of increased frequency of ADRs; however, further research is warranted.

Keywords: Diabetes mellitus, Diabetes Treatment Satisfaction Questionnaire, hemoglobin A1c, incretins, metformin, sitagliptin

Introduction

Diabetes mellitus (DM) is a common disease in geriatric population, with almost 50% of patients with type 2 DM (T2DM) being over 60 years of age. The prevalence of T2DM in people aged 65–74 years is reported to be 40%.[2-4]

Address for correspondence: Dr. Yogendra Kumar Gupta, Department of Pharmacology, All India Institute of Medical Sciences, New Delhi - 110 029, India. E-mail: yk.ykgupta@gmail.com

Quick Response Code: Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_89_17

How to cite this article: Singh H, Chakrawarti A, Singh H, Guruprasad P, Gupta YK. Evaluation of treatment satisfaction, efficacy and safety of dipeptidyl peptidase-4 inhibitors in geriatric patients with type 2 diabetes mellitus: A cross-sectionalcomparative study. J Family Med Prim Care 2018;7:70-6.
Dipeptidyl peptidase 4 (DPP4) inhibitors prevent degradation of endogenously released incretins, enhance their plasma levels, prolong their actions and finally leading to increased insulin level.\[10\]-\[12\] The levels of DPP4 increase with advancing age, therefore DPP4 inhibitors are attractive agents to be used in the elderly because of their beneficial effects.\[13\]-\[16\] They are associated with a low risk of hypoglycemia, few gastrointestinal (GI) side effects, few drug interactions, weight neutrality, better tolerability and fewer adverse events (AEs) as compared to metformin and sulfonylureas (SUs).\[13\]-\[16\] They have low risk of hypoglycemia, few gastrointestinal (GI) side effects, few drug interactions, weight neutrality, tolerability, and fewer adverse events (AEs) compared with metformin and sulfonylureas (SUs) in geriatric patients.\[13\]-\[16\] The DPP4 inhibitors are considered cardioprotective and have been used in acute coronary syndrome settings as well, which is advantageous in geriatric patients.\[16\]-\[18\]

Currently, DPP4 inhibitors such as sitagliptin, vildagliptin, saxagliptin, and newly approved teneligliptin are being prescribed as an adjunct to diet and exercise to improve glycemic control in Indian geriatric patients with T2DM, but data regarding their safety and efficacy and overall treatment satisfaction among T2DM geriatric patients are lacking. In the relative vacuum of data regarding treatment satisfaction and safety and efficacy of DPP4 inhibitors in geriatric patients, the aim of this observational study was to evaluate the treatment satisfaction and the safety and efficacy of DPP4 inhibitors in geriatric patients with T2DM.

Methods

Ethics

Permission to conduct this study was obtained from the institutional ethics committee of All India Institute of Medical Sciences, New Delhi, India, vide Reference No. IESC/T-492/30.09.2015, RT-13/28.10.2015. Written informed consent was obtained from all the patients prior to enrolling them in the study. The study was conducted according to the principles of Declaration of Helsinki and good clinical practices.

Study design

This was a single-center, cross-sectional, comparative observational study. It was conducted for 2 months in the Departments of Geriatric Medicine and Pharmacology.

Study population and study procedures

Geriatric patients with T2DM were screened and enrolled in the study subject to fulfilling inclusion criteria. Geriatric patients with T2DM who have taken antidiabetic medications at least for 3 months’ duration were included in the study; however, patients with T1DM and those who were not willing to give written informed consent were excluded from the study.

A total of 115 patients were enrolled in this study. Individual patient details, type of antidiabetic medications obtained, duration of treatment, any concomitant medications, etc., were noted in noted in case report form (CRF). For the purpose of the final analysis, patients were divided into two groups as follows:

- Group 1: Geriatric patients with T2DM receiving DPP4 inhibitor-based therapies either in monotherapy or in combination with other antidiabetic drugs (ADDs)
- Group 2: Geriatric patients with T2DM receiving non-DPP4 inhibitor-based therapies either in monotherapy or in combination with other ADDs.

Evaluation of treatment satisfaction

Diabetes treatment satisfaction was evaluated using the Diabetes Treatment Satisfaction Questionnaire (DTSQ). Permission to use DTSQ was obtained prior to the commencement of the study from Health Psychology Research Ltd., University of London (www.healthpsychologyresearch.com). The DTSQ is a validated and widely used tool to assess the treatment satisfaction among diabetic patients.\[19\]-\[22\] The DTSQ scores were compared among the two groups. It consists of a six item scale assessing treatment satisfaction and two items assessing perceived frequency of hyperglycemia and hypoglycemia (a total of 8 items). The scale total is computed by adding the six items, namely 1, 4, 5, 6, 7, and 8, to produce the treatment satisfaction scale total, which has a minimum of 0 and a maximum of 36. Items 2 and 3 denote the individual’s perception of hyperglycemia and hypoglycemia, respectively. DTSQ scores for treatment satisfaction total (items 1, 4, 5, 6, 7, and 8), perception of hyperglycemia (item 2), and perception of hypoglycemia (item 3) were computed for all patients and compared among the two groups.

Assessment of efficacy and safety

The last measured HbA1c (not older than 3 months) values were noted from the laboratory investigation reports of the patients (as a measure of efficacy) and were compared among the two groups. We also compared the percentage of patients who achieved HbA1c values <7% (as a measure of glycemic control). The individual adverse drug reactions (ADRs) were recorded in CRF and compared among the two groups as a measure of safety. Percentage of patients who experienced ADRs was also compared among the two groups.

Statistical analysis

Data were represented as percentages, mean ± standard deviation, and median (range) wherever applicable. Data were analyzed using the statistical software “R” version 3.2.2. Categorical data were analyzed using Chi-square test and Fisher’s exact test (wherever applicable). Continuous variables were analyzed using t-test for parametric data or Mann–Whitney test for nonparametric data. Difference in efficacy parameters between different DPP4 inhibitors was analyzed using analysis of variance (ANOVA) for parametric data and Kruskal–Wallis test for nonparametric data. \( P < 0.05 \) was considered statistically significant.
Results

Out of 115 patients who participated in the study, 42 were taking DPP4 inhibitors-based regimens (Group 1) and 73 were taking non-DPP4 inhibitors-based regimens (Group 2).

Demographic characteristics of the participants
• Age: Mean age of patients was 64 ± 4.4 years. Mean age of patients in Group 1 and Group 2 was 64.9 ± 5.6 and 63.5 ± 3.5 years, respectively (P = 0.1).
• Gender: Sixty-four male and 51 female patients participated in this study, 24 male and 18 female patients in Group 1 and 40 male and 33 female patients in Group 2 (P = 0.8).
• Weight: Mean weight of all patients was 70.4 ± 6.24 kg (69.2 ± 6.69 kg in Group 1 and Group 2, respectively, P = 0.37).

Prescribing pattern of antidiabetic drugs
Dipeptidyl peptidase 4 inhibitors
Three DPP4 inhibitors, i.e., sitagliptin, vildagliptin, and teneligliptin were prescribed among 42 patients. Fifteen patients were taking sitagliptin, with a mean dose of 88 ± 41.61 mg/day and a mean duration of 13.66 ± 6.67 months; 14 patients were taking vildagliptin, with a mean dose of 82.14 ± 24.86 mg/day and a mean duration of 16.12 ± 6.90 months; and 13 were taking teneligliptin, with a mean dose of 20.0 ± 0.0 mg/day and a mean duration of 6.07 ± 1.25 months.

Metformin
A total of 105 patients were taking metformin, with a mean dose of 1287 ± 502 mg/day and a mean duration of 40.6 months. Thirty-eight patients in Group 1 and 67 patients in Group 2 were taking metformin. Mean dose of metformin was 1223 ± 502 mg/day and 1324 ± 590 mg/day in Group 1 and Group 2, respectively. Difference in mean dose of metformin among two groups was not found to be statistically significant (P = 0.38). Mean duration of metformin use was 38 months and 41 months in Groups 1 and 2, respectively, and this difference was not statistically significant (P = 0.61).

Sulfonylureas
Sixty-nine patients were taking SUs, with a mean duration of 30.7 months (30.7 months in Group 1 and 30.8 months in Group 2, P = 0.9 for difference among the two groups). Ten patients in Group 1 and 59 patients in Group 2 were taking SUs (P = 0.001). Three different SUs were prescribed to patients, i.e., glimepiride, gliclazide, and glibenclamide. The most commonly used SU was glimepiride (total in 58 patients) followed by glibenclamide (6 patients) and gliclazide (5 patients).

Insulin
A total of 15 patients were taking insulin (7 in Group 1 and 8 in Group 2), with a mean duration of 28 months (30.5 months in Group 1 and 25.5 months in Group 2).

Other anti-diabetic drugs
Eight patients were taking pioglitazone (all in Group 2), with a mean dose of 15.93 ± 6.25 mg and a mean duration of 66 months. Two patients were taking voglibose (all in Group 2), with a mean dose of 0.2 mg and a mean duration of 36 months.

Number of anti-diabetic drugs
The mean number of ADD was 2.00 ± 0.69 in all patients (2.07 ± 0.7 in Group 1 vs. 1.97 ± 0.68 in Group 2, P = 0.46).

Monotherapy
Twenty three patients were taking ADD as monotherapy (8 in Group 1 and 15 in Group 2).

Diabetes Treatment Satisfaction Questionnaire
Overall DTSQ score was found to be 20.44 ± 4.57. Overall DTSQ score for perception of hyperglycemia was 2.33 ± 1.57 while that of perception of hypoglycemia was 1.27 ± 1.24. Group 1 patients had a significantly better overall DTSQ score (P = 0.01) [Table 1] and DTSQ score for perception of hyperglycemia (P = 0.008) [Table 1] as compared to Group 2, while no significant difference was observed in DTSQ score for perception of hypoglycemia between Groups 1 and 2 (P = 0.84) [Table 1]. No significant difference was observed in DTSQ scores among sitagliptin-, vildagliptin-, and teneligliptin-based regimens [Table 2].

Hemoglobin A1c
Mean value of HbA1c in all patients was 7.68 ± 1.42. Group 1 patients had significantly lower values of HbA1c as compared to Group 2 patients (P = 0.02, 95% confidence interval [CI], 0.06–1.14) [Table 3]. No significant difference was observed among sitagliptin-, vildagliptin-, and teneligliptin-based regimens with respect to HbA1c values [Table 4].

Percentage of patients who achieved glycemic control (hemoglobin A1c <7)
The proportion of patients who achieved HbA1c <7% was compared among the two groups. Significantly more number of patients in Group 1 had HbA1c <7% as compared to Group 2 (P = 0.002, 95% CI, 11.8%–48.1%) [Table 3].

No significant difference was observed among sitagliptin-,
Discussion

We observed a significant difference with respect to DTSQ score among geriatric patients taking regimens containing DPP4 inhibitor (one of sitagliptin, vildagliptin, or teneligliptin) and those taking other regimens. In addition, patients taking DPP4 inhibitor-containing regimens had significantly lower score for perception of hyperglycemia as compared to patients taking other regimens while no significant difference was observed between the two groups with respect to scores for perception of hypoglycemia.

To the best of our knowledge, this is the first study in India which evaluated the treatment satisfaction among geriatric patients with T2DM, and globally, limited data are available regarding the treatment satisfaction among diabetic patients taking DPP4 inhibitor-containing regimens and others. We came across only two studies in literature where DPP4 inhibitors and other regimens were compared for DTSQ scores among diabetic patients. Davies et al.[23] and Pratley et al.[24] used DTSQ scores among patients taking liraglutide or sitagliptin.

We observed that better glycemic control (low HbA1c levels) was associated with higher treatment satisfaction as indicated by significantly higher DTSQ scores among patients taking DPP4 inhibitor-containing regimens (had lower values of mean HbA1c) as compared to other patients (had higher values of mean HbA1c).

Redekop et al.[25] and Marra[26] also found significantly better DTSQ scores among patients having lower HbA1c levels as compared to those having higher HbA1c levels. This finding indicates that the DTSQ could be informative to some extent regarding glyco-metabolic parameters.

HbA1c values were assessed for comparing the efficacy between the two groups. We also assessed the proportions of patients meeting the goal of antidiabetic treatment recommended by various diabetic authorities such as American Diabetic Association, i.e., HbA1c <7%. A statistically significant difference was observed in HbA1c values among Group 1 and Group 2 patients. Also, significantly higher percentage of patients taking DPP4 inhibitor-based regimens had achieved HbA1c target of <7% as compared to the other group [Table 3].

Significantly higher percentage of patients taking regimens containing DPP4 inhibitors experienced ADRs as compared to

Table 2: Difference in Diabetes Treatment Satisfaction Questionnaire Scores among sitagliptin-, vildagliptin-, and teneligliptin-based regimens

| Parameter | Sitagliptin-based regimens (n=15) | Vildagliptin-based regimens (n=14) | Teneligliptin-based regimens (n=13) | P
|----------------|-------------------------------|-------------------------------|-------------------------------|-------------------------|
| 1. DTSQ (mean±SD) | 22.3±3.6 | 22.0±4.2 | 20.9±4.1 | 0.63 (one-way ANOVA)
| 2. DTSQ for perception of hyperglycemia, median (range) | 1 (0-4) | 1.5 (0-4) | 3 (0-4) | 0.58 (Kruskal–Wallis test)
| 3. DTSQ for perception of hypoglycemia, median (range) | 0 (0-3) | 1 (0-3) | 1 (0-3) | 0.95 (Kruskal–Wallis test)

DTSQ: Diabetes Treatment Satisfaction Questionnaire; SD: Standard deviation; ANOVA: Analysis of variance

Table 3: Difference in glycosylated hemoglobin and percentage of patients who achieved glycemic control (glycosylated hemoglobin <7.0%) among Group 1 and Group 2 patients

| Parameter | Group 1 (n=42) | Group 2 (n=73) | P (95% CI)
|----------------|---------------|---------------|-------------|
| HbA1c (%) | 7.07±1.22 | 7.68±1.48 | 0.02* (0.06%–1.14%)
| Percentage of patients who achieved HbA1c <7%, n (%) | 26 (62) | 24 (33) | 0.002* (11.8%–48.1%)

DTSQ: Diabetes Treatment Satisfaction Questionnaire; SD: Standard deviation; ANOVA: Analysis of variance

Table 4: Difference in glycosylated hemoglobin and percentage of patients who achieved glycemic control (glycosylated hemoglobin <7.0%) among sitagliptin-, vildagliptin-, and teneligliptin-based regimens

| Parameter | Sitagliptin (n=15) | Vildagliptin (n=14) | Teneligliptin (n=13) | P
|----------------|---------------------|---------------------|---------------------|----------|
| HbA1c (%) | 7.12±1.42 | 7.12±0.88 | 6.96±1.36 | 0.21 (one-way ANOVA)
| Percentage of patients who achieved HbA1c <7%, n (%) | 9 (60) | 8 (57.1) | 9 (69.2) | 0.85 (Chi-square test)

HbA1c: Glycosylated hemoglobin; ANOVA: Analysis of variance

vildagliptin-, and teneligliptin-based regimens with respect to the percentage of patients who achieved glycemic control [Table 4].

Adverse drug reactions

A total of 59 ADRs were reported in both groups. Significantly higher proportion of patients in Group 1 experienced ADRs as compared to Group 2 (33 ADRs in 27 patients in Group 1 vs. 26 ADRs in 26 patients in Group 2, P = 0.003). No significant difference was observed among the two groups with respect to the number of individual ADRs except nasopharyngitis which occurred exclusively in Group 1 as compared to Group 2 (6 in Group 1 vs. 0 in Group 2, P = 0.001) [Table 5]. No significant difference was observed among sitagliptin-, vildagliptin-, and teneligliptin-based regimens with respect to the percentage of patients who experienced ADRs (sitagliptin 47%, vildagliptin 71%, and teneligliptin 77%, P = 0.22). Also, no significant difference was observed among sitagliptin-, vildagliptin-, and teneligliptin-based regimens with respect to the number of individual ADRs.
Schweizer et al.[13] observed a significant reduction in HbA1c in geriatric patients with vildagliptin as add-on therapy to metformin; AEs and serious AEs (SAEs) were reported with a lower frequency in geriatric patients receiving vildagliptin than comparators.

We did not observe any difference among patients taking three DPP4 inhibitor-based therapies with respect to HbA1c values, proportion of patients who were meeting the target of HbA1c, and the number of total and individual ADRs.

Schwartz[14] evaluated the effectiveness and safety of different DPP4 inhibitors in geriatric T2DM patients who were treated with sitagliptin, saxagliptin, vildagliptin, alogliptin, BI-1356, DSP-7238, or PF-734200 administered as monotherapy or in combination with metformin, a thiazolidinedione, glimepiride, glibenclamide, or insulin. Quantitative data indicated that DPP4 inhibitors were associated with significant HbA1c reductions. They also observed a significantly lower risk of hypoglycemia with DPP4 inhibitors as compared to other agents.

Teneligliptin was recently approved (May 2015) in India for the treatment of T2DM as an adjunct to diet and exercise[15] and no reports are available on its use in geriatric patients in India. Kim et al.[16] and Kadowaki and Kondo[17] assessed the efficacy and safety of teneligliptin in combination with metformin[18] and glimepiride[19] in patients who were inadequately controlled with metformin and glimepiride monotherapy. They found a significant improvement in HbA1c with addition of teneligliptin and comparable safety to that of other drugs.

Teneligliptin seems to be an attractive option, but in our study, only 13 patients were taking teneligliptin and any conclusion drawn on the basis of this will not be highly meaningful.

Although we found a significant difference in the occurrence of ADRs in patients receiving regimens containing one DPP4 inhibitor, none of the patients developed serious ADRs or discontinued therapy. DPP4 inhibitors were mainly prescribed in combination with other ADD (mainly metformin); therefore, it is difficult to assign ADRs to one particular medicine, though the possibility cannot be ruled out.

Limitations of our study

1. Sample size was small and a less number of patients taking DPP4 inhibitor-based therapies participated in the study;
DPP4 inhibitors are not frequently prescribed at our center because they are costlier
2. Mean duration of use of DPP4 inhibitors in our study was about 1 year; therefore, our report does not address the long-term safety and efficacy of these agents
3. Treatment satisfaction is a subjective parameter and may vary with the number of factors.

DPP4 inhibitors seem to be associated with better treatment satisfaction and better efficacy outcomes in geriatric patients with T2DM but at the expense of increased frequency of ADRs. However, due to the cross-sectional nature of this study and limited sample size, the results cannot be generalized and require further validation.

**Acknowledgment**

We are thankful to Health Psychology Research Ltd., University of London (www.healthpsychologyresearch.com) for providing DTSQ.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Morley JE. The elderly type 2 diabetic patient: Special considerations. Diabet Med 1998;15 Suppl 4:S41-6.
2. Harris MI, Hadden WC, Knowler WC, Bennett PH. Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in U.S. Population aged 20-74 years. Diabetes 1987;36:523-34.
3. Knowler WC, Saad MF, Pettitt DJ, Nelson RG, Bennett PH. Determinants of diabetes mellitus in the Pima Indians. Diabetes Care 1993;16:216-27.
4. Croxson SC, Burden AC, Bodington M, Botha JL. The prevalence of diabetes in elderly people. Diabet Med 1991;8:28-31.
5. Krapek K, King K, Warren SS, George KG, Caputo DA, Mihelich K, et al. Medication adherence and associated hemoglobin A1c in type 2 diabetes. Ann Pharmacother 2004;38:1357-62.
6. Schectman JM, Nadkarni MM, Voss JD. The association between diabetes metabolic control and drug adherence in an indigent population. Diabetes Care 2002;25:1015-21.
7. Diabetes Attitudes, Wishes, and Needs (DAWN) Study. Barriers to Treatment. Available from: http://www.dawnstudy.com. [Last accessed on 2016 Jan 10].
8. Anderson RT, Balkrishnan R, Camacho F, Bell R, Duren-Winfield V, Goff D, et al. Patient-centered outcomes of diabetes self-care. Associations with satisfaction and general health in a community clinic setting. N C Med J 2003;64:58-65.
9. Lawson ML, Gerstein HC, Tsui E, Zinnman B. Effect of intensive therapy on early macrovascular disease in young individuals with type 1 diabetes. A systematic review and meta-analysis. Diabetes Care 1999;22 Suppl 2:S35-9.
10. Stonehouse AH, Darsow T, Maggs DG. Incretin-based therapies. J Diabetes 2012;4:53-67.
11. Dailey MJ, Moran TH. Glucagon-like peptide 1 and appetite. Trends Endocrinol Metab 2013;24:85-91.
12. Russell S. Incretin-based therapies for type 2 diabetes mellitus: A review of direct comparisons of efficacy, safety and patient satisfaction. Int J Clin Pharm 2013;35:159-72.
13. Schweizer A, Dejager S, Bosi E. Comparison of vildagliptin and metformin monotherapy in elderly patients with type 2 diabetes: A 24-week, double-blind, randomized trial. Diabetes Obes Metab 2009;11:804-12.
14. Schweizer A, Dejager S, Foley JE, Shao Q, Koithny W. Clinical experience with vildagliptin in the management of type 2 diabetes in a patient population ≥75 years: A pooled analysis from a database of clinical trials. Diabetes Obes Metab 2011;13:55-64.
15. Shankar R, Engel SS, Xu L, Golm GT, Davies MJ, Kaufman KD, et al. Sitagliptin provides similar glycemimic improvement with less hypoglycemia in the elderly with type 2 diabetes mellitus compared to sulfonylurea. Diabetes 2012;61 Suppl 1:A278.
16. Schwartz SL. Treatment of elderly patients with type 2 diabetes mellitus: A systematic review of the benefits and risks of dipeptidyl peptidase-4 inhibitors. Am J Geriatr Pharmacother 2010;8:405-18.
17. Bashir M, Pathan MF, Raza SA, Ahmad J, Khan AK, Ishaq O, et al. Role of oral hypoglycemic agents in the management of type 2 diabetes mellitus during Ramadan. Indian J Endocrinol Metab 2012;16:503-7.
18. Yoshida T, Akahoshi F, Sakashita H, Kitajima H, Nakamura M, Sonda S, et al. Discovery and preclinical profile of teneligliptin (3-[(2S,4S)-4-[4-(3-methyl-1-phenyl-1H-pyrazol-5-yl) piperazin-1-yl] pyrrolidin-2-ylcarbonyl] thiazolidine): A highly potent, selective, long-lasting and orally active dipeptidyl peptidase IV inhibitor for the treatment of type 2 diabetes. Bioorg Med Chem 2012;20:5705-19.
19. DTSQ. Available from: http://www.healthpsychologyresearch.com/questionnaires_details.asp?QID=713 and QC=0 and QT=0. [Last accessed on 2015 Sep 10].
20. Bradley C, Lewis KS. Measures of psychological well-being and treatment satisfaction developed from the responses of people with tablet-treated diabetes. Diabet Med 1990;7:445-51.
21. DAFNE Study Group. Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: Dose adjustment for normal eating (DAFNE) randomised controlled trial. BMJ 2002;325:746.
22. Witthaus E, Stewart J, Bradley C. Improved psychological outcomes after initiation of insulin treatment in patients with Type II diabetes. Diabetologia 2000;43 Suppl 1:A205.
23. Davies M, Pratley R, Hammer M, Thomsen AB, Cuddihy R. Liraglutide improves treatment satisfaction in people with type 2 diabetes compared with sitagliptin, each as an add on to metformin. Diabet Med 2011;28:333-7.
24. Pratley RE, Nauck MA, Bailey T, Montanya E, Filetti S, Garber AJ, et al. Efficacy and safety of switching from the DPP-4 inhibitor sitagliptin to the human GLP-1 analog liraglutide after 52 weeks in metformin-treated patients with type 2 diabetes: A randomized, open-label trial. Diabetes Care 2012;35:1986-93.
25. Redekop WK, Koopmanschap MA, Stolk RP, Rutten GE,
Singh, et al.: Treatment satisfaction, efficacy and safety of DPP4 inhibitors in geriatric patients with T2DM

Wolffenbuttel BH, Niessen LW, et al. Health-related quality of life and treatment satisfaction in Dutch patients with type 2 diabetes. Diabetes Care 2002;25:458-63.

26. Marra G; DIAB. & T.E.S Project Study Group. The DIAB & T.E.S project: How patients perceive diabetes and diabetes therapy. Acta Biomed 2004;75:164-70.

27. American Diabetes Association (ADA). Diabetes Guidelines Summary Recommendations from NDEI; 2015. Available from: http://www.ndei.org/uploadedFiles/CommonNDEI/Treatment_Guidelines/ADA%202015%20Summary%20PDF.pdf. [Last accessed on 2016 Jan 10].

28. Umezawa S, Kubota A, Maeda H, Kanamori A, Matoba K, Jin Y, et al. Two-year assessment of the efficacy and safety of sitagliptin in elderly patients with type 2 diabetes: Post hoc analysis of the ASSET-K study. BMC Endocr Disord 2015;15:34.

29. Mohan Dallumal R, Chua SS, Wu DB, Vethakkan SR. Sitagliptin: Is it effective in routine clinical practice? Int J Endocrinol 2015;2015:950571.

30. List of Approved Drugs from 01-01-2015 to 31-01-2015. Available from: http://www.cdsco.nic.in/forms/list.aspx?id=2034&id=11. [Last accessed on 2015 Jan 10].

31. Kim MK, Rhee EJ, Han KA, Woo AC, Lee MK, 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.

32. 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 2014;16:418-25.

33. Amori RE, Lau J, Pittas AG. Efficacy and safety of incretin therapy in type 2 diabetes: Systematic review and meta-analysis. JAMA 2007;298:194-206.

34. Brown NJ, Byiers S, Carr D, Maldonado M, Warner BA. Dipeptidyl peptidase-IV inhibitor use associated with increased risk of ACE inhibitor-associated angioedema. Hypertension 2009;54:516-23.