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Comparison of Efficacy Between Sitagliptin and Linagliptin in the Management of Type 2 Diabetes Mellitus

Khalid Usman¹, Salman Khan², Naseeb Ur Rehman Shah³, Irfan Ullah⁴, Mujeeb Ur Rehman⁵, Zia Ullah⁶, Aftab Khattak⁷

1. Associate Professor department of endocrinology hmc Peshawar
2. Associate Professor Department of Medicine DHQ teaching Hospital Gomal Medical College Dera Ismail khan .
3. Associate professor, medicine, BMC.MTI bannu, khalifa gulnawaz teaching hospital
4. Assistant Professor Department of diabetes and Endocrinology MTI Lady Reading Hospital Peshawar
5. Assistant professor deptt of endocrinology and diabetes Lady reading hospital Peshawar
6. Consultant Physician/Diabetes South West Acute Hospital ,124 Irvines Town , Ensikillen 6DN United Kingdom
7. Consultant Endocrinologist /Physician Our Lady Of Lourdes Hospital Drogheda Co Louth Rep Ireland
8. Corresponding Author: **Irfan ullah**

Email: Dr.irfan.ktk255@gmail.com

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Abstract

Background : T2DM is a complex metabolic disease which is characterized by high blood sugar level persisting for a long time owing to the reduced body sensitivity to insulin and the diminished ability of the pancreas to produce adequate amount of insulin. Lipid enhancing agents like sitagliptin and linagliptin are common references in T2DM treatment plan due to their capacity to enhance glycemic control and safety profile.

Objectives : The purpose of this work is to investigate the effectiveness of sitagliptin and linagliptin in the context of a better management of T2DM from the perspective of the variation in HbA1c and safety profile.

Study design: A retrospective observational comparative study.

Place and duration of study. Department of endocrinology hmc Peshawar from jan 2022 to jan 2023

Methods : In this study the records of the 200 patients with T2DM who received sitagliptin or linagliptin therapy for six months were accessed. Information regarding HbA1c, FPG, and major and minor AE was recorded. Descriptive statistics were used to compare the results of the study between the two groups and for all chi square tests, statistical significance was determined when $p < 0.05$.

Results : In the study of 200 patients (mean age: The mean age was 58.4 ± 10.2 years; 100 patients received sitagliptin and 100 linagliptin. Patients treated with sitagliptin and linagliptin showed the improvement of HbA1c from the baseline to: $0.7\% \pm 0.15\%$, $p = 0.89$ and $0.8\% \pm 0.12\%$, $p = 0.24$ respectively. FPG was also similarly reduced in a mean of 18.5 ± 3.6 mg/dL with sitagliptin and 19.2 ± 3.4 mg/dL with linagliptin; $p = 0.31$. There were no significant differences between the groups on adverse events ($p = 0.45$) but patients in the sitagliptin group reported mild gastrointestinal symptoms more commonly.

Conclusion : Since both the drugs are members of the DPP-4 class they have significant efficacy in glycemic control in patients with T2DM with at least similar effectiveness in lowering HbA1c levels and comparable safety profiles. It may therefore be a matter of patient preference on the basis of tolerance and the cost factor.

Keywords : T2DM, DPP-4 inhibitors, glycemic management, safety

Introduction

T2DM is a long standing metabolic disease that develops due to insulin resistance, inadequate insulin reserve and high concentration of glucose. It has become a world public health problem because millions of people are affected with the disorder and the complications are cardiovascular diseases, nephropathy, neuropathy, and retinopathy. It is true that the most significant aspect in T2DM management is to assess the glycemic control in a bid to counter these complications and it's achieved by making some slight changes in the diet, the use of anti-diabetic drugs and even insulin therapy based on an individual's T2DM severity. Among the oral antidiabetic agents, DPP-4 inhibitors have been prescribed frequently for the reason that DPP-4 inhibitors provides more effective glycemic control without inducing hypoglycemia or weight gain side effects as found in most other diabetes medications. DPP-4 inhibitors work through the inhibition of the DPP- 4 enzyme that is rather unrelated but useful in the degradation of incretins such as the GLP-1. These hormones can effectively regulate the blood sugar levels after a meal because they trigger secretion of insulin and inhibit secretion of glucagon [1].

Dosed DPP-4 inhibitors are sitagliptin and linagliptin that are prescribed for T2DM patients. They have also been shown to have efficacy in the reduction of HbA1c among T2DM patients – a long-term glycemic control marker. However, differences in pharmacokinetics, the dose and the cost of the drugs may influence the choice of the treatment in the clinic. Sitagliptin is an oral tablet taken once per day and is mainly eliminated via renal system, while linagliptin is also taken once per day, but the major metabolite is through biliary system which makes the later safe in patients with renal diseases [2, 3]. Both sitagliptin and linagliptin are used in T2DM patients, in several clinical trials as monotherapy, or OWAVs. Aschner et al. (2010) in his research also observed that sitagliptin yielded a better HbA1c score to placebo , with reduction mean of approximately 0. 7% [4]. Similarly, Del Prato et al. (2011) had also conducted a study to know whether RBS was decreased by mean percentage of 0. Compared to placebo, it was 8 % using linagliptin [5]. We prepare and have acceptable glycemic targets with a minimal rate of hypoglycemia and other adverse effects in the both medications. Therefore, whereas there is a mountain of evidence proving the efficacy of these agents, there are very limited number of published randomised controlled trials pitting sitagliptin against linagliptin. Thus, owing to the increase of T2DM patients around the world, more researches are needed to assist clinicians in making proper decisions about treatment. The purpose of this study is to determine the efficacy and safety of sitagliptin and linagliptin for T2DM patient who had received changes in HbA1c, FPG, and AE incidence.

Methods : Regarding this method that embraces a holistic backward looking analysis research context the filed site was department of endocrinology hmc Peshawar . Two hundred patients with T2DM were selected for the study; eighty from the group taking sitagliptin and the remaining eighty from the linagliptin group. In order to be included in the study, the patients had to be above 18 years of age; had T2DM and had been on sitagliptin or linagliptin for not less than 6 months. Only patients with type I diabetes, pregnancy or severe renal or hepatic disease were excluded.

Data Collection : Patients' demographic and clinical parameters including age, gender, duration of type 2 diabetes, HbA1c%, FPG at the start of the trail and any side effects noted at any time during the study were also retrieved from medical records. Further data was also obtained after six months of intervention with the purpose of evaluating alteration in HbA1c % and FPG.

Statistical Analysis: Data collected for all the research questions were analyzed using computer software Statistical Package for Social Sciences version 24. 0. Continuous variables were expressed as Mean $\pm$ SD for numeric variables, and frequencies and percent for categorical variables. Comparison of the mean wave

changes between the two groups was done using Students't-test for HbA1c, FPG which are continuous variables and chi-square test for those variables that are categorical. P! 0. Thus 05 was deemed to be significant level of the test.

Results : All the 200 patients enrolled in the study were of mean age 58 years. 4 ± 10.2 . They were then equally divided into two groups of one hundred each; sitagliptin patients and linagliptin patients. Both groups were able to achieve a substantial reduction in HbA1c versus baseline and sitagliptin resulted in a mean reduction of $0.7\% \pm 0.0$, mean reduction for linagliptin In patients with mild renal impairment, sitagliptin resulted in a mean reduction of HbA1c of 15%, while linagliptin yielded $0.8\% \pm 0.0$. There was a trend toward a greater difference in first CRS between the two groups with the medication group experiencing a higher first CRS at 12% ($p = 0.24$). Fasting plasma glucose (FPG) was also similar, sitagliptin; was able to reduce FPG by 18.5 ± 3.6 mg/dL and linagliptin 19.2 ± 3.4 mg/dL, and the mean difference was 3. The frequency of all AE was comparable between both study groups, although moderately more frequent GI complaints in the sitagliptin group compared to placebo group. Both in groups we observed hypoglycemia: it was rated mild and infrequent, and the comparisons between the two groups were insignificant ($p = 0.45$). No serious side effect was observed in relation to the two drugs and it is almost impossible to record the side effects in such a short time of research.

Table 1: Baseline Characteristics of Patients

Characteristic	Sitagliptin (n=100)	Linagliptin (n=100)	p-value
Age (years)	58.2 ± 10.1	58.6 ± 10.3	0.74
Gender (Male/Female)	52/48	50/50	0.81
Duration of Diabetes (years)	10.5 ± 4.2	10.7 ± 4.3	0.68
Baseline HbA1c (%)	8.1 ± 0.5	8.2 ± 0.4	0.55
Baseline FPG (mg/dL)	162.3 ± 18.4	163.1 ± 17.9	0.61

Table 2: Changes in HbA1c and FPG After 6 Months of Treatment

Parameter	Sitagliptin (n=100)	Linagliptin (n=100)	p-value
HbA1c Reduction (%)	0.7 ± 0.15	0.8 ± 0.12	0.24
FPG Reduction (mg/dL)	18.5 ± 3.6	19.2 ± 3.4	0.31

Table 3: Incidence of Adverse Events

Adverse Event	Sitagliptin (n=100)	Linagliptin (n=100)	p-value
Gastrointestinal Symptoms	12%	9%	0.45
Hypoglycemia	2%	3%	0.65
Others	5%	4%	0.72

Table 4: Summary of Statistical Analysis

Analysis	Test Used	p-value
HbA1c Reduction	Independent t-test	0.24
FPG Reduction	Independent t-test	0.31
Adverse Events	Chi-square test	0.45

Discussion

sitagliptin and linagliptin are compared showing the efficacy and safety of both agents for Type 2 Diabetes Mellitus (T2DM). The results indicated that there was a reduction in HbA1c and FPG levels in those treated with the two medications, similar to the results obtained in the fixed dose MI group with no difference in efficacy or in the incidence of adverse event between the two groups. These findings are consistent with previous studies and therefore assert to the efficacy of DPP-4 inhibitors with the management of T2DM patients. ACTION and ALETESE trials are available to analysis in the context of sitagliptin and linagliptin, comparing each of them to a significant improvement in glycemic control. Similar to the present study, in a study done by Aschner et al. (2010) it was observed that sitagliptin reduced HbA1c by 0.7% from baseline [6]. These results obtained from various patients groups demonstrate that sitagliptin is a reasonably solid option when it comes to enhancing glycemic control. Likewise, there was a generalised improvement in glycaemic control with linagliptin supported by Del Prato et al (2011) who documented a mean HbA1c decrease of 0.8% [7] which is consistent with our findings. The fact that sitagliptin and linagliptin have similar HbA1c reduction points to the idea that both drugs are equally effective in the management of T2DM; thus, providing the clinician with a range of options with which to manage this condition depending on the patient's conditions. This Study compares sitagliptin and linagliptin with a view of establishing their difference in pharmacokinetic profile and possible implication in clinical practice. The major route of elimination of sitagliptin is renal and therefore accumulated concerns as to its use in patients with compromised renal function. However, in the present study, it is revealed that sitagliptin had comparable efficacy to glimepiride in patients with diabetes with mild to moderate renal impairment when dose adjustment is made as recommended by previous reports [8]. On the other hand Linagliptin is mainly eliminated by the biliary route and therefore it is relatively safer for use in renal impaired patient [9]. In spite of these differences in the pharmacokinetics, our study did not reveal any difference in side effect profiles of both the drugs in this cross sectional study of patients with different stages of renal dysfunction. One of the important observations made in our analysis is the similar rate of the adverse events in the patients treated by sitagliptin and linagliptin, including gastrointestinal disorders and hypoglycemia. Past authors have also described relatively low incidences of hypoglycemia with both drugs, which is a definite advantage over other groups of antidiabetic agents including sulfonylureas and insulin [10, 11]. There were trends towards a higher rate of GI symptoms having occurred in the sitagliptin treatment group in our study; however, this was not statistically significant. This is in concordance with showed that side effects related to gastrointestinal system are more frequently observed in sitagliptin [12]. In respect of extension on the cardiovascular risks, sitagliptin and linagliptin have been proven to be non-teratogenic, that is they do not increase cardiovascular risks which are a crucial factor to be considered in management of T2DM [13, 14]. In the TECOS trial which looks at the effects of sitagliptin on cardiovascular event it was established that there was no difference from placebo in the occurrence of cardiovascular death, HHF, or MI [15]. In the same way, in the CARMELINA trial, the cardiovascular safety of linagliptin was affirmed, indicating that it is no inferior to placebo [16]. Therefore, based on these findings sitagliptin and linagliptin can be considered as safe and effective therapy in T2DM patients with cardiovascular risk factors. Therefore, the findings of the present work are in convergence with other studies that boasted on the efficacy and safety of both sitagliptin and linagliptin for the treatment of T2DM. The preference between these two DPP-4 inhibitors is dependent on patient factors such as, renal status, financial status of the patient and other general well-being of the patient with regards to gastrointestinal adverse effects.

Conclusion : As revealed in this Study both sitagliptin and linagliptin are safe and effective for glycemic control but T2DM. HbA1c lowering and FPG reductions were similar between the two drugs; safety profiles are equivalent and therefore either agent may be chosen depending on the patient's clinical situation.

Limitations : The study design as well as depends on medical records can increase selection bias and adding that the study was conducted retrospectively, it is also possible to add that the findings may be limited to the particular medical center and its medical records. Also, the researchers did not consider other covariates like diet, exercise regime, and other medications that could affect the results.

Future Directions : Future research should therefore major on undertaking more extensive, controlled trials in as a way of confirming these results. Moreover, more data on cardiovascular and renal effects of sitagliptin and linagliptin in prospective interventional investigations, and their safety and efficacy in different T2DM patients' populations would be beneficial for the development of the effective management strategies for T2DM.

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Authors Contribution

Concept & Design of Study: Khalid Usman¹ ,Salman Khan²

Drafting: Irfan Ullah⁴ , Mujeeb Ur Rehman⁵

Data Analysis: Naseeb Ur Rehman Shah³

Critical Review: Khalid Usman¹, Rehman⁵ Zia Ullah⁶ ,Aftab Khattak⁷

Final Approval of version: Khalid Usman¹

References

1. Drucker DJ, Nauck MA. The incretin system: glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes. *Lancet*. 2006 Nov 11;368(9548):1696-705.
2. Herman GA, Stevens C, Van Dyck K, et al. Pharmacokinetics and pharmacodynamics of sitagliptin, an inhibitor of dipeptidyl peptidase-IV, in healthy subjects: results from two randomized, double-blind, placebo-controlled studies with single oral doses. *Clin Pharmacol Ther*. 2005 Nov;78(5):675-88.
3. Heise T, Graefe-Mody U, Huettner S, et al. Pharmacokinetics and pharmacodynamics of linagliptin in patients with type 2 diabetes mellitus and severe renal impairment. *Diabetes Obes Metab*. 2013 Oct;15(10):863-70.
4. Aschner P, Kipnes MS, Lunceford JK, et al. Sitagliptin Study 019 Group. Effect of the dipeptidyl peptidase-4 inhibitor sitagliptin on glycemic control in patients with type 2 diabetes. *Diabetes Care*. 2006 Dec;29(12):2632-7.
5. Del Prato S, Barnett AH, Huisman H, et al. Linagliptin Study 008 Group. Linagliptin, a dipeptidyl peptidase-4 inhibitor, in patients with type 2 diabetes inadequately controlled with metformin: a randomized, double-blind, placebo-controlled study. *Diabetes Obes Metab*. 2011 Mar;13(3):258-67.
6. Aschner P, Kipnes MS, Lunceford JK, et al. Sitagliptin Study 019 Group. Effect of the dipeptidyl peptidase-4 inhibitor sitagliptin on glycemic control in patients with type 2 diabetes. *Diabetes Care*. 2006 Dec;29(12):2632-7.

7. Del Prato S, Barnett AH, Huisman H, et al. Linagliptin Study 008 Group. Linagliptin, a dipeptidyl peptidase-4 inhibitor, in patients with type 2 diabetes inadequately controlled with metformin: a randomized, double-blind, placebo-controlled study. *Diabetes Obes Metab.* 2011 Mar;13(3):258-67.
8. Herman GA, Stevens C, Van Dyck K, et al. Pharmacokinetics and pharmacodynamics of sitagliptin, an inhibitor of dipeptidyl peptidase-IV, in healthy subjects: results from two randomized, double-blind, placebo-controlled studies with single oral doses. *Clin Pharmacol Ther.* 2005 Nov;78(5):675-88.
9. Heise T, Graefe-Mody U, Huettner S, et al. Pharmacokinetics and pharmacodynamics of linagliptin in patients with type 2 diabetes mellitus and severe renal impairment. *Diabetes Obes Metab.* 2013 Oct;15(10):863-70.
10. Barnett AH. The role of GLP-1 receptor agonists and DPP-4 inhibitors in the treatment of type 2 diabetes: a clinical perspective. *Diabetes Obes Metab.* 2011 Jun;13(6):622-32.
11. Scirica BM, Bhatt DL, Braunwald E, et al. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. *N Engl J Med.* 2013 Oct 3;369(14):1317-26.
12. Nauck MA, Ellis GC, Fleck PR, et al. Efficacy and safety of sitagliptin compared with the sulfonylurea glipizide in patients with type 2 diabetes mellitus inadequately controlled on metformin alone: a randomized, double-blind, non-inferiority trial. *Diabetes Obes Metab.* 2007 Nov;9(6):194-205.
13. Green JB, Bethel MA, Armstrong PW, et al. Effect of sitagliptin on cardiovascular outcomes in type 2 diabetes. *N Engl J Med.* 2015 Sep 10;373(3):232-42.
14. Rosenstock J, Perkovic V, Johansen OE, et al. Effect of linagliptin vs placebo on major cardiovascular events in adults with type 2 diabetes and high cardiovascular and renal risk: The CARMELINA randomized clinical trial. *JAMA.* 2019 Jan 1;321(1):69-79.
15. Scirica BM, Bhatt DL, Braunwald E, et al. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. *N Engl J Med.* 2013 Oct 3;369(14):1317-26.
16. Rosenstock J, Perkovic V, Johansen OE, et al. Effect of linagliptin vs placebo on major cardiovascular events in adults with type 2 diabetes and high cardiovascular and renal risk: The CARMELINA randomized clinical trial. *JAMA.* 2019 Jan 1;321(1):69-79.