https://doi.org/10.3329/cbmj.v14i1.79340

Comparison of Efficacy and Safety of Vildagliptin and Linagliptin in Patients of Type 2 Diabetes Mellitus with Chronic Kidney Disease

*Ahmed S[1], Hasan MJ[2], Bari MA[3], Islam MA[4], Alam MR[5], Jahan F[6], Hasan R[7], Helal ASMJ[8]

Abstract

Both vildagliptin and linagliptin are dipeptidyl peptidase-4 (DPP-4) inhibitors used to manage blood sugar levels in patients with type 2 diabetes mellitus (T2DM), including those with chronic kidney disease (CKD). This randomized comparative study was conducted in the Department of Medicine, Community Based Medical College, Bangladesh (CBMC,B) Hospital, Mymensingh Bangladesh, between January and December 2023, to compare the efficacy and safety of vildagliptin and linagliptin in patients of type 2 diabetes mellitus (T2DM) with chronic kidney disease (CKD). A total of 120 type 2 diabetes mellitus (T2DM) patients with chronic kidney disease (CKD) were enrolled and randomly divided into two groups. Group A (60 patients taking vildagliptin 50 mg) and Group B (60 patients taking linagliptin 5 mg). Both groups received respective medication along with metformin 500 mg and glimepiride 2 mg. Baseline demographic and diagnostic findings showed similar results between Group A and Group B. Both groups experienced significant improvements in FBG and PPG levels, along with a notable reduction in creatinine levels. LDL-C levels decreased in both groups, but the change was only statistically significant in Group B. Additionally, creatinine and AST levels significantly decreased in both groups. At follow-up, Group B had significantly lower PPG levels compared to Group A. Both vildagliptin and linagliptin are effective and safe for type 2 diabetes patients with chronic kidney disease. However, linagliptin shows some superiority over vildagliptin in controlling postprandial glucose levels.

CBMJ 2025 January: Vol. 14 No. 01 P: 96-100

Keywords: Type 2 diabetes mellitus, chronic kidney disease, efficacy, vildagliptin, linagliptin

Introduction

The prevalence of chronic kidney disease (CKD) is rising globally, with higher rates in developing countries.[1] Diabetic nephropathy (DN) has become the most common underlying cause of end-stage renal disease (ESRD) requiring dialysis in many countries.[2] Renal impairment (RI) is prevalent among patients with type 2 diabetes[3], as diabetes is a leading cause of kidney failure and ESRD.[4] Managing patients with type 2 diabetes and severe RI presents significant challenges, as therapeutic options are limited due to contraindications and / or the

1. *Dr. Sultan Ahmed, Associate Professor, Department of Medicine, Community Based Medical College, Bangladesh.
2. Dr. Mahmud Javed Hasan, Associate Professor and Head of Department of Nephrology, Community Based Medical College, Bangladesh.
3. Dr. Md. Abdul Bari, Associate Professor, Department of Medicine, Community Based Medical College, Bangladesh.
4. Professor Dr. Md. Aminul Islam, Professor, Department of Medicine, Community Based Medical College, Bangladesh.
5. Dr. Md. Rezaul Alam, Assistant Professor, Department of Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
6. Dr. Ferdous Jahan, Assistant Professor, Department of Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
7. Dr. Rafiqul Hasan, Associate Professor, Rangamati Medical College, Bangladesh.
8. Dr. ASM Julfekar Helal, Associate Professor, Department of Nephrology, Ad-Din Medical College Hospital, Dhaka, Bangladesh.

Address of Correspondence:
Email: drsultan1975@gmail.com

increased risk of hypoglycemia in this patient group.[5] Hypoglycemia is more common in patients with renal impairment (RI) due to decreased renal gluconeogenesis.[6] Overexposure to insulin secretagogues or exogenous insulin often increases the risk of hypoglycemia.[7] Dipeptidyl peptidase-4 (DPP-4) inhibitors, such as vildagliptin and linagliptin, are generally well tolerated and approved for use in patients with severe RI. Their glucose-dependent mechanism of action means they are typically associated with a low risk of hypoglycemia, making them an attractive treatment option for these difficult-to-treat patients.[8] All DPP-4 inhibitors enhance glycemic control by extending the meal-induced increases in glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) by slowing the inactivation rate of these peptides. However, there are differences in their mechanisms of action, particularly in their catalytic binding kinetics, which might lead to clinical variations. For instance, vildagliptin blocks DPP-4 through substrate-like binding to the enzyme's active site for an extended period.[8,9] In contrast, linagliptin operates through competitive enzyme inhibition8. Notably, only vildagliptin has been demonstrated to block the inactivation of GLP-1 and GIP between meals and overnight.[9,10] The objective of this study was to compare the efficacy and safety of vildagliptin and linagliptin in T2DM patients with chronic kidney disease.

Methods

This randomized comparative study was conducted in the Department of Medicine, Community Based Medical College, Bangladesh (CBMC,B) Hospital, Mymensingh, Bangladesh, between January and December of 2023. We enrolled 120 type 2 diabetic patients with chronic kidney disease in this study. Participants were randomly assigned into two groups. Group A, consisting of 60 patients, received vildagliptin (50 mg) once daily, while Group B, also with 60 patients, received linagliptin (5 mg) daily. Both groups received respective medication as adjunctive therapy alongside metformin (500 mg) and glimepiride (2 mg).

Inclusion Criteria: Male and female patients with type 2 diabetes mellitus and chronic kidney disease were included. Additional criteria were fasting blood glucose (FBG) levels greater than 126 mg/dl, postprandial blood glucose (PPBG) over 200 mg/dl, and HbA1c levels between 7–10%.

Exclusion Criteria: Patients diagnosed with type 1 diabetes mellitus were not included in the study. The follow-up data were collected after 24 weeks of treatment.

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 27.0 for Windows. To compare the mean values between groups, the student’s t-tests were utilized. A p-value of less than 0.05 was considered indicative of statistical significance. This threshold was used to determine meaningful differences between the treatment groups for various clinical parameters. The study was approved by the Ethical Review Committee of Community Based Medical College, Bangladesh (CBMC,B), Mymensingh, Bangladesh.

Results

In this study, the mean age of the participants was 52.1 years in group A and 51.9 years in group B. 66.7% were males and 33.3% were females for group A, while group B comprising

68.3% males and 31.7% females. BMI measured 27.3 kg/m² in group A compared to 27.1 kg/m² in group B. Mean systolic blood pressure was 132.2 mm Hg in group A and 131.8 mm Hg in group B, while mean diastolic pressure was 84.2 mm Hg and 84.1 mm Hg in group A and group B respectively. Disease duration averaged 6.8 years for group A and 6.9 years for group B. The baseline diagnostic findings revealed close similarities between group A and group B, with no significant differences observed (p>0.05) (Table-I).

Among the group A participants, there was a significant improvement in FBG (p=0.018) and PPG (p<0.001) levels and additionally, there was a noteworthy reduction in creatinine levels (p=0.0262). Although LDL-C levels decreased, this change was not statistically significant (p=0.076). Changes in HDL-C, eGFR, and ALT were not statistically significant (p>0.05). However, there was a significant reduction in AST levels (p<0.001) (Table-II).

Among the group B participants, FBG (p=0.002) and PPG (p<0.001) levels significantly improved. Additionally, there was a substantial reduction in LDL-C levels (p<0.001). The creatinine levels also significantly decreased (p<0.001). There was a modest, yet significant reduction in AST levels (p=0.048). However, changes in HDL-C, eGFR, and ALT were not statistically significant (p>0.05) (Table-III). At the follow-up stage, the comparison between groups A and B revealed that differences were not statistically significant (p>0.05). However, PPG levels were significantly lower in group B compared to group A (p=0.040) (Table-IV).

Table-I: Demographic data of the participants (N=120)

Variables	Group A (n=60)	Group B (n=60)
	Mean ±SD/%	
Mean Age (in years)	52.1±12.7	51.9±12.5
Sex		
Male	66.70%	68.30%
Female	33.50%	31.70%
BMI (Kg/m^2)	27.3±5.4	27.1±5.5
SBP (mm Hg)	132.2±17.5	131.8 ± 16.9
DBP (mm Hg)	84.2±7.9	84.1±8.2
Duration of disease (in years)	6.8±1.8	6.9±1.9

Table-II: Comparison between baseline and follow-up diagnostic findings in group A (n=60)

Diagnostic findings	Baseline	Follow-up	p-value
	Mean ±SD		
FBG (mg/dl)	147.9±33.5	135.4±22.4	0.018
PPG (mg/dl)	227.6±9.4	178.4±12.6	<0.001
LDL-C (mg/dl)	148.5±29.6	126.2±25.7	0.076
HDL-C (mg/dl)	56.3±11.8	57.3±11.8	0.643
eGFR (ml/min/1.37m^2)	102.4±25.6	99.7±26.9	0.5744
Creatinine (mg/dl)	0.81±0.2	0.68±0.4	0.0262
AST (IU/L)	34.2±15.2	32.3±12.6	<0.001
ALT (IU/L)	44.5±27.5	4 1.9±19.3	0.550

Table-III: Comparison between baseline and follow-up diagnostic findings in group B (n=60)

Diagnostic findings	Baseline	Follow-up	p-value
	Mean ±SD		
FBG (mg/dl)	148.2±32.8	129.7± 29.4	0.002
PPG (mg/dl)	227.3±9.2	173.5±13.2	<0.001
LDL-C (mg/dl)	149.2±28.8	117.4±26.5	<0.001
HDL-C (mg/dl)	56.5±11.1	59.2±12.4	0.211
eGFR (ml/min/1.37m^2)	101.7±26.2	103.3±22.9	0.722
Creatinine (mg/dl)	0.79±0.2	0.61±0.2	<0.001
AST (IU/L)	33.9±16.1	30.4±13.4	0.048
ALT (IU/L)	43.8±26.6	40.2±18.4	0.390

Table-IV: Comparison between diagnostic findings in both groups at the follow-up stage

Diagnostic findings	Group A (n=60)	Group B (n=60)	p-value
	Mean ±SD		
FBG (mg/dl)	135.4±22.4	129.7± 29.4	0.235
PPG (mg/dl)	178.4±12.6	173.5±13.2	0.040
LDL-C (mg/dl)	126.2±25.7	117.4±26.5	0.067
HDL-C (mg/dl)	57.3±11.8	59.2±12.4	0.392
eGFR (ml/min/1.37m^2)	99.7±26.9	103.3±22.9	0.432
Creatinine (mg/dl)	0.68±0.4	0.61±0.2	0.228
AST (IU/L)	32.3±12.6	30.4±13.4	0.425
ALT (IU/L)	41.9±19.3	40.2±18.4	0.622

Discussion

The mean age of patients was 52.1 years in Group A and 51.9 years in Group B, with a male predominance observed in both groups. These demographic trends align with findings from other similar studies.[11,12] The baseline diagnostic findings in our study showed close similarities between Group A and Group B, with no significant differences across health indicators, as evidenced by p-values greater than 0.05 in all parameter comparisons. In Group A, vildagliptin significantly improved fasting blood glucose (FBG), postprandial glucose (PPG), and creatinine levels, suggesting enhanced glucose control and kidney function. While LDL-C levels decreased, this change wasn't statistically significant. HDL-C, eGFR, and ALT showed no significant changes. A notable reduction in AST levels hinted at improved liver function. These results align with findings from another study.[13] In the linagliptin group, there was a significant improvement in fasting blood glucose (FBG) and postprandial glucose (PPG) levels, enhancing glycemic control. LDL-C levels substantially decreased, benefiting cardiovascular health. Significant reductions in creatinine levels suggest improved renal function and a modest reduction in aspartate transaminase (AST) levels indicates potential liver health benefits. No significant changes were observed in high-density lipoprotein cholesterol (HDL-C), estimated glomerular filtration rate (eGFR), and alanine transaminase (ALT). Overall, linagliptin positively impacted glucose control, cholesterol levels, and kidney function, with some improvements in liver health, mirroring findings from Zaman *et al.*[14] At the follow-up stage, comparing the vildagliptin (group A) and linagliptin (group B) groups revealed no statistically significant differences in most diagnostic findings. However, Group B had significantly lower postprandial glucose (PPG) levels (p=0.040), indicating a slight advantage in postprandial glucose control. Overall, both groups showed improvements, but Group B had a notable edge in managing PPG levels, aligning with findings by Zaman *et al.*[14] Previous reports indicate that DPP-4 inhibitors effectively decrease HbA1c levels, helping patients achieve glycemic control both as monotherapy and in combination therapy.[15,16] These inhibitors differ in their elimination pathways, which influence their clinical use. Linagliptin and sitagliptin are primarily eliminated unchanged, experiencing minimal metabolism. In contrast, vildagliptin undergoes cytochrome P450 (CYP)-independent hydrolysis, with recent data indicating that DPP-4 itself is responsible for 60% of its elimination.[17,18]

Conclusion

In managing type 2 diabetes patients having chronic kidney disease, both vildagliptin and linagliptin were found safe and effective treatment options. However, linagliptin may offer some advantages over vildagliptin, particularly in

controlling postprandial glucose levels. This distinction can be crucial for optimizing glycemic control, leading to improved patient outcomes.

References

1. *Tahrani AA, Barnett AH, Bailey CJ. Pharmacology and therapeutic implications of current drugs for type 2 diabetes mellitus. Nat Rev Endocrinol. 2016;12(10):566-92.*
2. *Rhee CM, Leung AM, Kovesdy CP, Lynch KE, Brent GA, Kalantar-Zadeh K. Updates on the management of diabetes in dialysis patients. Semin Dial. 2014;27(2):135-45.*
3. *de Boer IH, Rue TC, Hall YN, Heagerty PJ, Weiss NS, Himmelfarb J. Temporal trends in the prevalence of diabetic kidney disease in the United States. JAMA. 2011;305(24):2532-9.*
4. *Villar E, Zaoui P. Diabetes and chronic kidney disease: lessons from renal epidemiology. [Article in French]. [Abstract]. Nephrol Ther. 2010;6(7):585-90.*
5. *Lubowsky ND, Siegel R, Pittas AG. Management of glycemia in patients with diabetes mellitus and CKD. Am J Kidney Dis. 2007;50(5):865-79.*
6. *Gerich JE, Meyer C, Woerle HJ, Stumvoll M. Renal gluconeogenesis: its importance in human glucose homeostasis. Diabetes Care. 2001;24:382-91.*
7. *Arem R. Hypoglycemia associated with renal failure. Endocrinol Metab Clin N Am. 1909;18:103-21.*
8. *Scheen AJ. Pharmacokinetics and clinical use of incretin-based therapies in patients with chronic kidney disease and type 2 diabetes. Clin Pharmacokinet. 2015;54:1-21.*
9. *Ahrén B, Schweizer A, Dejager S, Villhauer EB, Dunning BE, Foley JE. Mechanisms of action of the dipeptidyl peptidase-4 inhibitor vildagliptin in humans. Diabetes Obes Metab 2011;13:775-83.*
10. *Davis JA, Singh S, Sethi S, Roy S, Mittra S, Rayasam G, et al. Nature of action of Sitagliptin, the dipeptidyl peptidase-IV inhibitor in diabetic animals. Indian J Pharmacol. 2010;42(4):229-33.*
11. *Kothny W, Lukashevich V, Foley JE, Rendell MS, Schweizer A. Comparison of vildagliptin and sitagliptin in patients with type 2 diabetes and severe renal impairment: a randomised clinical trial. Diabetologia. 2015;58(9):2020-6.*
12. *Rizzo MR, Barbieri M, Marfella R, Paolisso G. Reduction of oxidative stress and inflammation by blunting daily acute glucose fluctuations in patients with type 2 diabetes: role of dipeptidyl peptidase-IV inhibition. Diabetes Care. 2012;35(10):2076-82.*
13. *Suthakaran C, Bhaskaran S. Comparative effectiveness of sitagliptin and vildagliptin in the management of patients with type 2 diabetes mellitus undergoing haemodialysis: an Indian rural tertiary care centre experience. Int J Basic Clin Pharmacol. 2018;7(7):1268-72.*
14. *Zaman ZA, Sinha HK. Comparison between the effect of vildagliptin and linagliptin on glycaemic control, renal function, liver function, and lipid profile in patients of T2DM inadequately controlled with a combination of metformin and glimepiride. J Dent Med Sci. 2017;16:27-31.*
15. *McKeage K. Linagliptin: an update of its use in patients with type 2 diabetes mellitus. Drugs. 2014;74(16):1927-46.*
16. *Neumiller JJ. Pharmacology, efficacy, and safety of linagliptin for the treatment of type 2 diabetes mellitus. Ann Pharmacother. 2012 Mar;46(3):358-67.*
17. *Lo C, Toyama T, Wang Y, Lin J, Hirakawa Y, Jun M, et al. Insulin and glucose-lowering agents for treating people with diabetes and chronic kidney disease. Cochrane Database Syst Rev. 2018;9(9):CD011798.*
18. *He H, Tran P, Yin H, Smith H, Batard Y, Wang L, et al. Absorption, metabolism, and excretion of [14C] vildagliptin, a novel dipeptidyl peptidase 4 inhibitor, in humans. Drug Metab Dispos. 2009;37(3):536-44.*