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Effect of Different Dipeptidyl Peptidase-4 Inhibitors on Lipid Profile of Type II Diabetic Patients

Omran T. Z.
College of Pharmacy, University of Al-Ameed, Karbala, Iraq
Email: tukafaji@alameed.edu.iq

Ismaeel G. L.
College of Pharmacy, University of Al-Ameed, Karbala, Iraq

***Abstract*---**Objective: In this research study, we aimed to study the effect of dipeptidyl peptidase-4 inhibitors (Gliptins drug) on the lipid profile of diabetic type 2 patients. Materials/methods: Type 2 diabetic (200) patients taking Gliptin ± metformin and willing to participate in the study were included. Lipid profile tests (total cholesterol, HDL, non-HDL, LDL, VLDL, triglycerides level) of the patients were done in a pathological laboratory on routine health checkups. The mean and S.E.M of each parameter were calculated. All data were subjected to a Student's t-test. Comparison between the treatments was done by using one-way ANOVA- Bonferroni multiple comparison tests. Results: All 200 patients have completed the questionnaire and monitored twice for six months (initial visit and final visit). Of the total participants, 109 (54.50%) were males and 91 (45.50%) were females. Ninety tow (46%) were taking vildagliptin + metformin while 73 (36.5%) patients were taking vildagliptin, 20 (10%) were taking sitagliptin + metformin, 15 (7.5%) were taking linagliptin and only 1 (0.5%) patients were taking sitagliptin Conclusions: The present findings showed that vildagliptin can reduce the total cholesterol level, Non-HDL level, and triglycerides significantly. Linagliptin can reduce the total cholesterol Level and non-HDL significantly. Combination therapy of vildagliptin + metformin can reduce the total cholesterol level and non-HDL level significantly. While the combination therapy of sitagliptin + metformin can reduce the LDL level significantly.

***Keywords*---**cholesterol level, diabetes mellitus, lipid profile, metformin, vildagliptin.

Introduction

Diabetes is a metabolic disease that has been diagnosed based on the sustained high concentration of glucose in the blood. The criteria for diagnosis of diabetes mellitus include Fasting plasma glucose > 126mg/dl, symptoms of DM plus Random plasma glucose level > 200 mg /dl, or a 75 g test of oral glucose tolerance where 2-h plasma glucose > 200 mg/dl (1). The appearance of diabetes becomes obvious when there is an insufficiency in the scale of insulin and when there is unresponsive to its effect by the different body cells. The damage that occurs in eyes, kidneys, and nerve functions along with cardiovascular disorders and some cases amputation of lower limbs are related to the intricacies of diabetes disease (2). An autoimmune disease that results from the destruction of pancreatic beta cells causes diabetes of type 1(3). To avoid complications like ketoacidosis or in severe cases coma and maybe death, the insulin level is vital for such patients and must be under control.

The predominant features of patients with type 2 diabetes are insulin resistance and can be the disorders that are related to the secretion of insulin (4). These individuals do not require insulin for their treatment. The predominant type of diabetes is type 2 and it is often motivated by overweight and in genetically inclined patients (3). Diabetes is a disease that non-recuperate, the progression of the disease and its complications can be handled by different means leading to control of the glycemic index of the patients (5, 6).

One of the important established factors that bring about cardiovascular jeopardy in diabetic type 2 patients is their lipid profile levels and these patients are vulnerable to undergo dyslipidemia (7, 8). These macrovascular complications could be miniatured by controlling hyper-cholesterolemia (9, 10). The elevated level of triglycerides, low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and the scarcity in the level of high-density lipoprotein cholesterol (HDL-C) are all the exponents for the abnormalities in lipid profile (9, 11). These reference values along with apolipoprotein glycation and continuous elevation of the oxidation rate of LDL contributed to the atherosclerosis cells proliferation (12). By concerning the metabolism rate of lipid and glucose levels in patients with type 2 diabetes, it was found that the glucose detraction agents can positively affect the lipid profile.

Gliptins are DPP-4 inhibitors that act selectively, it is also termed incretin enhancers. This group includes vildagliptin, sitagliptin, saxagliptin, linagliptin, alogliptin, dutogliptin, and gemigliptan. Sitagliptin, vildagliptin, and saxagliptin are approved for use in India (13). It is found that gliptins have the metier in elevating the level of endogenous incretin by the prohibition of the swift degradation of both GLP-1 and GIP levels (14). The glycaemic control and its improvement level with DPP-4 inhibitors are moderate and could be effectual in combination with other hypoglycemic drugs like metformin, Thiazolidinedione, and Sulphonylurea i.e they are considered as an appealing option in type 2 diabetes treatment (15).

These drugs can be taken in a single dose once /day, less causing hyperglycemia, do not raise weight gain, and well-tolerated. (16). These distinctive countenances

are against the widespread adverse effects of other available hypoglycaemic medicines. Although they have all the previously indicated advantages, they could be unconsumed as the primary choice for the standard treatment because less data safety is available and considerably of soaring cost (17).

It can be suggested for the treatment in overweight patients because they are weight-impartial. Beta-cell growth and proliferation are affected by raised levels of GLP-1, so it requisites to evaluate the effective role of Gliptins in banning the failure of beta-cell in diabetic patients (18). A further study is coveted to emphasize the possible prohibition of the decadence of glucose tolerance.

Patients Materials and Methods

Two hundred patients with type 2 Diabetes mellitus taking Gliptin ± metformin and willing to participate in the study were included. The study includes informing the patients about the detailed procedure and written consent were obtained. Their demographic data, history of illness, and drug history had noted and their medical records were checked. This study involves only the collection of patient data without intervention. Ratification of the research work was achieved by the ethics committee of Inamdar Multispecialty Hospital, Pune India (Ref. No. IMH/EC/62-12-13).

Lipid profile tests (total cholesterol, HDL, non-HDL, LDL, VLDL, triglycerides level) of the patients were done in a pathological laboratory on routine health checkups. The values of these investigations at the initial visit and final visit after 6 months duration of Gliptins treatment were noted as mentioned on the medical records of the patients. Any side effect of the drug reported by patients/mentioned on their medical records was also noted. The mean and S.E.M of each parameter were calculated. All data were subjected to the student's t-test. Comparison between the treatments was done by using one-way ANOVA- Bonferroni multiple comparison tests.

Results

A total of 200 type 2 diabetic patients have completed the questionnaire and were monitored twice for six months (initial visit and final visit). Of the total participants, 109 (54.50%) were males and 91 (45.50%) were females as presented in figure 1.

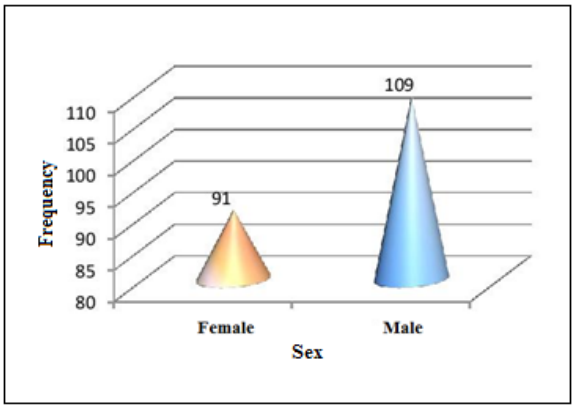

Figure 1. Distribution of patients according to gender

Sixty tow (31%) of patients were of the age group of 50-60 years while 3 (1.5%) of the age group 80-90 years were founded. The age's mean of the patients was 55.53 years with S.D. 11.37 as presented in figure 2.

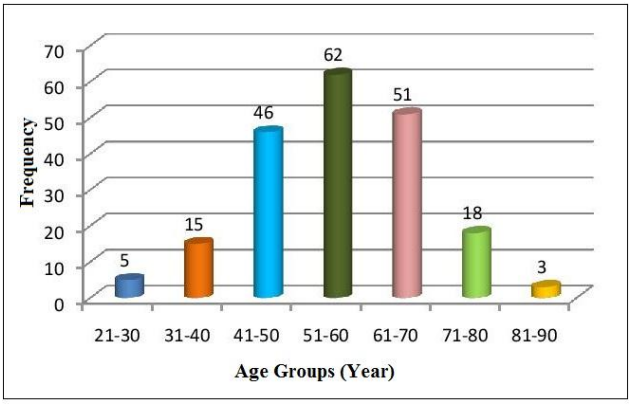

Figure 2. Distribution of patients according to age

Ninety tow (46%) of patients were taking vildagliptin + metformin while 73 (36.5%) patients were taking vildagliptin, 20 (10%) were taking sitagliptin + metformin, 15 (7.5%) were taking linagliptin and only 1 (0.5%) patients were taking sitagliptin as presented in figure 3.

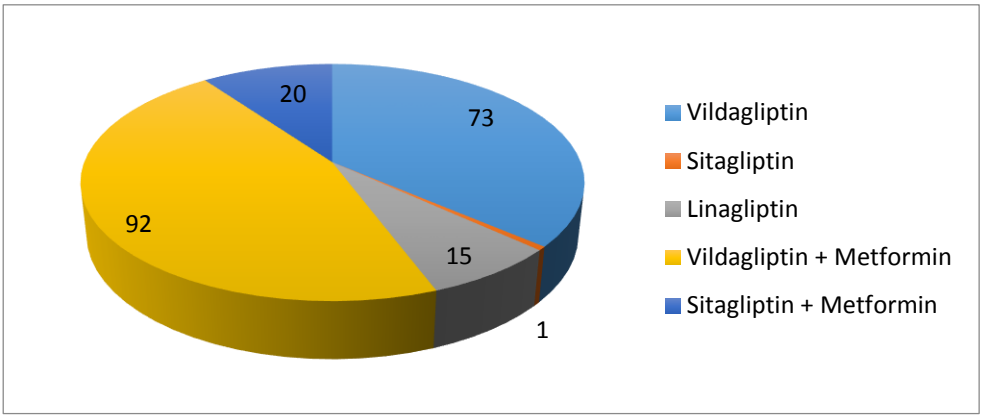

Figure 3. Distribution of patients according to various Gliptins

The total cholesterol level of vildagliptin treatment at the initial visit was 170.8 ± 4.04 mg/dl and at the final visit, it was 148 ± 3.77 mg/dl. A highly significant decrease ($p<0.001$) in the level of total cholesterol was spotted at the final visit which indicates that vildagliptin had good control on the total cholesterol level. When all the treatments were compared with each other, no significant decrease ($p >0.05$) was observed in total cholesterol as presented in Table 1.

Table 1
Comparison of the effect of Gliptins and its combinations on total cholesterol level (mg/dl) at the initial and final visit

Treatment	Initial visit	Final visit	*P*-value
Vildagliptin (n= 73)	45.62 ± 1.12	43.55 ± 1.28	>0.05
Sitagliptin (n=1)	36	30	
Linagliptin (n=15)	45.13 ± 2.98	42.93 ± 2.29	>0.05
Vildagliptin + metformin(n=92)	43.64 ± 0.98	43.74 ± 1.06	>0.05
Sitagliptin + metformin(n=20)	48.75 ± 3.66	46.21 ± 2.35	<0.05

Mean ± SEM were explicit for all the values. The data were analyzed using the student's t-test. * indicate ($p<0.05$), ** indicate ($p<0.01$), and *** indicate ($p<0.0001$).

The HDL level of the patients on the treatment of vildagliptin at the initial visit was found to be 45.62 ± 1.12 mg/dl and at the final visit, it was 43.55 ± 1.28 mg/dl. No significant difference ($p>0.05$) in HDL level was observed between the initial visit and final visit.When all the treatment groups were compared with each other, no significant difference ($p<0.05$) was observed in HDL level as presented in Table 2.

Table 2
Comparison of effect of Gliptins and its combinations on HDL level (mg/dl) at initial and final visit

Treatment	Initial visit	Final visit	*P*-value
Vildagliptin (n= 73)	170.8 ± 4.04	148 ± 3.77 ***	<0.001
Sitagliptin (n=1)	166	112	

Linagliptin (n=15)	179.3 ± 11.61	147 ± 6.48*	<0.05
Vildagliptin + metformin (n=92)	167.1 ± 3.75	149 ± 3.54**	<0.001
Sitagliptin + metformin (n=20)	163.3 ± 9.69	151 ± 14.3	>0.05

The LDL level in patients taking vildagliptin at the initial visit was 94.75 ± 3.35 mg/dl and at the final visit, it was 95.92 ± 14.92 mg/dl. No significant decrease ($p>0.05$) in LDL level was found when the initial visit and final visit were compared. When all the treatment groups were compared with each other, no significant decrease ($p<0.05$) was observed in LDL level as presented in Table 3

Table 3
Comparison of the effect of Gliptins and its combinations on LDL level (mg/dl) at the initial and final visit

Treatment	Initial visit	Final visit	*P*-value
Vildagliptin (n= 73)	94.75 ± 3.35	95.92 ± 14.92	>0.05
Sitagliptin (n=1)	85	47	
Linagliptin (n=15)	95.53 ± 8.69	79.33 ± 6.49	>0.05
Vildagliptin + metformin (n=92)	92.14 ± 3.07	91.59 ± 10.16	>0.05
Sitagliptin + metformin (n=20)	88.37 ± 5.70	72.58 ± 4.98*	>0.05

The non-HDL level for the patients on the treatment of vildagliptin at the initial visit was 125.9 ± 4.16 mg/dl and at the final visit, it was 104.1 ± 3.52 mg/dl. A highly significant decrease ($p<0.0001$) was observed in the non-HDL level between the initial visit and final visit which indicates that vildagliptin had good control on the non-HDL level. When all the treatment groups were compared with each other, no significant decrease ($p<0.05$) was observed in non-HDL levels as presented in Table 4.

Table 4
Comparison of the effect of Gliptins and its combinations on Non-HDL level (mg/dl) at the initial and final visit

Treatment	Initial visit	Final visit	*P*-value
Vildagliptin (n= 73)	125.9 ± 4.16	104.1 ± 3.52***	0.001
Sitagliptin (n=1)	130	82	
Linagliptin (n=15)	134.1 ± 11.41	106.1 ± 6.14*	<0.05
Vildagliptin + metformin (n=92)	123.9 ± 3.81	104.6 ± 3.52**	<0.001
Sitagliptin + metformin (n=20)	116.7 ± 8.70	105.2 ± 13.78	>0.05

The VLDL level of the patients on the treatment of vildagliptin was found to be 29.49 ± 2.37 mg/dl at the initial visit and final visit; it was 26.42 ± 2.51 mg/dl. No significant decrease ($p>0.05$) in VLDL level was observed between the initial visit and final visit. When all the treatment groups were compared with each other, no significant decrease ($p>0.05$) was observed in the VLDL level as presented in Table 5.

Table 5
Comparison of the effect of Gliptins and its combinations on VLDL level (mg/dl) at the initial and final visit

Treatment	Initial visit	Final visit	*P*-value
Vildagliptin (n= 73)	29.49 ± 2.37	26.42 ± 2.51	>0.05
Sitagliptin (n=1)	45	55	
Linagliptin (n=15)	29.13 ± 3.28	27.27 ± 2.57	>0.05
Vildagliptin + metformin (n=92)	28.10 ± 1.39	26.77 ± 1.21	>0.05
Sitagliptin + metformin (n=20)	21.48 ± 2.50	31.26 ± 12.76	>0.05

The triglycerides level of the patients on the treatment of vildagliptin at the initial visit was 146.7 ± 8.23 mg/dl and at the final visit, it was 121.7 ± 6.13 mg/dl. A significant decrease ($p<0.05$) in triglycerides level was observed between the initial visit and final visit indicating that vildagliptin had good control on triglycerides level. As presented in Table 6 when all the treatment groups were compared with each other, no significant decrease ($p<0.05$) was observed in triglycerides level.

Table 6
Comparison of effect of Gliptins and its combinations on triglycerides level (mg/dl) at initial and final visit

Treatment	Initial visit	Final visit	*P*-value
Vildagliptin (n= 73)	146.7 ± 8.23	121.7 ± 6.13*	<0.05
Sitagliptin (n=1)	227	175	
Linagliptin (n=15)	154.7 ± 19.86	131.1 ± 13.01	>0.05
Vildagliptin+ metformin (n=92)	146.0 ± 6.93	133.2 ± 6.38	>0.05
Sitagliptin + metformin (n=20)	118.8 ± 13.61	151.5 ± 64.11	>0.05

Discussion

There are various drugs used for the management of diabetes mellitus type 2. Gliptins are recent oral drugs for the treatment of type 2 diabetes mellitus, level of blood glucose reduced by a novel mechanism i.e by the prohibition of the enzyme dipeptidyl peptidase-IV, thereby increasing the circulating levels of incretins (19). Controlling the glycemic index when compared with a thiazolidinedione, metformin, and sulphonylureas were found to be more leverage. They are potentially an attractive therapeutic option in the treatment of type 2 diabetes (20).

A total of 200 patients participated in the study comprising 109 (54.50%) males and 91 (45.50%) females with an average age of 55 years. It was found that about 92 (46%) of the patients were taking vildagliptin + metformin, 73 (36.5%) patients were taking vildagliptin, 20 (10%) were taking sitagliptin + metformin, 15 (7.5%) were taking linagliptin and only 1 (0.5%) patient was taking sitagliptin. The effect of Gliptins alone and in combination with metformin studied on metabolic syndrome at two-point visits i.e. with an interval of six months.

Considering the lipid profile, the effect of Gliptins on total cholesterol was found that vildagliptin, linagliptin, and vildagliptin + metformin showed a significant

decrease between the initial visit and the final visit where they reduced the total cholesterol to the normal level. Hence, these three drugs can be given to diabetic patients for preventing or controlling their metabolic syndrome as they have approximately the same effect on total cholesterol. A study by Kusunokiet et., (21) have found similar results to our investigation as did a meta-analysis review article by Monami et al. (22).

The combination therapy of sitagliptin + metformin had no significant decrease between the initial visit and the final visit so they do not produce a noted reduction in total cholesterol level. Similar results were found in the literature on the effects of DPP-4 inhibitors on lipids (22, 23). A study by Caroline (24) found that the effect on lipid profile was not significant in patients with sitagliptin.

For HDL, all four treatments of monotherapy and combination therapy had no significant decrease between the initial visit and the final visit, so they do not produce any reduction of HDL level. As they prevent the reduction in HDL level so this leads further to control the metabolic syndrome, diabetes mellitus, and cardiovascular diseases which in turn suggest that these drugs are preferred for the treatment of the late diseases. Studies have found similar results (9, 25) while on the contrary, a study by cha et al. found that Sodium-glucose linked transporter (SGLT2) is a preferable add-on to metformin (25).

LDL considered as bad cholesterol, so lowering LDL level having advanced in controlling the metabolic syndrome. Vildagliptin and vildagliptin + metformin showed the same effect on LDL level where there was no significant decrease between the initial visit and the final visit. Linagliptin showed a reduction in LDL near to the normal level but there was no significant decrease between the initial visit and the final visit. Only sitagliptin + metformin showed a significant decrease between the initial visit and final visit, therefore this combination may be the preferred treatment for controlling the bad cholesterol in a diabetic patient having metabolic syndrome. The test for non-HDL cholesterol is not usually part of screening for the total cholesterol. When the triglyceride level of the patients is above 200 mg/dl, then non–high-density lipoprotein cholesterol (non–HDL-C) is a more precise therapeutic target than LDL cholesterol.

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Conflict of interest

The authors had no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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