International Journal of Research and Review
Vol.7; Issue: 12; December 2020
Website: www.ijrrjournal.com
Original Research Article *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

Effect of Vildagliptin on Cardiac and Endothelial Function as Compared to Metformin in Type 2 Diabetes Mellitus Patients with Cardiomyopathy

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ABSTRACT

AIM: The main objective of the study was to evaluate the effect of vildagliptin on cardiac and endothelial function as compared to metformin in type 2 diabetes mellitus patients with cardiomyopathy.

Materials and Methods: This was a retrospective study which was conducted at a tertiary out patients department clinic at Chapra district in Bihar. One group of patients received vildagliptin 50 mg BID along with other oral therapy and insulin but were not on metformin. While other group received metformin 1000 to 2000 mg OD or BID along with other oral therapies and insulin but were not on vildagliptin. Demographic data were collected by using predesigned proforma in Microsoft excel sheet and electrocardiographic data at baseline and 1 year follow up were also documented.

Result: It has been found that patients who were on vildagliptin group were having much improved echocardiographic values as compare to the patients who were on metformin based treatment. Both systolic and diastolic blood pressure were well controlled in vildagliptin group (132.5±3.2 to 124.3±3.6 mmHg and 86.2±2.8 to 78.3±2.9 mmHg, respectively) as compare to metformin group (138.2±6.1 to 133.1±5.7 and 88.4±3.2 to 83.5±4.1 respectively) (p=0.005). Ejection fraction (EF) were significantly improved in vildagliptin based group (from 65.8±2% to 69.8±1.7%) as compare to metformin based group (from 64.3±2.9% to 65.4±1.7%)(p=0.005).

Conclusion: This retrospective observation demonstrated in patients treated with a dipeptidyl peptidase-4 inhibitor over 12 months, a significant improvements in endothelial diastolic and LV systolic function, as compared to the patients treated with metformin over 12 months.

Keywords: Diabetes Mellitus, Cardiac function, Metformin, Dipeptidyl peptidase-4 inhibitor.

INTRODUCTION

A lot of vascular damage may accrue in the pre diabetic period in association with insulin resistance (IR) [1]. Insulin, a peptide hormone secreted from pancreatic β cells into portal circulation is response to glucose, free fatty acids and amino acids facilitates their cellular uptake and processing of building blocks for storage in the forms of glycogen, triglycerides and protein [2]. Resistance to insulin stimulated glucose uptake is present in the majority of patients with impaired glucose tolerance (IGT) or non-insulin dependent diabetes mellitus. And in approximately 25% of nonobese individuals with normal oral glucose tolerance [3].

Impaired endothelial function is not only antecedent to atherosclerosis, but is also demonstrable in the early stages of type 2 diabetes and is likely to precede the onset of microalbuminuria [4]. People with impaired glucose tolerance (IGT), first degree relatives of type 2 diabetes have increased circulating concentration of markers of ED, including soluble vascular cell adhesion molecule (sVCAM), soluble intracellular adhesion molecule (sICAM), endothelin (ET-1) and von Willebrand factor (vWF). This data support the notion that there is macrovascular risk well before the development of overt type 2 diabetes [5].

Incretin-based therapies like dipeptidyl peptidase-4 inhibitor (DPP4i), like vildagliptin, a new class of anti-hyperglycaemic drugs which as compare to conventional therapy [6-9]. Like metformin, have different mechanisms of action. Multiple potentially beneficial effects, including reduction of cardiovascular risk, protective effects on endothelial function, reduction in ischaemic/reperfusion injury, cholesterol and blood pressure lowering, improvements in LV contractile performance and anti-fibrotic effects have been demonstrated by vildagliptin along with other dipeptidyl peptidase-4 inhibitor (DPP4i), in patients with T2DM [6-9].

The main objective of the study was to evaluate the effect of vildagliptin on cardiac and endothelial function as compare to metformin in type 2 diabetes mellitus patients with cardiomyopathy.

MATERIALS AND METHODS

This was a retrospective study which was conducted at a tertiary out patients department clinic at Chapra district in Bihar. Patients' data were recorded from the patients OPD chart, clinical reports and mainly from the clinical records maintain at the investigation centres. Any patients who were diabetic and having documented cardiomyopathy were included in this study. Patients who were fails to maintain their clinical reports, discontinued their treatment for any reason and the patients who denied to participate in the study were excluded. For those patients who fulfils the inclusion criteria a sign informed consent were obtained.

Patients were mainly divided into two groups. One group of patients received vildagliptin 50 mg BID along with other oral therapy and insulin but were not on metformin. While other group received metformin 1000 to 2000 mg OD or BID along with other oral therapies and insulin but were not on vildagliptin.

Demographic data were collected by using predesigned proforma in Microsoft excel sheet and electrocardiographic data at baseline and 1 year follow up were also documented.

Microsoft excel sheet were used to collect the data thereafter with help of SPSS 22.0 data were analysed. A descriptive bivariate analysis was performed; for the chi-squared distribution, significance was assumed to be <0.05.

RESULTS

Table 1 shows the clinical characteristics of participants in both vildagliptin and metformin group. It was observed that both the group has almost similar characteristic and mirror image of each other's.

Table 1: Clinical characteristics of participants in both vildagliptin and metformin group.

Characteristics	Vildagliptin Group (N=30)	Metformin Group (N=35)	P Value
Age (Years)	59.7±12.3	62.1±11.9	0.891
Males (%)	19 (63%)	21 (60%)	0.2=498
Diabetes Duration (Years)	15.2±5.7	14.7±8.1	0.386
BMI (Kg/m2)	32.3±4.2	33.6±4.7	0.671
Hypertension (%)	25 (83%)	29 (82.8%)	0.372
Smoking History (%)	21(70%)	24 968.6%)	0.734
Dyslipidemia	27 (90%)	32 (91%)	0.842
Stroke (%)	7 (23%)	6 (17%)	0.693
Peripheral Vascular Disease (%)	2 (6.6%)	1(2.9%)	0.859
HBA1c (%)	7.4±1.1	7.3±1.2	0.836
Total Cholesterol (mg/dl)	212.32±21.27	201.32±19.89	0.698
Triglyceride (mg/dl)	211.21±17.85	218.68±18.26	0.738
LDL Cholesterol (mg/dl)	135.72±11.47	139.83±15.58	0.812
HDL Cholesterol (mg/dl)	31.4±4.5	30.3±3.9	0.937

Table 2 demonstrates the changes in ultrasound characteristics of patients after 1 year treatment with Vildagliptin and metformin group. It has been found that patients who were on vildagliptin group were having much improved echocardiographic values as compare to the patients who were on metformin based

treatment. Both systolic and diastolic blood pressure were well controlled in vildagliptin group (132.5±3.2 to 124.3±3.6 mmHg and 86.2±2.8 to 78.3±2.9 mmHg, respectively) as compare to metformin group (138.2±6.1 to 133.1±5.7 and 88.4±3.2 to 83.5±4.1 respectively) (p=0.005). Ejection fraction (EF) were significantly inproved in vildagliptin based group (from 65.8±2% to 69.8±1.7%) as compare to metformin based group (from 64.3±2.9% to 65.4±1.7%) (p=0.005).

Table 2: Change in ultrasound characteristics of patients after 1 year treatment with Vildagliptin and metformin group.

Characteristics	Vildagliptin Group (N=30)		Metformin Group (N=35)		P Value
	Baseline	Follow up	Baseline	Follow up	
Heart rate(bpm)	74.2±2.1	68.7±2.2	72.3±1.8	69.8±1.9	0.005
Systolic BP (mmHg)	132.5±3.2	124.3±3.6	138.2±6.1	133.1±5.7	0.005
Diastolic BP (mmHg)	86.2±2.8	78.3±2.9	88.4±3.2	83.5±4.1	0.005
LA Dimension (mm)	36.3±1.1	34.3±1.1	35.5±1.1±	34.2±1.1±	0.005
LA volume index (mL/m2)	28.3±1.7	26.2±1.4	31.1±1.8	30.6±1.7	0.005
LV mass index (g/m2)	84.6±6.2	77.4±2.9	87.4±3.9	88.5±4.3	0.005
LV EF(%)	65.8±2	69.8±1.7	64.3±2.9	65.4±1.7	0.005
FMD (%)	2.5±1.5	7.4±1.5	2.9±1.5	3.1±1.3	0.005

DISCUSSION

Dilated cardiomyopathy (DCM) is common in this part of the world, while restrictive cardiomyopathy is prevalent in the western countries [10-12]. In the recent years, significant controversy is noted about the definition, frequency, natural history and optimal treatment for many of these myocardial disorders [13-15]. Hence, the uses of endomyocardial biopsy in the evaluation of the patients with myocardial disease have been advocated by various centers all over the world.

In this retrospective study diabetic patients who were on vildagliptin based treatment demonstrated greater improvement in LV GLS compared to patients who were on metformin based therapy. These findings were observed despite the fact that both groups had comparable lipid profiles, glycaemic control, blood pressure, age and BMI at baseline as well as at follow-up. Several previous trials have established same reports with vildagliptin [16-18].

At high doses metformin should not be used in patients with diabetes and heart failure according to the recommendations of the international guidelines because of a risk of lactic acidosis. In patients with recent diabetes than sulfonylurea monotherapy, metformin monotherapy is associated with a lower risk of heart failure development [19]. Metformin reduced mortality of ambulatory patients with diabetes and heart failure during two years observation, treatment [20].

The severity and the type of heart failure are related with the findings of EMB. Patients with greater myocardial cellular diameter suffer from greater systolic and diastolic dysfunction [21]. The degree of fibrosis is dependent on the increased diameter of myocardial cells. This is noted in alcohol related heart disease, wherein myocardial cells are also enlarged in size. In contrast, following doxorubicin therapy, the myocardial cells remain normal or become smaller but fibrosis is prominent. Idiopathic or alcoholic cardiomyopathy shows the least fibrosis [22].

The ultrastructural studies of the biopsy tissue demonstrate the uniqueness of cardiomyopathies and sometimes provide clue to the pathogenesis [23]. Patients with doxorubicin induced cardiomyopathy show chromatin clumping and severe disarrangement in the nucleolus. In contrast, patients with viral cardiomyopathy developed super normal nuclei with nucleoli [24].

CONCLUSION

This retrospective observation demonstrated in patients treated with a dipeptidyl peptidase-4 inhibitor over 12 months, a significant improvements in endothelial. diastolic and LV systolic

function, as compared to the patients treated with metformin over 12 months.

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How to cite this article: Dubey KM. Effect of vildagliptin on cardiac and endothelial function as compared to metformin in type 2 diabetes mellitus patients with cardiomyopathy. International Journal of Research and Review. 2020; 7(12): 217-221.

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