Effect of Metformin Monotherapy and Combination Therapy with Glimepiride on Lipid Profile in Drug Naive Type-2 Diabetes Patients: A Prospective Observational Study

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Abstract

Background: Dyslipidemia is an important risk factor for development of macrovascular disease. Altered lipid metabolism and abnormality in serum lipid profile results atherogenic dyslipidemia this can worsen the prognosis of diabetic patients and increases risk of cardiovascular disease and stroke. This study aims to evaluate the effect of metformin monotherapy and combination therapy with glimepiride on lipid profile of drug naive type-2 diabetes patients after 10-12 weeks of treatment.

Methods: In this study, prescriptions of 120 OPD (Outpatient department) patients of drug naive type-2 diabetes were collected. The detailed observation of: demographic, drug details and investigations done were noted in a specially designed preform. The data was analyzed statistically and results were expressed as numbers and percentage.

Results: The total of 120 patients prescriptions was analyzed. Among these male was 62.5% and female were 37.5%, most common affected age group was between 31-50 years with mean age of 43.82 yrs. Metformin was most commonly prescribed drug 42% followed by its combination with glimepiride 58%. Average blood glucose level prior therapy was 193.4mg/dl and post therapy it was 135.2mg/dl. After 10-12 weeks of metformin monotherapy and combination therapy with glimepiride LDL was significantly reduced from 92.3mg/dl to 83.2mg/dl, TG was reduced from 145.5mg/dl to 132 mg/dl and HDL increased from 29.1 mg/dl to 32.9 mg/dl.

Conclusion: Metformin monotherapy and combination therapy with glimepiride appreciably improved dyslipidemia in drug naive type-2 diabetes patients.

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Keywords: Metformin; Glimepiride; Lipid

Introduction

Diabetes is a chronic, progressive disease characterized by hyperglycemia and altered metabolism of carbohydrate, lipid and protein. Altered lipid metabolism and abnormalities in serum lipid profile is characterized by low HDL-C, high triglycerides and total cholesterol and normal or raised LDL-C, which results in "Atherogenic Dyslipidemia" and this worsens the prognosis of diabetic patients by accelerating atherosclerosis and increasing risk of cardiovascular diseases and stroke (1). The incidence of diabetes mellitus (DM) is increasing substantially worldwide. Over the past three decades, the global burden of diabetes mellitus (DM) has swelled from 30 million in 1985 to 536 million in 2021 and 6.7 million deaths, with current trends indicating that these rates will only continue to rise (2). The latest estimates by the international diabetes federation project that 643 million (1 in 10 persons) worldwide will have DM by 2030 and 783 million by 2045 (3).

Proper control and treatment of DM is critical as both the prevalence and economic burden of the disease continue to mount. As CVD is the most prevalent cause of mortality and morbidity in patients with DM, a primary goal of diabetes treatment should be to improve the cardiovascular (CV) risk

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of diabetic patients (4). However, one challenge associated with treating DM and reducing CV events is the complex and multifaceted nature of the relationship linking DM to CVD. CV risk factors including obesity, hypertension and dyslipidemia are common in patients with DM, particularly those with T2DM (5). Diabetes treatment includes diet modification, lifestyle changes, pharmacological therapy with insulin and oral anti-diabetic agents. The drugs used in diabetes not only decrease blood sugar levels effectively but also have effect on lipid profile.

Therefore, we aim to review the effects of commonly used oral hypoglycemic on serum lipids - total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TGs) and free fatty acids (FFAs) in patients with diabetes and minimize the risk for atherogenic cardiovascular disorder and cerebrovascular accident by early detection and treatment of lipid abnormalities. Drug utilization pattern of anti-diabetic agents can further help us to follow a treatment protocol and to enhance approach to drug selection for best management and in prevention of co-morbidities

Methods

A prospective observational study was conducted in Non Communicable Diseases (NCD) clinic, Belagavi Institute of Medical Sciences, Belagavi after obtaining institutional ethical committee clearance.

Prescription of 120 OPD (Outpatient department) patients of drug naive patients of type-2 diabetes was collected for 3 months on random sampling method of first come basis. The Prescriptions collected in 3 months were followed up till end of 6th month. Total duration of the study was 6 months. The detailed observation about demographic data, drug details and investigations prior and post therapy done were noted in a specially predesigned proforma. Lipid profiles were evaluated by Erba excel-640 and the levels were noted for patients. Each patient's prescription was collected based on following inclusion and exclusion criteria -

Inclusion criteria:

1. Drug naive patients with type 2 diabetes mellitus attending OPD only
2. Age between 18 to 60 years of either sex
3. HbA1c greater than 6.5% and Fasting Blood Sugar (FBS) greater than 110mg/dl of blood

Exclusion criteria:

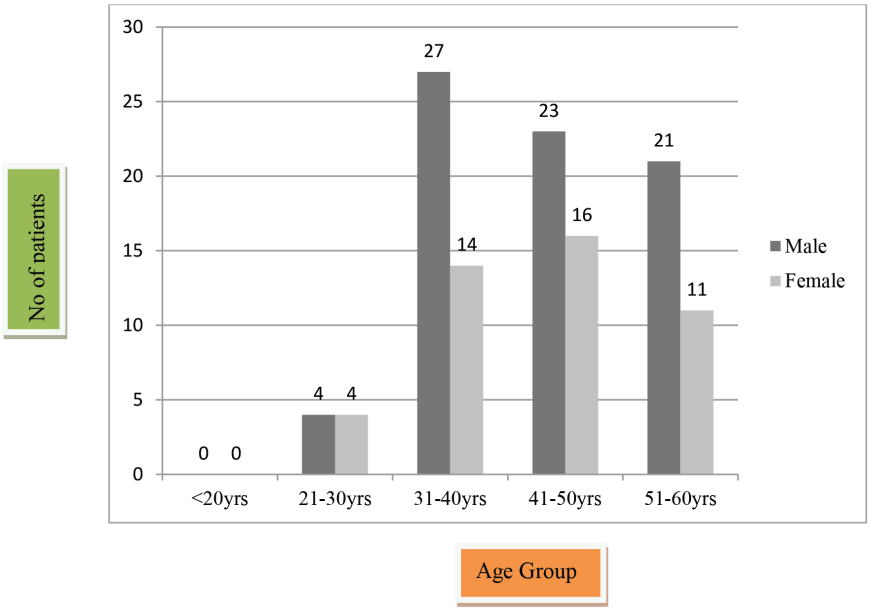
1. Inpatients of type 2 diabetes mellitus
2. Patients on anti-diabetic or hypoglycemic agents.
3. Pregnant or lactating mothers.
4. Patients with renal/ hepatic dysfunctions/ cardiovascular diseases.
5. Patients with any cardiac comorbidity.

During course of the study, data regarding preliminaries was collected during daily oupatient timings from 9.00AM to 4 PM on regular working days and data regarding investigations were collected during followup of the patient or next visit to OPD by author. The important investigations required for the study like fasting blood glucose, postprandial blood glucose, random blood glucose, HbA1c and total lipid profile were done in the central lab of institution using proper sophisticated standard equipments according to GLP (Good Laboratory Practices) guidelines. The same was monitored during each data collection visit. The data collected was entered in Microsoft Excel sheet and later analyzed statistically and results were expressed as numbers and percentage. To compare before and after values of lipid profile Non parametric test (Wilcoxon signed rank test) is applied.

Results

In our study a total of 120 patients' data were analyzed. Male were 62.5% and female 37.5%, most commonly affected drug naïve type 2 diabetes patients age group was between 31-50 years with mean age of 43.82 yrs. as shown in "Figure 1".

Figure 1. Gender & Age group distribution



Drugs prescribed were procured from hospital pharmacy, Number of patients prescribed with metformin monotherapy 500 mg oral twice daily were 50(42%) and combination with glimepiride 1 mg twice daily oral were 70(58%).

Average random blood glucose level was 193.4 mg/dl prior therapy was recorded. After twelve weeks of metformin monotherapy and combination therapy with glimepiride, average random blood glucose level was 135.2mg/dl, total average of LDL in both the groups was significantly reduced from 92.3mg/dl to 83.2mg/dl, total average of triglycerides in both the groups were reduced from 145.5mg/dl to 132 mg/dl and total average of HDL in both the groups increased from 29.1 mg/dl to 32.9 mg/dl as shown in "Table 1" with stastical significance (P <0.001) in LDL,VLDL,TGs and TC values.

Table 1. Mean difference in parameters before (Pre) and after (post) treatment on lipid profile

	Mean ±SD	Median	IQR	Z Statistic	P Value	Confidence interval for mean
LDL Pre	94.79±29.76	94.8	39.5	7.595	<0.001	89.39 to 100.19
Post	83.78±28.32	84.8	33.4			78.63 to 88.92
HDL Pre	35.12±4.58	34.4	4.4	2.71	=0.007	34.29 to 35.95
Post	36.76±6.16	35.3	7.9			35.65 to 37.88
VLDL Pre	32.11±7.24	33.4	7.8	4.419	<0.001	30.79 to 33.42
Post	30.12±5.39	30.7	7.4			29.14 to 31.1
TG Pre	147.11±27.9	144.5	32	8.705	<0.001	142.05 to 152.18
Post	131.05±24.75	134.1	35.7			126.55 to 135.54
TC Pre	189.09±35.31	186.1	46.9	8.984	<0/001	182.69 to 195.51
Post	167.22±30.57	166.4	32.8			161.68 to 172.77

Favorable effect of metformin combination therapy with glimepiride 69(60.5%) is more significant on lipid profile when compared to metformin monotherapy 45(39.5%).

114(95%) patients showed significant change in lipid profile while 6(5%) patients showed irregular changes in the lipid profile. There was no adverse effect of any drugs used in the study.

Discussion

In this study both metformin monotherapy and combination therapy with glimepiride appreciably improved dyslipidemia as well as good reduction in average blood glucose levels in type 2 diabetes patients. The lipid-modifying effect may be attributable to insulin sensitization, reduction of irreversibly glycated LDL-C and weight loss (6). In practice, people with dyslipidemia who are ineligible for lipid-lowering agents may benefit from metformin therapy and those patients who have mild dyslipidemia along with diabetes can be treated with antidiabetic drugs most preferably metformin and glimepiride, without the use of statins and other lipid lowering agents. Moreover, there is a synergistic effect between metformin and statin, which may further reduce cardiovascular events in at-risk individuals. Overall, metformin and glimepiride are safe and efficacious approach to alleviate dyslipidemia in people with newly diagnosed T2DM.

Cardiovascular disease is a major cause of mortality and morbidity in people with type 2 diabetes mellitus (T2DM). Studies have consistently identified dyslipidemia as an important risk factor for the development of micro and macrovascular disease which is in turn due to increased oxidative stress (7,8). The results of this study is comparable with study done by Shashikala et al., (9) where there is no statistically significant decrease in LDL-C. When data was compared with many studies it has shown that metformin therapy reduces cardiovascular events in overweight people with T2DM (10-12). This study also showing more favorable effect of combination therapy with glimepiride than metformin monotherapy on serum lipid profile in drug naïve type 2 diabetic individuals is comparable with the study done by Abhijit das et al., (13). A study on Medline data search by Buse et al., has showed that metformin at higher doses reduced triglycerides, but effect on other lipids were inconclusive (14).

Furthermore metformin when used in different combinations yields favourable lipid profile which could be related to beneficial changes in gut microbiota (15). Strengths of the study: very simple but effective study in describing the effect of metformin in monotherapy and combination therapy on lipid profile of drug naïve

type 2 diabetes patients with no adverse effects in the entire duration of study. Limitations: study sample size was not large enough. And plasma adiponectin levels should have been done to predict very strong positive correlation between increased HDL levels (16). But still with this sample size it was adequate enough to arrive to a conclusion that metformin monotherapy and combination therapy with glimepiride has good favourable lipid profile in drug naive type 2 diabetes patients and more so with combination therapy of glimepiride.

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Conflict of interest

The authors declare no conflict of interest, financial or otherwise.

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