Original Article

A study of Glimepiride versus Metformin plus Glimepiride with respect to Glycemic control and lipid profile in type II diabetes mellitus patients

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Abstract

Introduction: Diabetes Mellitus is a very commonly occurring metabolic disorder characterized by hyperglycemia and altered metabolism of lipids, proteins, and carbohydrates which is due to absolute or relative deficiency of insulin or insulin resistance. **Aims and Objectives:** To Study of Glimepiride versus Metformin plus Glimepiride With Respect to Glycemic Control and Lipid Profile in Type II Diabetes Mellitus Patients. **Methodology:** The present study was a open label hospital based prospective study undertaken to study effects of two classes of antidiabetic drugs on lipid profile and oxidative stress. The study period was October 2013 to October 2015. The study was approved by the Ethical Committee of the Medical College. The study population was carried out in all patients with both sexes of Diabetes Mellitus at Rural Hospital. A total of 60 patients with Diabetes Mellitus with Simple Random Sampling satisfying inclusion and exclusion criteria were included in the study. The patient clinically diagnosed as type 2 Diabetes Mellitus Group I (N=30): Diagnosed cases of T2DM being treated with hypoglycemic drug Glimepiride alone. Group II (N=30): Diagnosed cases of T2DM being treated with a combination of Glimepiride and Metformin. Data were double entered using Microsoft excel 2007 and analyzed using SPSS version 11. The ANOVA test where applied in the following results whenever necessary. **Result:** The difference between fasting blood glucose levels in Group 1 (Glimipride) and Group 2 (Metformin + Glimepiride) was statistically significant at 6 months, 12 months and 18 months i.e. $p<0.05$.the difference between postprandial blood glucose levels and HbA1c in Group 1 (Glimepiride) and Group 2 (Metformin + Glimipride) was statistically significant at 6 months, 12 months and 18 months i.e. $p<0.05$.the difference between MDA levels in Group 2 (Glimipride) and Group 4 (Metformin + Glimipride) was statistically significant at 6 months, 12 months and 18 months i.e. $p<0.05$. The difference between total cholesterol, triglycerides, LDL and HDL in Group 1 (Glimipride) and Group 2 (Metformin + Glimipride) was statistically significant at 6 months, 12 months and 18 months i.e. $p<0.05$. **Conclusion:** Combination treatment with metformin plus Glimepride was more effective in improving hyperglycemia, oxidative stress and lipid status in type 2 diabetics.

Keywords: Glimepiride, Metformin, Malondialdehyde level (MDA), GlycemicControl, Lipid Profile.

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INTRODUCTION

Diabetes Mellitus is a very commonly occurring metabolic disorder characterized by hyperglycemia and altered metabolism of lipids, proteins, and carbohydrates which is due to absolute or relative deficiency of insulin or insulin resistance. Diabetes is not an epidemic anymore but has turned into pandemic for the whole world.[1] The worldwide survey reported that diabetes is affecting nearly 10% of the population.[2] According to the World Health Organization (WHO) projections, the prevalence of diabetes is likely to increase by 35% by the year 2025.[3] India has a high prevalence of diabetes and the numbers are increasing at an alarming rate. In India alone, diabetes is expected to increase to 79.4 million by 2030.[4] A body of evidence exists concerning the involvement of oxidative stress in the aetiology of diabetes and its later complications.[5] Oxidative stress arises in cells and tissues through the increased production of reactive oxygen

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species (ROS) and/or from decreases in the antioxidant defence system.[6] Oxidative stress, through the production of reactive oxygen species, is increased in hyperglycemia and elevated free fatty acids (FFA) which occur during Diabetes Mellitus (both type 1and2). Several mechanisms seem to be involved in the generation of OS in the presence of elevated glucose concentrations; they include glucose auto-oxidation, enhanced glucose flux through polyol pathway and non-enzymatic and progressive glycation of proteins with consequent increased formation of glucose-derived advanced glycosylation end products.[7] Under normal physiological conditions, a widespread antioxidant defense system protects the body against the adverse effects of ROS generation. The defense mechanism's efficiency is altered in diabetes and the ineffective scavenging of free radicals may therefore play a crucial role in determining tissue damage in the patients[8]the increased oxidative stress plays a key role in development of micro and macro vascular diabetic complications, leading to a significant impact on quality of life. Long-term complications involve almost all vital organs such as heart, eyes, kidney, blood vessels and nervous system. Previous studies have established that early intensive glycemic control reduces the risk of diabetic complications both micro and macro vascular. In vivo studies have revealed that oxidative stress occurs before the complications of diabetes.

MATERIAL AND METHODS

The present study was an open label hospital based prospective study undertaken to study effects of two classes of antidiabetic drugs on lipid profile and oxidative stress. The study period was October 2013 to October 2015.The study was approved by the Ethical Committee of the Medical College. The study population was carried out in all patients with both sexes of Diabetes Mellitus at Rural Hospital. A total of 60 patients with Diabetes Mellitus with Simple Random Sampling satisfying inclusion and exclusion criteria were included in the study. The patient clinically diagnosed as type 2 Diabetes Mellitus with: Duration of type 2DM less than 5 years since diagnosis Patient on Glimepride alone. Patient on Metformin alone. Patient on Glimepride + Metformin included into study while Patients not willing to participate in study. Patient diagnosed as T2DM but time since diagnosis exceeds 5 years Patient receiving other hypoglycemic drug (Excluding Glimepride, Metformin) Excluded from the study. Following investigations were done in above groups at duration of 0, 6, 12and 18 months: Fasting and post prandial blood glucose estimation. HbA1c estimation, MDA estimation, Serum lipid profile estimation. Study subjects selected as following groups. Group I (N=30): Diagnosed cases of T2DM being treated with hypoglycemic drug Glimepride alone. Group II (N=30): Diagnosed cases of T2DM being treated with a combination of Glimepride and Metformin. Data were double entered using Microsoft excel 2007 and analyzed using SPSS version 11. The ANOVA test where applied in the following results whenever necessary.

RESULT

Table 1: Comparison of Blood glucose levels among study groups 1 and group 2

Variable	Time point	Group 1	Group 2	P value
FBS	Baseline	191.43±36.97	190.23±35.71	P>0.05
	6 months	106.70±10.00	102.53±10.78	P<0.05*
	12 months	99.33±8.91	94.63±6.55	P<0.05*
	18 months	94.73±6.18	92.13±8.33	P<0.05*
PPS	Baseline	283.73±35.95	289.70±43.53	P>0.05
	6 months	168.97±18.99	164.13±17.04	P<0.05*
	12 months	158.26±14.13	152.78±17.49	P<0.05*
	18 months	147.36±14.76	144.30±12.63	P<0.05*
HbA1c	Baseline	9.18±0.63	9.06±0.85	P>0.05
	6 months	6.91±0.40	6.18±0.65	P<0.05*
	12 months	6.78±0.50	6.14±0.66	P<0.05*
	18 months	6.53±0.51	6.14±0.57	P<0.05*

(* P<0.05 Statistically Significant)

In the above table it was observed the difference between fasting blood glucose levels in Group 1 (Glimipride) and Group 2 (Metformin + Glimipride) was statistically significant at 6 months, 12 months and 18 months i.e. p<0.05. Similarly the difference between postprandial blood glucose levels and HbA1c in Group 1 (Glimipride) and Group 2 (Metformin + Glimipride) was statistically significant at 6 months, 12 months and 18 months i.e. p<0.05.

Table 2: Comparison of MDA and lipid profile levels among study group 1 and group 2

Variable	Time point	Group 2	Group 4	P value
MDA	Baseline	5.04±0.60	5.20±0.60	P>0.05
	6 months	2.75±0.52	2.67±0.49	P<0.05*
	12 months	2.69±0.51	2.53±0.40	P<0.05*
	18 months	2.63±0.47	2.38±0.31	P<0.05*
TC	Baseline	186.33±12.45	191.33±16.59	P>0.05
	6 months	165.43±21.63	169.33±15.89	P<0.05*
	12 months	162.93±16.80	161.36±13.64	P<0.05*
	18 months	176.13±15.39	158.23±13.56	P<0.05*
TG	Baseline	187.53±15.31	192.43±13.73	P>0.05
	6 months	156.76±14.23	138.26±14.61	P<0.05*
	12 months	158.62±17.93	128.67±8.02	P<0.05*
	18 months	145.76±15.33	124.53±4.69	P<0.05*
LDL	Baseline	105.67±15.47	100.66±12.98	P>0.05
	6 months	94.76±11.74	89.86±12.13	P<0.05*
	12 months	92.73±14.37	88.67±11.25	P<0.05*
	18 months	90.43±11.89	86.94±9.97	P<0.05*
HDL	Baseline	36.80±5.16	38.70±4.92	P>0.05
	6 months	38.16±4.89	40.63±4.42	P<0.05*
	12 months	37.23±3.72	41.80±5.17	P<0.05*
	18 months	40.34±6.68	43.43±4.27	P<0.05*

(* P<0.05 Statistically Significant)

In the above table it was observed that the difference between MDA levels in Group 1 (Glimipride) and Group 2 (Metformin + Glimipride) was statistically significant at 6 months, 12 months and 18 months i.e. $p<0.05$. Similarly the difference between total cholesterol, triglycerides, LDL and HDL in Group 1 (Glimipride) and Group 2 (Metformin + Glimipride) was statistically significant at 6 months, 12 months and 18 months i.e. $p<0.05$.

DISCUSSION

Type 2 diabetes mellitus patients are more prone to cardiovascular complications (CVD), which can occur earlier and more frequently as compared to non-diabetic patients.[9] Dyslipidemia, an established risk factor for CVD, is strikingly common in patients with type 2 diabetes, affecting almost 50% of this population.[10] In addition to hyperglycemia and hypertension, dyslipidemia is a modifiable CVD risk factor that remains largely uncontrolled in patients with Type 2 diabetes mellitus.[10] Hyperglycemia increases the risk of microvascular complications,[11] while dyslipidemia is a major risk factor for macrovascular complications in patients with type 2 diabetes.[12,13] Elevated low-density lipoprotein cholesterol (LDL-c) is a major risk factor for CVD.[12] As such, management of LDL-c is the primary goal of therapy for diabetic dyslipidemia.[14-16] Furthermore, type 2 diabetes increases the risk of CVD mortality independent of LDL-c levels, adding to the greater overall cardiovascular risk in this population.[17]Therefore, aggressive lipid treatment goals have been recommended for patients with type 2 diabetes.[14-16,18] In present study, there was significant reduction in fasting blood glucose level, postprandial blood glucose and glycosylated haemoglobin by 51.57%, 50.16% and 32.15% respectively, from the baseline after 18 months of treatment with a combination. Similar findings were seen in the study by CharpentierG *et al*[19], where Metformin and Glimepride combination treatment was significantly more efficient in controlling glycosylated haemoglobin, fasting blood glucose and post-prandial blood glucose than either Glimepride or Metformin alone. In present study, significant reductions were observed in total cholesterol, serum triglyceride and LDL cholesterol in patients treated with a combination of Metformin and Glimepride as compared to monotherapy. The combined therapy with Metformin and Glimepride also showed significant increase in HDL levels as compared to monotherapy with Metformin or Glimepride alone. Similar findings were seen also in study done by Md. Akram Minhaj and Md. Waris[20] who observed after 21 weeks, statistically significant reductions were observed in case of total cholesterol, serum triglyceride and LDL cholesterol in patients treated with combination of Metformin and Glimepride.

CONCLUSION

The combination of Glimepride and Metformin therapy improves hyperglycemia more potently and helps in decreasing Malondialdehyde level, one of the markers of oxidative stress effectively as compared to monotherapy of either Glimepride or Metformin in diabetic patients. Thus, this study was suggesting that combination treatment with metformin plus Glimepride was more effective in improving hyperglycemia, oxidative stress and lipid status in type 2 diabetics.

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