Original Research Article

Comparison of effects of metformin with combination of glimepride and metformin in type 2 diabetes patients

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Abstract

Background: The use of a fixed-dose combination pill of sulfonylurea and metformin has recently increased. Using a fixed-dose combination pill can improve patient compliance. **Aim:** To compare the effects of metformin with combination of glimepiride and metformin in type 2 diabetes patients. **Material and Methods:** A total of 120 patients with Type 2 DM with simple random sampling were included in the study. Study subjects selected as Group I (N=30): Diagnosed cases of T2DM being treated with Metformin alone and Group II (N=30): Diagnosed cases of T2DM being treated with a combination of Glimepiride and Metformin. Fasting and post prandial blood glucose estimation, HbA1c, MDA estimation and Serum lipid profile estimation was done at duration of 0, 6, 12 and 18 months. **Results:** 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 of Metformin and Glimepiride as compared to monotherapy with Metformin alone. Total cholesterol, serum triglyceride and LDL cholesterol also reduced significantly in combination therapy. **Conclusion:** Combination treatment with Metformin plus Glimepiride was more effective in improving hyperglycemia, oxidative stress and lipid status in type 2 diabetics.

Key Word: Type 2 Diabetes mellitus, Metformin, Metformin Glimepiride combination, hyperglycemia, oxidative stress

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INTRODUCTION

Diabetes mellitus,a common 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. In addition to hyperglycemia and hypertension, dyslipidemia is a modifiable CVD risk factor that remains largely uncontrolled in patients with Type 2 diabetes mellitus.[1] Metformin has been the most recommended monotherapy of type 2 diabetes mellitus (T2DM).[2,3] The American Diabetes Association (ADA) recommended metformin as the first drug of choice for treating T2DM patients, especially those who are overweight.[3]Glimepiride is of the latest generation sulfonylureas for treating T2DM. It has a lower cardiovascular risk than conventional sulfonylureas do.[4,5] Considering the compliance and cost-effectiveness, the use of a fixed-dose combination pill of sulfonylurea and metformin has recently increased. Using a fixed-dose combination pill can improve patient compliance compared with taking multiple pills,[6] and is expected to minimize the side-effects caused by high-dose monotherapy while effectively controlling blood glucose level. Hence, in present study, we sought to compare the effects of metformin with combination of glimepiride and metformin in type 2 diabetes patients.

MATERIAL AND METHODS

The present study was open label hospital based prospective study undertaken to study effects of metformin with combination of glimepiride and metformin. A total of 120 patients with Diabetes Mellitus with simple random sampling satisfying inclusion and exclusion criteria were included in the study. The study was approved by the Institutional Ethical Committee of the Medical College.

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Inclusion criteria

The patient clinically diagnosed as type 2 Diabetes Mellitus with:

- duration of type 2DM less than 5 years since diagnosis
- Patient on Metformin alone
- Patient on Glimepiride + Metformin combination

Exclusion criteria

1. Patients not willing to participate in study.
2. Patient diagnosed as T2DM but time since diagnosis exceeds 5 years
3. Patient receiving other hypoglycemic drug (excluding Glimepiride, Metformin)

Study Variables

Diabetes mellitus: The presence of diabetes mellitus was defined as either a fasting glucose level ≥126 mg/dL or a 2-hr glucose value of ≥200 mg/dL after 75 g oral glucose loading. A person who is diagnosed to be diabetic based on biochemical tests already and either taking treatment or not taking treatment.

Methodology

Study subjects selected as following groups.

- Group I (N=30): Diagnosed cases of T2DM being treated with Metformin alone.
- Group II (N=30): Diagnosed cases of T2DM being treated with a combination of Glimepiride and Metformin.

Following investigations were done in above groups at duration of 0, 6, 12and 18 months: 1) Fasting and post prandial blood glucose estimation.2) HbA1c estimation 3) MDA estimation 4) Serum lipid profile estimation.

Sample Collection

After 12 hours of fasting, venous blood sample was collected in different bulbs under aseptic condition.

- Fluoride bulb, used for fasting and post prandial blood glucose estimation by GOD POD method.
- Plain bulb, used for Malondialdehyde (MDA) estimation by kit method.
- EDTA bulb, used for Glycosylated hemoglobin (HbA1c) estimation.
- Plain bulb, used for Serum lipid profile estimation by chemical analysis.

Baseline levels of all above parameters measured at the time of enrollment of subjects in the study. Study subjects were again reassessed for same parameters after a follow up of 6 months, 12 months and 18 months. The sera were analyzed for markers MDA, Total Cholesterol, Triglycerides, High density lipoproteins, HbA1c, Fasting and post prandial blood glucose. Statistical Analysis Data were double entered using Microsoft excel 2007 and analyzed using SPSS version 11.Data were summarized in frequency tables, pie chart and histogram. Categorical variables were reported as proportion. Continuous data were described as means (standard deviation) or medians (interquartile range) depending on the distribution of data. The ANOVA test where applied in the following results whenever necessary.

RESULTS

It was observed that mean age in Group I and Group II was 51.93 ±10.37 and 53.30 ±9.26 years respectively. There was no statistical difference among age in different study groups. It was observed that change of fasting blood glucose at 18 months from baseline was maximum in Group II (51.57%) as compared to Group I (51.23%). Change of postprandial blood glucose at 18 months from baseline was maximum in Group II (50.16%) i.e. combined treatment of Metformin and Glimepiride as compared to Group I (45.82%) i.e. only Metfromin. The change in mean Glycosylated haemoglobin at the end of 18 months of therapy was highest in Group II (32.15%) as compared to Group I (28.51%). This showed that glycemic control was superior in combined therapy of Metformin and Glimepiride patients as compared to monotherapy.

Table 1: Comparison of Blood glucose levels among study groups I and II

Variable	Time point	Group 3	Group 4	P value
FBS	Baseline	202.43±36.47	190.23±35.71	P<0.05*
	6 months	110.27±9.38	102.53±10.78	P<0.05*
	12 months	103.26±7.82	94.63±6.55	P<0.05*
	18 months	98.73±7.71	92.13±8.33	P<0.05*
PPS	Baseline	292.23±48.43	289.70±43.53	P<0.05*
	6 months	172.83±18.66	164.13±17.04	P<0.05*
	12 months	165.63±12.40	152.78±17.49	P<0.05*
	18 months	158.34±17.33	144.30±12.63	P<0.05*
HbA1c	Baseline	9.33±0.72	9.06±0.85	P<0.05*
	6 months	7.09±0.44	6.18±0.65	P<0.05*
	12 months	6.83±0.46	6.14±0.66	P<0.05*
	18 months	6.67±0.47	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 I (Metformin) and Group II (Metformin + Glimepiride) was statistically significant at baseline, 6 months, 12 months and 18 months i.e. p<0.05. Similarly, the difference between postprandial blood glucose levels and HbA1c in Group I (Metformin) and Group II (Metformin + Glimepiride) was statistically significant at baseline, 6 months, 12 months and 18 months.

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

Variable	Time point	Group 3	Group 4	P value
MDA	Baseline	5.17±0.63	5.20±0.60	P<0.05*
	6 months	2.97±0.66	2.67±0.49	P<0.05*
	12 months	2.76±0.49	2.53±0.40	P<0.05*
	18 months	2.68±0.45	2.38±0.31	P<0.05*
TC	Baseline	193.33±17.48	191.33±16.59	P<0.05*
	6 months	176.23±18.09	169.33±15.89	P<0.05*
	12 months	172.43±14.69	161.36±13.64	P<0.05*
	18 months	173.26±15.47	158.23±13.56	P<0.05*
TG	Baseline	190.27±16.48	192.43±13.73	P<0.05*
	6 months	135.67±14.80	138.26±14.61	P<0.05*
	12 months	131.13±8.53	128.67±8.02	P<0.05*
	18 months	128.56±7.17	124.53±4.69	P<0.05*
LDL	Baseline	101.53±16.04	100.66±12.98	P<0.05*
	6 months	90.96±7.47	89.86±12.13	P<0.05*
	12 months	90.70±11.96	88.67±11.25	P<0.05*
	18 months	90.67±11.78	86.94±9.97	P<0.05*
HDL	Baseline	39.07±5.22	38.70±4.92	P<0.05*
	6 months	40.16±4.71	40.63±4.42	P<0.05*
	12 months	40.14±4.72	41.80±5.17	P<0.05*
	18 months	41.43±4.53	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 I (Metformin) and Group II (Metformin + Glimepiride) was statistically significant at baseline, 6 months, 12 months and 18 months i.e. p<0.05. Similarly, the difference between total cholesterol, triglycerides, LDL and HDL in Group I (Metformin) and Group II (Metformin + Glimepiride) was statistically significant at baseline, 6 months, 12 months and 18 months i.e. p<0.05.

DISCUSSION

The present prospective study was undertaken to determine effect of oral antidiabetic drugs on glycosylated haemoglobin levels, serum lipid profile, and oxidative stress in patients with type 2 diabetes mellitus. 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 of Metformin and Glimepiride as compared to monotherapy with Metformin alone. Similar findings were seen in the study by Charpentier G *et al*,[7] where Metformin and Glimepride combination treatment was significantly more efficient in controlling glycosylated haemoglobin, fasting blood glucose and post-prandial blood glucose than Metformin alone. Similarly, in study by Gonzalez-Ortiz M *et al*,[8] the percentage of patients that showed a decrease in glycosylated haemoglobin of 1% or higher were 21.2% and 47.0% in the Metformin and in the combined therapy groups, respectively (p<0.001). The percentage of patients with decreased glycosylated haemoglobin of 7% or less was 9.0% and 23.5% in the Metformin and in the combined therapy groups, respectively (p =0.01). The combined use of Glimepride plus Metformin in a single presentation for 3 months showed to be more efficacious and safe in patients with type 2 Diabetes Mellitus than monotherapy. In present study, significant reductions were observed in total cholesterol, serum triglyceride and LDL cholesterol in patients treated with a combination of Metformin and Glimepiride as compared to monotherapy. The combined therapy with Metformin and Glimepiride also showed significant increase in HDL levels as compared to monotherapy with Metformin or Glimepiride alone. Similar findings were seen also in study done by Md. AkramMinhaj and Md. Waris[9] 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. The effect of monotherapy as discussed above shows that both the drugs individually decrease Malondialdehyde level with different mechanisms. 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 Metformin in diabetic patients. The patients treated with Metformin and Glimepride in combination resulted in the significant reduction in blood glucose levels, plasma malondialdehyde, total cholesterol, serum triglyceride, and LDL cholesterol while increased the HDL cholesterol throughout the study.

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