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Effects of Monotherapy and Combination Therapy Involving Metformin and Glimepiride on HbA1c and Lipid Profile in Patients with Type II Diabetes Mellitus

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***K. Saravanan, P.K. Manna and G.P.Mohanta**

Department of Pharmacy, Annamalai University, Annamalai Nagar-608002. India.

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ABSTRACT

To compare the effects of an insulin sensitizer, metformin, with an insulin secretagogue, Glimepiride, on Glycosylated hemoglobin level (HbA1c) and lipid profile in type II diabetes patients. This is a prospective cross sectional study carried out on 120 type II diabetic Patients were selected according to the prescription divided in three groups Metformin (N=40), Glimepiride (N=40), a combination of Glimepiride with metformin (N=40). We observed the levels of HbA1c and lipid profiles, in the 0^{th}, 12^{th} and 24^{th} weeks of the treatment period. The HbA1c level significantly reduced in12^{th} and 24^{th} weeks in metformin and Glimepiride alone groups as well in the combination groups. However, the reduction was more profound in the Glimepiride plus metformin combination as that of single therapyy groups. Further, the Glimepiride treatment group displayed non-significant changes in serum TG However, in combination therapy of Glimepiride with Metformin there was a significant decrease in serum TC, LDL-c, TG and significant increase in HDL-c levels at 12^{th} and 24^{th} week as compared to the 0 week Metformin improve lipid profile when used in type II diabetic patients and reduce the risk of cardiovascular complications.

1. INTRODUCTION

Diabetes mellitus is a chronic condition and is characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both[1]. Due to this the amount of glucose in the blood increases and leads to hyperglycemia[2]. The major complications are diabetic neuropathy and nephropathies, peripheral vascular disease, foot ulcers and limb amputations affecting 30% of those aged 40 or more[3]. Symptoms of diabetes include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision[4]. The ultimate or primary goal of therapy for type 2 diabetes is to prevent the mortality and morbidity related to the microvascular and macrovascular complications. Since these diseases are lifelong disorders, reduction in the number of tablets and daily doses is a very important consideration from the patient's point of view. It is increasingly obvious that to achieve this on a global perspective, we will need to identify better and more effective treatment strategies to maintain tight glycemic control[5,6]. The typical pattern of dyslipidaemia seen in type 2 diabetes is normal or slightly elevated total cholesterol, elevated triglycerides and low levels of high density lipoprotein (HDL)-cholesterol levels. Low density lipoprotein (LDL) -cholesterol levels are variably elevated, but not significantly different from non-diabetic patients[7]. In recent years there has been an increase in the number and classes of medications available for the treatment of type 2 diabetes. Given the implications of macrovascular disease in this population, an understanding of the alterations in the major lipid classes and subclasses that occur as a result of the broad range of antidiabetic medications may enhance approaches to drug selection for the treatment of type 2 diabetes[8]. The present study aims to compare the efficacy of Metformin, Glimepiride and combination of metformin with Glimepiride patients with type 2 Diabetes mellitus and to assess the percentage reduction in HbA1c, lipid profiles of total cholesterol, triglyceride, (HDL) high density lipoprotein, (LDL) low density lipoprotein in different three groups.

2. MATERIALS AND METHODS

The institutional Human Ethical Committee of Annamalai University has been approved the study of being carried out at the Raja Muthaih Medical College and Hospital (RMMCH). A prospective cross-sectional study was conducted on 120 Type 2 diabetic patients, which includes 69 males and 51 females were recruited as per the inclusion and exclusion criteria. Patients who

are regularly visiting hospital for the treatment from March 2012 to May 2013 have been taken as subjects for this study. Patients were recruited as per the inclusion and exclusion criteria

(a) Inclusion criteria

- ✓ Patients who diagnosed with Type-2 diabetes complications
- ✓ Patients with age of 30 years and above
- ✓ Fasting glucose > 140 mg/dl
- ✓ Postprandial blood glucose level (at 2hr) > 200 mg/dl
- ✓ Patients with associated diseases of Hypertension,
- ✓ Coronary artery diseases, Bronchial Pneumonia, Asthma.

(b) Exclusion criteria

- ✓ Patients who diagnosed without Type-2 diabetes complications
- ✓ Patients below the age group of 30 years.
- ✓ Patients who are not willing to participate in the study.
- ✓ Nursing or pregnant women.
- ✓ Hepatic or renal disease patients
- ✓ Patients with History of Ketoacidosis

(3) Grouping of patients

(a) Grouping of patients based on a treatment regimen prescribed. Each study group had 40 patients. The study groups were as follows:

Group I- Patients treated with Metformin (500 mg) for 24 weeks.

Group II - Patients treated with Glimipiride (2 mg) for 24 weeks.

Group III- Patients treated with combination therapy of Glimepiride (2 mg) + Metformin (500 mg) for 24 weeks.

(b) Assess the patients out comes through

(a) HbA1c

(b) Lipid profiles.

(4) Biochemical estimations

1**.** Estimation of Glycosylated Hemoglobin [HbA1c] (VARIANT II TURBO Analyser) were measured at baseline, 12th and 24th weeks of the treatment period.

2. Estimation of total cholesterol (Allain et al., 1974)

3. Estimation of Triglycerides (GPO-PAP method)

4. Estimation of High Density Lipoprotein Cholesterol (HDL – C)) (Matsuzaki et al.1995)

5. Estimation of Low Density Lipoprotein Cholesterol (LDL – C)

The estimation of LDL-cholesterol was determined by using the formula of Friedwald *et al* (1972) as shown below:

LDL Cholesterol = (Total Cholesterol) – (HDL- Cholesterol) – (Triglyceride/5)

The lipid profiles of total cholesterol, (HDL) high density lipoprotein, (LDL) Low density lipoprotein and triglyceride levels were measured at baseline, 12th and 24th weeks of the treatment period.

(5) Statistical analysis

Biochemical parameters were expressed as Mean ± SD results were analyzed statistically by one way (ANOVA) followed by Dunnett's test. Value of $p < 0.05$ were considered significant.

6. RESULTS AND DISCUSSION

Table 1. Gender distribution

Gender	Number of patients	Percentage
Male	69	57.5
Female	51	42.5
Body mass index (Mean ± SD)	28.16±2.15	ND

Table 2. Duration of Diabetes (in years)

Years	Number of patients	Percentage
>5	43	35.8
6-10	59	49.1
11-15	18	15

Totally 120 diabetes patients were included in the study. Of which, 69 (57.5%) patients were male and 51 (42.5%) patients were as females (Table -1). The duration of diabetes of the subjects recruited in the present study were as follows, 43 patients (35.8%) presented for less than 5 years. 59 (49.1%) patients elicited for 6-10 years. and 18 patients (15%) showed that 11-15 years (Table- 2).

Table 3. Co-morbidity conditions of patients with Type ll diabetes mellitus

Diagnosis	Number of patients	Percentage
Hypertension	33	27.5
Peripheral Neuropathy	21	17.5
Gastritis	6	5
UTI	7	5.8
Parkinson's	2	1.6
LRTI	9	7.5

The patients were presented with following co-morbid conditions highest number of Co morbidity like Hypertension (27.5%) and Neuropathy (17.5%) others UTI (5.8) Parkinson's (1.6) and LRTI (7.5%) (Table-3)

Table 4: Effect of Metformin, Glimepiride single and its combination treatment on Glycosylated haemoglobin level

Timeline (in weeks)	Metformin	Glimipiride	Glimepiride + Metformin
0	9.47±0.78	8.89±0.28	11.76±0.58
12	6.92±0.52*	6.14±0.16*	7.85±0.26*
24	6.07±0.45*	5.85±0.54*	6.52±0.42*

All values are expressed as Mean ± SD, N=40, One way ANOVA, repetatial analysis was done using Dunnet post test. All the values are compared with 0 week.* denotes statistically significant ($p<0.05$)

In the present study, the levels of HbA1c was significantly ($p<0.05$) reduced in 12th and 24th weeks in metformin and glimepiride single groups as well in the combination groups. However, the reduction was more profound in the glimepiride and metformin combination as that of monotherapy groups (Table- 4).

Table 5: Effect of Metformin single treatment on lipid profiles of (TC,LDL,HDL,TG)

Timeline (In Weeks)	TC (mg/dl)	LDL(mg/dl)	HDL (mg/dl)	TG (mg/dl)
0	195.23±12.26	119.72±12.45	43.46±1.25	126.42±9.12
12	154.24±11.25*	85.42±9.28*	47.21±1.81^{NS}	118.28±9.28^{NS}
24	110.72±9.26*	80.25±9.47*	50.15±1.75*	81.45±10.15*

All values are expressed as Mean ± SD, N=40, One way ANOVA, repetatial analysis using Dunnet post test all values are compared with 0 week.* denotes statistically significant ($p<0.05$).

Table 6: Effect of Glimepiride single treatment on lipid profiles of (TC,LDL,HDL,TG)

Timeline (In Weeks)	TC (mg/dl)	LDL (mg/dl)	HDL (mg/dl)	TG (mg/dl)
0	201.28±14.12	120.48±11.0	37.45±1.11	231±30.45
12	196.36±12.25^{NS}	110.76±12.75^{NS}	40.26±1.05 ^{NS}	206±20.25^{NS}
24	142.42±11.25*	87.45±9.76*	46.42±0.92*	200±22.56^{NS}

All values are expressed as Mean ± SD, N=40, One way ANOVA, repetatial analysis using Dunnet post test all values are compared with 0 week.* denotes statistically significant ($p<0.05$).

Table 7: Effect of Glimepiride and Metformin combination therapy treatment on lipid profiles of (TC,LDL,HDL,TG)

Timeline (In Weeks)	TC (mg/dl)	LDL (mg/dl)	HDL (mg/dl)	TG (mg/dl)
0	210.26±12.12	138.45±12.45	46.25±1.36	154.10±15.62
12	158.25±7.72*	89.26±9.12*	51.22±1.28^{NS}	101.25±10.12*
24	114.85±9.75*	81.92±8.29*	54.52±1.65*	86.55±9.25*

All values are expressed as Mean ± SD, N=40, One way ANOVA, repetatial analysis using Dunnet post test all values are compared with 0 week.* denotes statistically significant ($p<0.05$).

Effect of Metformin, Glimepiride single and its combination treatment on lipid profiles of (TC,LDL,HDL,TG)

Treatment with metformin alone displayed a significant decrease in serum TC and LDL-c levels, and significant increase in HDL-c levels at 12th and 24th week as compared to the 0 week. However, metformin alone significantly decreased the TG level only at the 24th week (Table - 5). Meanwhile, in the glimepiride alone treated group there was a significant decrease in TC and LDL-C and increase in HDL-c at 24th week only and not in 12th week changes. Further, the glimipiride treatment group displayed non-significant changes in serum TG (Table- 6).

However, in combination therapy of glimepiride with metformin there was a significant decrease in serum TC, LDL-c, TG and significant increase in HDL-c levels at 12th and 24th week as compared to the 0 week (Table -7).

The tight glycemic control and reduction of elevated lipid levels are primary goals in the prevention of cardiovascular complications in type 2 diabetics. Poor glycemic control in type 2 diabetes associated with hyperlipidemia are independent risk factors for cardiovascular events. Thus, an ideal antidiabetic agent would improve both glycemic control and dyslipidemias

(7) CONCLUSION

The present study was combination therapy of glimepiride and metformin there was a significant decrease in serum TC, LDL-c, TG and significant increase in HDL-c levels at 12th and 24th week

as compared with single therapy. Diabetes mellitus is the one of the major problems of cardiovascular diseases, Hence the study revealed that the combination therapy of Glimepiride with metformin improves the lipid profile than the metformin and glimepiride single treatment, when used in type II diabetes patients and reduced the risk of cardiovascular complication.

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