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Comparative study of efficacy of glimepiride and metformin versus glibenclamide and metformin for type 2 diabetic patients

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ABSTRACT

Diabetes Mellitus is a syndrome with disordered metabolism and inappropriate hyperglycemia due to either a deficiency of insulin secretion or to a combination of insulin resistance and inadequate secretion to compensate. Type 2 diabetes is the most prevalent form and results from insulin resistance with a defect in compensatory insulin secretion. The study aims to compare the clinical efficacy of glimepiride plus metformin versus glibenclamide plus metformin in patients with type 2 diabetes mellitus and to assess the percentage reduction in fasting plasma glucose, post prandial glucose levels and HbA_1C. A prospective observational study conducted for a period of 6 months. We included 96 type 2 diabetic patients in which 52 patients were taking glimepiride plus metformin (group A) and 44 patients were taking glibenclamide plus metformin (group B). A 'p' value of < 0.05 was considered to be statistically significant. The primary efficacy was measured by comparing HbA1C, FBS, PPBS and serum cholesterol level. After 6 months of treatment the HbA_1C value decreased more significantly in group A (1.6%) than group B (1.29%), PPBS and cholesterol level also reduced more significantly in group A patients. But FBS value was more significantly reduced in group B patients. Glimepiride plus metformin combination therapy can be considered as the best combination in patients with increased glycaemic control as compared to glibenclamide plus metformin therapy.

Keywords: Comparative Study, glimepiride, metformin, glibenclamide, type 2 diabetes mellitus.

INTRODUCTION

Diabetes mellitus is one of the leading causes of death and disability worldwide. According to recent estimates, approximately 285 million people worldwide (6.6%) in the 20–79 year age group have diabetes in 2010 and by 2030, 438 million people (7.8%) of the adult population, is expected to have diabetes. The International Diabetes Federation (IDF) estimates the total number of people in India with diabetes to be around 50.8 million in 2010, rising to 87.0 million by 2030[1].

Diabetes mellitus is a chronic condition and is characterized by hyperglycemia resulting from defect in insulin secretion, insulin action or both[2]. Due to this the amount of glucose in the blood increases and leads to hyperglycemia[3]. The major complications are diabetic neuropathy and nephropathies, peripheral vascular disease, foot ulcers and limb amputations affecting 30% of those aged 40 or more[4]. Symptoms of diabetes include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision[5].

Diabetes is a chronic condition that requires continues medication and life style modification to prevent acute complication and to reduce long term complications[6]. Blood sugar level cannot be controlled as β-cell function worses over time, independent of whether the treatment was diet alone, sulfonyl urea, metformin, or insulin. If blood

sugar level cannot be controlled by a single agent, should prompt by the addition of another oral agent or insulin. The best-tested oral combination is sulfonylurea plus metformin. Adding one sulfonylurea to metformin at full dosage can reduce HbA_1C by 1.5 % to 2 %[7].

The present study aims to compare the efficacy of glimepiride plus metformin Vs glibenclamide plus metformin in patients with type 2 Diabetes mellitus and to assess the percentage reduction in FPG, PPG levels and HbA_1C in both groups.

MATERIALS AND METHODS

This prospective observational study was conducted in Al Madeena Institute of Medical Science (ALMAS Hospital), Kottakkal, Kerala for 6 months. Patients who were diagnosed with diabetes mellitus and those who were on treatment with glimepiride plus metformin or glibenclamide plus metformin and patients whose HbA1C >7%, blood sugar level >140mg/dl, obese patients and age between 30-65 yrs were included in the study. Patients with current insulin therapy or received insulin for more than 6 weeks in last three month, history of adverse reaction to sulfonylurea or metformin, patient with renal dysfunction, pregnancy, breast feeding and patients with hepatic dysfunction were excluded from the study. Prior to data collection, patients were informed confidently about the aim and objectives of the study and that the information collected would not be relieved to any one and participation would be their choice. Age, sex, height, weight, other associated disease were noted, BMI were calculated and patients were given instruction to monitor their blood glucose level, HbA_1C and lipid profile at the initial visit to the hospital. Patients were informed to check glucose level regularly at the interval of 2 months. Patient's records were maintained for six months after their first visit to hospital. HbA_1C were examined before treatment and after 6 months of treatment. Primary parameters used for the study were fasting plasma glucose, post prandial glucose, HbA_1C and BMI. Secondary parameters were serum cholesterol, serum creatinine, serum urea and serum uric acid level.

Information collected was recorded in a Master Chart. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2010) developed by Centre for Disease Control, Atlanta, Graph pad prism 6 and Microsoft excel. Using this software range, frequency, percentage, mean, standard deviation, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to find the significant difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

RESULTS AND DISCUSSION

A total of 96 patients were included in our study in which 52 patients were in group A (glimepiride plus metformin) and 44 patients were in group B (glibenclamide plus metformin). Demographic details among the subjects of group A reveals that out of 52 patients 4 patients (7.7%) were below 40 years, 12 patients (23.1%) were between 41-50 years, 32 patients (61.5%) were between 51-60 years and 4 patients (7.7%) were above 60 years. Demographic details among the subjects of group B reveals that out of 44 patients 2 patients (4.5%) were below 40 years, 11 patients (25%) were between 41-50 years, 26 patients (59.1%) were between 51-60 years and 5 patients (11.4%) were above 60 years (Table 1).

Table 1: Age Distribution of type 2 Diabetic Patients (n= 96)

Age Group (in Years)	Group A		Group B	
	No	%	No	%
Up to 40 Yrs	4	7.7	2	4.5
41 – 50	12	23.1	11	25
51 – 60	32	61.5	26	59.1
Above 60	4	7.7	5	11.4
Total	52	100	44	100
Range	37 - 65 yrs		32 - 55 yrs	
Mean	53.1 yrs		53. 4 yrs	
'p' value	0.9441			

In both the groups majority of the patients were females and the sex distribution of the study population is shown in (Table-2).

Table 2: Sex Distribution of type 2 Diabetic Patients (n= 96)

Sex	Group A		Group B	
	No	%	No	%
Male	22	42.3	20	45.5
Female	30	57.7	24	54.5
'p' value	0.9178			

Out of 52 patients in group A, the duration of DM was 1 to 9 years and out of 41 patients in group B, the duration of DM was 2 to 10 years (Table-3).

Table 3: Duration of type 2 Diabetic mellitus (n= 96)

Duration of illness (in year)	Group A patients	Group B patients
Range	1-9 years	1-10 yrs
Mean	4.0	4.57
'p' value	0.3604	

(Table-4) shows the current treatment of type 2 diabetic patients. Group A showed that 30 patients (57.6 %) had history of DM and in group B 25 patients (56.8%) had history of DM. These values show that there is an increased chance of DM for people who are having family history of DM ($p < 0.05$).

Table 4: Current Treatment of type 2 Diabetic Patients (n= 96)

Current Treatment	Group A		Group B	
	No	%	No	%
Nil	25	48.1	17	38.6
Diet	13	25	14	31.8
Diet + Exercise	14	26.9	13	29.5
Total	52	100	44	100
'p' value	0.4699			

Average height of patients in group A and B were in the range of (164.8+ 4.2) cm and (165.4 + 34.8) cm respectively. Initial average weight of patients in group A and B were found to be in the range of (72.5 ±4.3) kg and (71± 5) kg respectively. Initial average BMI of patients in group A and B were found to be (26.7 ± 1.0) and (26.1 ± 0.85) respectively. There was no statically significant difference in the mean height, weight and BMI of the two groups ($p > 0.05$). Average systolic blood pressure of patients in group A was found to be (127.1±10.7) mm/Hg and in group B (126.1.±7.2) mm/Hg and the average diastolic pressure in group A was found to be (81.0 ± 8.4) mm/Hg and in group B (81.0. ±6.5) mm/Hg. Mean blood pressure value of both groups did not show any statistically significant difference ($p > 0.05$). Average urea level of patients in group A and B were found to be (26.1±8.7) and (24.5±.71) respectively. Average serum creatinine level of patients in group A and B were in the range of (0.9±0.07) and (0.9±0.069) respectively. Average uric acid level of patients in group A and B were in the range of (4.19± 0.47) and (4.13 ±0.48) respectively. Final urea, creatinine and uric acid levels of patients were not significant and were found to be normal. There was no statistically significant difference in the mean urea, creatinine and uric acid values of the two groups ($p > 0.05$).

Changes in fasting blood sugar level of patients were shown in table-5. Regimen B had better impact on decreasing FBS than regimen A.

Table 5: Changes in Fasting Blood Sugar level (n= 96)

Fasting Blood Sugar	Group A patients		Group B patients	
	Mean	SD	Mean	SD
Initial Value	171.8	22.5	179.9	24.4
At 3 Months' Follow up	140.2	13.5	134.6	11.2
At 6 Months' Follow up	107.3	11.9	105.2	9.8
Change in FBS	64.5	14.6	74.7	18.0
% of Change in FBS	37.1	5.0	41.0	5.0
'p' value	0.0011			

Changes in Post Postprandial Blood Sugar level were shown in table-6. Regimen A had better impact on PPBS than regimen B.

Table 6: Changes in Post Prandial Blood Sugar level (n= 96)

Post Prandial Blood Sugar	Group A		Group B	
	Mean	SD	Mean	SD
Initial Value	220.2	30.0	226.6	31.8
At 3 months' follow up	199.5	22.8	202.8	34.5
At 6 months' follow up	168.1	24.4	184.2	35.8
Change (Decrease) in PP BS	52.1	11.6	42.4	20.9
% of Change in PP BS	23.6	4.3	18.9	9.5
'p' value	0.0024			

HbA_1C values showed (Table-7) significant decrease in group A (1.65 ± 0.39) than in group B (1.29 ± 0.52) at the end of 6 months.

Table 7: Changes in HbA_1C value (n= 96)

HbA_1C	Group A		Group B	
	No	%	No	%
Initial Value	8.01	0.47	8.16	0.51
At 6 months' follow up	6.36	0.19	6.87	0.47
Change (decrease) in HbA_1C	1.65	0.39	1.29	0.52
% of Change in HbA_1C	20.4	3.86	15.61	5.8
'p' value	0.0001			

Average serum cholesterol level changed from first visit (180±19.5), (215.8±24.2) to 6 month follow up (163.1± 16.6), (210.2±24.0) in group A and B respectively (Figure-1). There was a statistically significant difference in the serum cholesterol value of the two groups ($p < 0.05$).

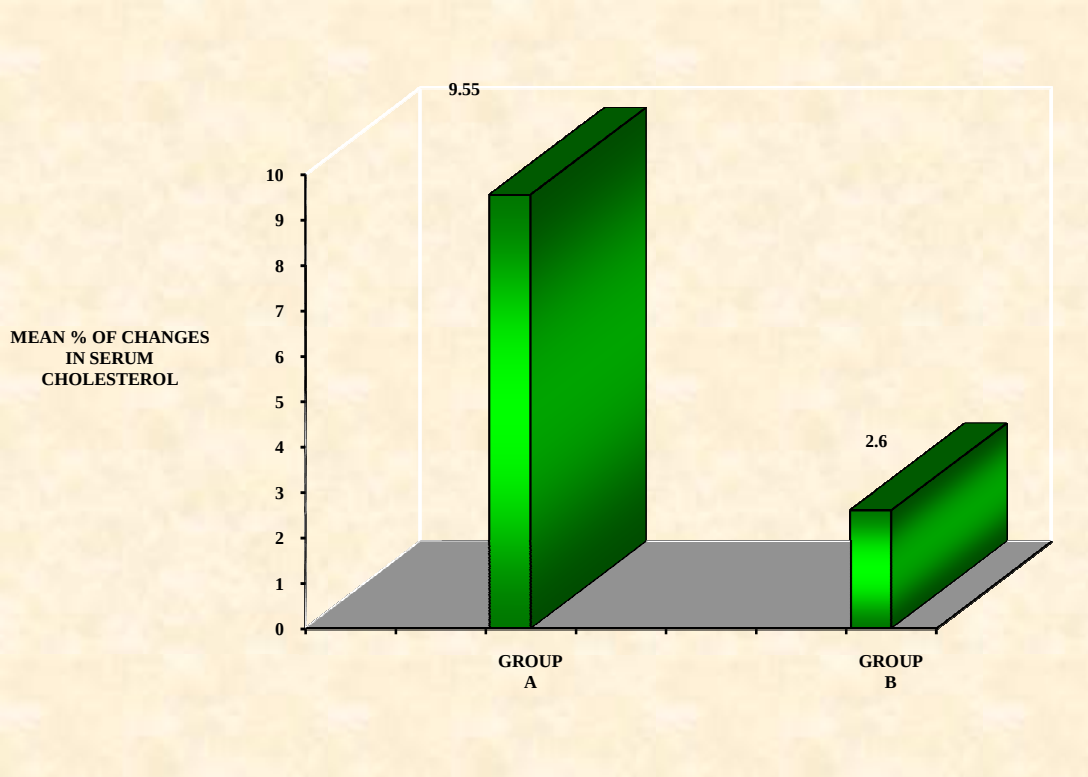

Fig. 1: Changes in Serum Cholesterol level of Type 2 Diabetic Patients

Average initial BMI were (26.7±1.0), (26.08±0.85) and after 6 months were (25.23±1.11), (24.88±0.95) in group A and B respectively. Patients in both the groups did not undergo any statistically significant change in BMI after six months of taking the drugs ($p > 0.05$).

CONCLUSION

Our study showed that glimepiride plus metformin combination significantly reduced the glycosylated haemoglobin level, postprandial glucose level and serum cholesterol level during the course of treatment. Glibenclamide plus metformin combination significantly decreased fasting blood sugar level throughout the study period. Hence

glimepiride plus metformin combination therapy can be considered as the best combination in diabetic patients with increased glycaemic control as compared to glibenclamide plus metformin therapy.

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