International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 2(3): May-June 2012

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences **Research Article……!!!**

Received: 04-05-2012; Revised; Accepted: 08-05-2012

EFFECT OF METFORMIN IN COMBINATION WITH GLIMEPIRIDE ON GLYCEMIC STATUS AND WEIGHT IN PATIENT WITH TYPE 2 DIABETES MELLITUS

Sanjeev I[1], Siddhant K[2], Jagdish D[2]*, Kunal C[2]

1. Diabetic Care Centre, Rachanakar Colony, Station Road, Aurangabad (MS) India
2. SRM Clinical Research Pvt. Ltd., Aurangabad (MS) India.

Keywords:

Type II Diabetes mellitus, Metformin, glimepiride, Glycemic status, Weight

For Correspondence:

Jagdish D

SRM Clinical Research Pvt. Ltd., Aurangabad (MS) India

E-mail:

jagdish.dj99@gmail.com

ABSTRACT

The aim of the present study is to observe the effect of metformin in combination with Glimepiride in patient with type 2 Diabetes Mellitus. Subjects and method: This is an open-label; observational study carried out to study the effect of metformin when it is given in combination with glimepiride on glycaemic status and weight in patient with type 2 Diabetes Mellitus. Patients with Glycosylated Haemoglobin more than 7% were included in the study. 25 patients were enrolled in the study for 12 weeks. The evaluation was conducted by observing the change in the FPG, PPG and weight at base line and at the end of study. Result: At week 12, the significant reductions in Glycemic status (FBG and PPG) were found in the patients. Also the greater significant reductions were observed in case of weight in same patients. Conclusion: Metformin-glimepiride tablets resulted in significantly reductions in Glycemic status and weight in patients with type 2 diabetes mellitus.

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders of carbohydrate metabolism in which glucose is underutilized, producing hyperglycemia resulting from a defect insulin secretion, insulin action, or both.[1,2] It is an endocrine disorder, more than 100 million (6% of the population) of people world-wide are affected inspite of enormous facilities available to control its growth.[3] Type 2 diabetes is caused by two primary metabolic defects: progressive pancreatic cell dysfunction and insulin resistance.[4] Typically, at the time of diabetes diagnosis, nearly 50% of Cell function has been lost and less than 60% of normal insulin sensitivity is present.[5] Diabetes is a chronic illness that requires continuing medical care and patient self-management education to prevent acute complications and to reduce the risk of long-term complications.[6]The lifestyle modification, diet and exercise o moderate intensity are used to improve insulin sensitivity and are recommended as an integral part of treatment of Type 2 diabetes.[7] When the lifestyle modification, diet and exercise fails to maintain the adequate glycaemic control, oral hypoglycaemic agents are introduced as a treatment approach.[4, 5] Oral Hypoglycemic Agents (OHAs) can be used either alone or in combination with other OHAs or insulin. The Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes recommends a target haemoglobin A1C concentration of 7.0% or less for all patients with diabetes. Currently, there are five major classes of oral antidiabetic agents: sulphonylureas – insulin secretagogues that target cell dysfunction; metformin – a biguanide that improves insulin sensitivity, thiazolidinediones – insulin sensitizers that lower peripheral insulin resistance; _ glucosidase inhibitors – intestinal enzyme inhibitors that slow carbohydrate absorption; meglitinides – rapid but short-acting, nonsulphonylurea secretagogues. [8-10]The goal levels of diabetes related parameters during treatment is given in Table No. 1.Insulin is also important in type 2 DM when blood glucose levels cannot be controlled by diet, weight loss, exercise and oral medications. Insulin is indicated in the following situations: 1) when diet and oral hypoglycaemic drugs fail to control hyperglycaemia and achieve therapy targets 2) diabetes during pregnancy when diet alone is inadequate, 3) when oral hypoglycaemic drugs are contraindicated, 4) during stressful conditions such as infection and surgery. [1, 2, 9]

Table No. 1 Blood-glucose targets for people with Diabetes

Parameter	Normal	Goal	Action suggested if
Pre-prandial Fasting Glucose	<110 mg/dl	80-120 mg/dl	<80 or >140 mg/dl
2h postprandial Glucose	<140 mg/dl	<140 mg/dl	>180 mg/dl
Bedtime	<120 mg/dl	100-140 mg/dl	<100 or >160 mg/dl
HbA1c	≤6%	< 6.5 %	>8 %

Combination therapy: It is always beneficial to switch over the patients on combination therapy, when there is high secondary failure associated with monotherapy and devastating long term consequence of poor glycemic control. A reasonable goal of treatment is to maintain good glycemic control through combination therapy so as to keep HbA1c value below 7% for a particular patient. Initiation of combination drug therapy at low dosages can minimize the side effects associated with high dose therapy of either agent, yield additive clinical benefits, and possibly curtail cost of treatment. For many drugs, 50% of the dosage needed to achieve the maximal therapeutic effect will produce well over 50% of that effect. [2, 11]

MATERIAL AND METHOD

Subject:

A total of 25 type 2 diabetic patients were enrolled in this study. Patients with age more than 35 yrs, of either sex, glycosylated haemoglobin > 7% and blood sugar level > 140 mg/dl were included in the study. The written consent was also taken from each patient in local language. Patients with current insulin therapy or received insulin for more than six weeks in last 3 months, who had known hypersensitivity to Biguanides and sulphonylurea, who are on chronic medication known to affect glucose metabolism were excluded from the study. Also the patients with renal disease or renal dysfunction, with congestive heart failure, hepatic insufficiency, alcoholic person and pregnant and lactating women were planned to exclude from the study.

Study Design:

This was a single centre, open-label, observational study conducted at the Diabetic Care Centre, Rachanakar Colony, Station Road, Aurangabad (MS) India. For conducting this observational study the protocol was generated and submitted to the Institutional Review Board (IRB) of SRM Clinical Research Services Pvt. Ltd. All subjects gave written informed consent to participate in the study. Total 25 patients were enrolled in this study. The dose of drug i.e. metformin in combination with Glimepiride given to the patients was at the sole discretion of the doctors and was not concerned with the investigators as the study is purely observational. After the screening of the patients they were given instructions on diabetic diet and their blood glucose level, both fasting and postprandial and weight was monitored at the initial visit to the hospital. Patient's records were maintained for the next three month after their initial visit to hospital. Also they were asked for the determination of FPG and PPG regularly. Records of age, sex, associated diseases were maintained. Observation of the subjects were done see changes in fasting plasma glucose, Postprandial plasma glucose and weight from baseline to 3 month after enrolment of the patient into the study. FPG and PPG were analysed by using one way ANOVA.

RESULTS

A total of 25 patients were screened of whom 21 completed the study successfully. 3 patients due to withdrawal of consent and 1 was switched to another treatment were excluded from the study. Out of the patients those participated in the study, 48.38% of patients were male while 51.61% of patients were female. An average weight of the patients was found 61.34 ± 0.5436. The mean age was 48.95 ± 2.032 yrs.

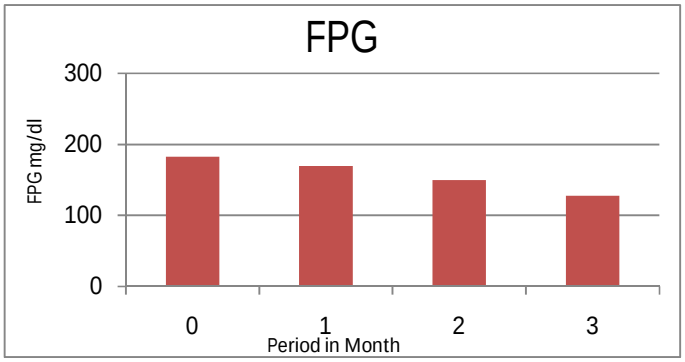
The baseline characteristics of all patients at randomization are summarized in the table 2.

Table No. 2:- The baseline characteristics of all patients at randomization

Parameters	Metformin plus Glimepiride
Sex (Male/Female)	12/13
Age (yrs)	48.95 ± 2.032
weight (kg)	61.34 ± 0.5436
FBG (mg/dl)	181.8 ± 9.49
PPG (mg/dl)	240.0 ± 16.65

FPG AND PPG: FPG values were found to be reduced by-54.59 ± 10.84 mg/dl. The significant reductions in the fasting plasma glucose were found (P: 0.0001). (Shown in Fig No.1)

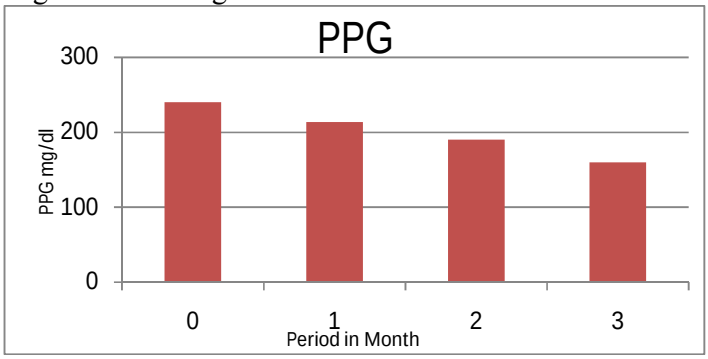
Fig No.1: - Change in FPG from baseline to the 3 months



Data was analyzed by ANOVA.P<0.001=extremely significant***,P<0.01= Very significant** Values are expressed as mean ±SEM

The PPG values were reduced throughout the study period of 3 month by 79.06 mg/dl. The PPG values were significantly reduced in both the groups (P<0.0001). (Shown in fig No.2)

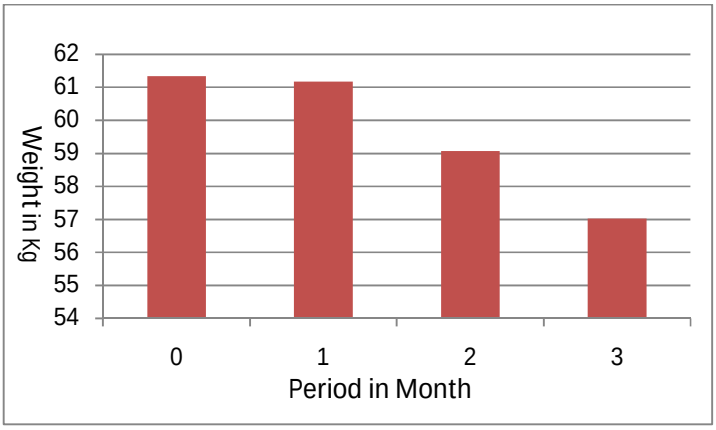
Fig No.2: - Change in PPG from baseline to the 3 months



Data was analyzed by ANOVA. P<0.001= extremely significant ***. Values are expressed as mean ±SEM.

Weight: Also the weight of the subjects was reduced throughout the study period of 3 month by 57.02 kg. The reduction in weight was significant (P<0.0001) and is Shown in fig No.3

Fig No.3: - Change in weight of subjects



Data was analyzed by ANOVA, P<0.001= extremely significant *** Values are expressed as mean ±SEM

DISCUSSION

Type 2 diabetes arises in the settings of insulin resistance in muscle, adipose tissue and liver and a progressive decline in pancreatic cell function.[5] A traditional stepwise approach to diabetes therapy involves the use of a single oral agent titrated to maximum dosage, each of which targets a single pathological defect of type 2 diabetes as its primary mechanism of action, with requirement of poor glycaemic control as an indication for addition of a second oral agent.[12-13]

The aim of our study was to observe the effect on glycemic status and weight in patients receiving metformin in combination with glimepiride. During the study it has been found that type 2 diabetes affected both the sex equally and mostly it is pronounced at the age of 48.26 ± 1.604 yrs. while 58% of patients were found to be at the greater risk of hypertension or other cardiovascular complication. Treatment with metformin glimepiride tablets simultaneously targets insulin resistance and insulin deficiency of type 2 diabetes, which may account for the greater effects on glycaemia. The greater mean changes from the baseline in case of fasting plasma glucose and postprandial glucose were found (-54.59 mg/dl and 79.06 mg/dl). Also the changes in weight of the patients from baseline were found (57.02 kg). The statistical analysis using ANOVA concludes that the reduction in FPG and PPG and weight is significant (P<0.0001). The reductions in the blood sugar level were found in both groups due to the synergistic effect. The synergistic effect of both combinations may be due to the different mechanism of action of individual drugs in the both combination.

These results demonstrate that treatment with metformin-glimepiride was efficacious in improving glycaemia by achieving therapeutic goals for fasting plasma glucose and postprandial glucose in patients with type 2 diabetes.

CONCLUSION

From the assumption described in results and discussion the present study concludes that the combination of Metformin-glimepiride reduced the Fasting and post-prandial plasma glucose as well as weight significantly throughout the study period of 12 weeks. So the Metformin-glimepiride combination can be considered as the best combination in patients with increased blood sugar level in diabetic patients.

REFERENCES

1. Bastaki S.,Diabetes mellitus and its treatment,Int J Diabetes & Metabolism,2005,13,111-134
2. Dipirio J.T., Pharmacotherapy: A pathophysiologic approach, 6th ed., 1999, 1333-1364.
3. Datta A., Diabetes Mellitus evaluation techniques Int. J. of Green pharmacy, 2006, 15-28.
4. Defronzo R. A., Pharmacologic Therapy Diabetes, Ann. Intern. Med.,1999.131(4),281-303.
5. Garber A., Klein E., Bruce S., Sankoh S., and Mohideen P., 2006. Metforminglibenclamide versus metformin plus rosiglitazone in patients with type 2 diabetes inadequately controlled on metformin monotherapy Diabetes, Obesity and Metabolism, 2006,8, 156–163.
6. American Diabetes Association, Standards of medical care for patients with diabetes mellitus, Diabetes Care, 2003; 26, S33–S50.
7. Kaufman M., Many Dimensions of Diet Counseling for Diabetes, Am. J. clinical nutrition, 1964, 15, 45-49.
8. Current concept in diabetes care, Module 6 – Treatment of Diabetes Mellitus, 2003 LifeScan, Inc.
9. Sundaram A., Newer antidiabetic drugs, Int. J. Diab. Dev. Countries, 1998, 18, 24-30.
10. Stumvoll M, Nurjhan N, Perriello G et al. Metabolic effects of metformin in non–insulin-dependent diabetes mellitus. N Engl J Med 1995; 333: 550–554.
11. Riddle M., Combining sulfonylurea and other oral agents, Am. J. Med., 2000,108, 15S-22S.
12. Landstedt-Hallin L., Arnert P., Bolindert J., The role of sulphonylurea in combination therapy assassed in a trial of sulphonylurea withdrawal, Diab. Med., 16, 827-834
13. Tosi F., Muggeo M., Brun E., Spiazzi G., Perobelli L., Zanolin E., Gori, M., Coppini A., Moghetti P., Combination Treatment With Metformin and Glibenclamide Versus Single-Drug Therapies in Type 2 Diabetes Mellitus: A Randomized, Double-Blind, Comparative Study, Metabolism, 2003. 52, 7, 862- 867.