A PROSPECTIVE STUDY OF EFFECT OF REPAGLINIDE MONOTHERAPY VERSUS ITS COMBINATION WITH METFORMIN IN TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT

BACKGROUND

Diabetes mellitus is a chronic metabolic disorder and complications are due to persistent hyperglycaemia. So to prevent or delay the complication, near-euglycaemia needs to be achieved. For that various drugs are used.

MATERIAL AND METHODS

This is a prospective, randomised open labelled study conducted in the Department of General Medicine, Amalapuram. Various parameters were measured before and after 16 weeks of study like FPG, PPPG, HbA1c, LDL, TG, and total cholesterol.

RESULTS

There was decrease in all the parameters in both the groups, but c-peptide level was decreased more in group B than group A and also increase in HDL concentration was more in group B.

CONCLUSION

When one antidiabetic drug is not sufficient to maintain euglycaemia and to prevent complication, various combinations are used. So various drug combinations to be evaluated and study to be conducted to establish the efficacy and more therapeutic options.

KEYWORDS

Repaglinide, metformin, diabetes mellitus.

HOW TO CITE THIS ARTICLE: Mohammed AA, Narsimha Raju AV, Swami KSR. A prospective study of effect of repaglinide monotherapy versus its combination with metformin in type 2 diabetes mellitus patients. J. Evid. Based Med. Healthc. 2016; 3(31), 1401-1403. DOI: 10.18410/jebmh/2016/321

INTRODUCTION: Diabetes mellitus is not a single disease entity but rather a group of metabolic disorders sharing the common underlying feature of hyperglycaemia. Morbidity associated with longstanding diabetes results from several serious complications, caused mainly by lesion involving both large and medium sized muscular arteries (macrovascular disease) and capillary dysfunction in target organs (microvascular diseases). Pathogenesis of these disorders is multifactorial, although persistent hyperglycaemia seems to be key mediators.(1) So the goals of therapy of both types of diabetes mellitus are to 1) eliminate the symptom related to hyperglycaemia 2) reduce or eliminate the longterm microvascular and macrovascular complication.(2)

Treatment goals for adults with diabetes are

HbA1c less than 7.0%
Preprandial capillary plasma glucose→80 – 180 mg/dL
Peak postprandial capillary plasma glucose →180 mg/dL
LDL <100 mg/dL.
HDL >40 mg/dL (male)
>50 mg/dL (female)
TG <150 mg/dL.

As recommended by the American Diabetes Association.(3)

For treatment of type-2 diabetes mellitus various oral hypoglycaemic agents are available. In present study, we have studied the effect of repaglinide monotherapy and its combination with metformin on type-2 diabetes mellitus.

MATERIAL AND METHODS: This is a prospective, randomised open labelled study conducted in the Department of General Medicine, Amalapuram during Jan-2015 to January 2016. Diabetic patients attending the regular outpatient department were selected for this study. Before start of the study permission form Institutional Ethics Committee was obtained and written consent from the

Financial or Other, Competing Interest: None.
Submission 27-03-2016, Peer Review 06-04-2016,
Acceptance 12-04-2016, Published 18-04-2016.
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DOI: 10.18410/jebmh/2016/321

patient was also taken in regional language. Patients were enrolled on the basis of inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Fasting plasma glucose – 140 to 220 mg. Without renal and hepatic disorder. Both sex age between 40 to 65 yrs.	Diabetic ketoacidosis. Hepatic and renal disease Pregnancy. H/O drugs hypersensitivity.

Patients were divided into two groups having 20 members each. Before start of the study all the parameters was measured like FPG, PPPG, HbA1c, LDL, TG, and total cholesterol. Patients were followed up to 16 weeks and each parameter was repeated at the end of the study. But fasting plasma glucose and postprandial glucose was repeated every 15 days. All the details of the patients like phone number and address of the patient were kept and were always in touch with them about their compliance with the treatment. Plasma glucose was measured by hexokinase method, c- peptide was measured by radioimmunoassay, glycosylated haemoglobin was measured by spectrophotometer, total cholesterol was estimated by ZAK modified method. HDL was estimated by precipitation method, LDL was estimated by W.T. Friedewald, R.I. Levy and D.C. Fredrickson and serum triglyceride was estimated by method of Neri and Frienge. Patients in group A were taking repaglinide 2 mg and patients in group B were taking repaglinide 2 mg and metformin 500 mg.

RESULTS:

Characteristics	Group A Repaglinide (mean) (N=20)	Group B Repaglinide plus metformin (mean) r=20
Age (years)	548	56.2
Sex	12/8	13/7
Weight (kg)	72.4	70.6
FPG (mg/dL)	160 mg/dL	158 mg/dL
PPPG (mg/dL)	228 mg/dL	236 mg/dL
C-peptide (nmol/L)	1.32	1.24
HbA1c (%)	8.2	8.6
HDL (mg/dL)	42.2	40.2
LDL (mg/dL)	136.2	144.4
Chol (mg/dL)	198.2	186.2
T.G (mg/dL)	196.2	182.4

Table 1: Parameters before start of the study

Character	Group A	% change	Group B	% Change
FPG (mg/dL)	138.2 mg/dL	13.75%	122.4	22.53
PPPG (mg/dL)	176.4 mg/dL	22.80%	172.4	26.94
HbA1c (%)	7.4	9.7%	7.2	16.27
C-peptide (nmol/L)	1.28	3.0%	1.10	11.29

Table 2: Changes in the percentage of mean FPG, PPPG, HbA1c and C-peptide in Group A and Group B after 16 weeks

Character	Group A (mean)	% Change	Group B (mean)	% Change
HDL (mg/dL)	46.2	9.4	48.2	19.9
LDL (mg/dL)	1110.4	18.94	114.6	20.63
TG (mg/dL)	160.6	18.14	154.6	15.01
Chol (mg/dL)	168.4	15.10	153.8	17.4

Table 3: Percentage change in the mean of lipid profile in Group A and Group B

Mean age of the patients in group A was 54.8 years and group B years was 56.2. There were twelve males and 8 females in group A and there were 13 males and seven females in group B. Fasting plasma glucose in group A and Group B was 160 mg/dL and 158 mg/dL respectively. Postprandial plasma glucose was 228 mg/dL and 236 mg/dL respectively. C-peptide concentration in the start of the study was 1.32 nmol/L in group A and 1.28 nmol/L in group B. HbA1c % was 8.2 and 8.6 respectively in both groups. HDL concentration in the start of the study in group A was 42.2 and group B was 40.2. LDL concentration was 136.2 mg/dL and 144.4 mg/dL in both the groups. Total cholesterol was 198.2 mg/dL and 186.2 mg/dL in group A and group B respectively. Triglyceride was 196.2 mg/dL in group A and 182.4 mg/dL in group B.

All the patients were followed up to 16 weeks and at the end of the study in group A, the FPG was reduced to 138.2 mg/dL, PPPG was reduced to 176.4 mg/dL, HbA1c was reduced to 7.4 and C-peptide was reduced to 1.22. Similarly, in group B, FPG was reduced to 122.4 mg/dL, PPPG was also reduced to 172.4 mg/dL, glycosylated haemoglobin changed to 7.4% and C-peptide level was reduced to 1.10 nmol/L.

Similarly, there was a change in lipid profile in both the groups. HDL concentration was increased in both the groups. In group A it was 46.2 mg/dL and in group B it was 48.2 mg/dL. In group A LDL was decreased to 110.4 and in group B it was 114.6. Total cholesterol was reduced to 168.4 in group A and 153.8 in group B. There was a change in TG also, in both groups that is 160.6 mg/dL and 154.6 mg/dL respectively.

DISCUSSION: Various drugs are used for the treatment of diabetes mellitus. When monotherapy fails to control the blood glucose levels, then combination of drugs with various mechanism of action are used. Repaglinide is the first clinically available insulin secretogenous drug that specifically enhances early phase prandial insulin response by increasing the sensitivity of β- cells to elevated glucose

levels.[4,5] Metformin, a biguanide that acts directly against insulin resistance, is regarded as an insulin sensitising drug and is considered to be cornerstone in the treatment of type -2 diabetes mellitus.

In our study, we have found that percentage change in mean of FPG in group A was less than group B that is 13.75% and 22.53%, but change in PPPG was nearly same in both groups that is 22.80% and 26.9% respectively which is similar to the study of Robert G Moses et al.[6] Glycosylated haemoglobin concentration has been decreased in both the groups, but percentage change in mean of HbA1c was better in Group B, which is similar to the study of Kawamori et al.[6,7] C–peptide level is the marker of insulin secretion. It is secreted at equimolar concentration with insulin. Its concentration after 16 weeks of treatment has not been changed much in Group A, but there is gross decrease in group B because of addition of insulin sensitiser.[7] HDL concentration was increased in both the groups, but in group B its concentration increased more than group A. In both the groups, LDL, triglyceride and total cholesterol level have been decreased, which is similar to the study of other authors.[8,9,10]

CONCLUSION: Diabetes mellitus is a chronic metabolic disorder which affects multiple organs. So to prevent this, near-euglycaemia to be maintained. Various drugs are available to maintain the plasma glucose to normal level. When one drug is not sufficient to maintain the euglycaemia, two drugs with different mechanism of action are used. Present study is also an effort to compare a combination therapy with monotherapy. Various such studies are required to make a combination as per individual metabolic needs.

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