

A PROSPECTIVE STUDY OF EFFICACY OF INSULIN SECRETAGOGUES AND INSULIN SENSITIZER IN TYPE – 2 DIABETES MELLITUS

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ABSTRACT

BACKGROUND

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin. In 2014, the global prevalence of diabetes was estimated to be 9% among the adults above 18 yrs. of age. More than 80% of the diabetes deaths occur in low and middle income countries.

METHOD

Present study is designed to study the effects of Repaglinide on type-2 diabetes mellitus in comparison with metformin. Subjects were randomized into two groups; one group A was given metformin 500 mg OD consisting of 20 patients, other group B was given Repaglinide 0.5 mg 30 min. before food, this group also consists of 20 patients.

RESULT

Fasting plasma glucose was decreased in both the groups, but percentage reduction in postprandial glucose was significantly higher in group A.

CONCLUSION

Hyperlipidaemia is the major cardiovascular risk factor in type 2 DM. Overall change in lipid profile was better in group B than group A.

KEYWORDS

Insulin secretagogues, Insulin sensitizer, Efficacy.

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INTRODUCTION: Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin.¹ In 2014, the global prevalence of diabetes was estimated to be 9% among the adults above 18 yrs. of age. More than 80% of the diabetes deaths occur in low and middle income countries.² WHO projects that diabetes will be the 7th leading cause of death in 2030,³ various therapeutic agents have been used for the treatment of type-2 diabetes mellitus along with diet and exercise. Among these therapeutic agents, there are two major groups of drugs that include insulin secretagogues and insulin sensitizer. Repaglinide is an oral insulin secretagogues of meglitinide class, which stimulates insulin release by closing K_{ATP} channels in pancreatic β cells. Metformin is another class of drug which increases the activity of AMP-dependent protein kinase.⁴ Present study is designed to study the effects of Repaglinide on type-2 diabetes mellitus in comparison with metformin.

MATERIAL AND METHOD: This is a prospective study carried out in the department of general medicine,

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Rangaraya Medical College, Kakinada, Andhra Pradesh, between Jan 2013 to Dec 2015. Patients included in this study were those who were attending the regular OPD of General Medicine. Before start of the study permission from institutional ethics committee was obtained and written consent from the patient was also taken in regional language. Consent was obtained in predesigned form, which is in two languages. Each patient was advised to visit the hospital every month and there contact details were taken along with address every month, all the parameters were evaluated.

Subjects were randomised into two groups; one group A was given metformin 500 mg OD consisting of 20 patients, other group B was given Repaglinide 0.5 mg 30 min. before food, this group also consists of 20 patients. Before start of the study, various parameters like BMI, fasting plasma glucose (FPG), postprandial plasma glucose (PPPG), HDL, LDL, total cholesterol, triglyceride was estimated and PPPG and FPG was repeated every month but other parameters were measured after 6 months and 12 months. Patients were advised to be on diet restriction and 45 min exercise every day. Plasma glucose was measured by hexokinase method, HbA1c was measured by using high performance required chromatography with reference to range 4.3 to 6.1%. HDL was estimated by ZAK modified method, LDL by by W.D Friedewald, R. I. Lavya and D.C. Frederickton and triglyceride was estimated by Debnath modification of Neri and Frienge.

| Inclusion Criteria | Exclusion Criteria |
|--|-------------------------------|
| Newly diagnosed | Diabetic ketoacidosis |
| Without renal and hepatic complication | H/o Hypersensitivity to group |
| Male/Female age 30 to 60 years | Hepatic and renal disease |
| FPG 140 to 220 mg/dL | Pregnancy |

RESULT: Forty newly diagnosed type-2 diabetes mellitus patients were enrolled for this study of both the sexes, as per inclusion and exclusion criteria, they were divided into two groups, were given 0.5 mg metformin for twelve months, in the start of the study in group (A). Before start of the study, all parameters were measured. Out of twenty patients in group A, 12 were male and 8 were female. Mean HbA1c of the patients before start of the study was 8.1, body mass index was 30.4, mean FPG and PPPG was 140.6 mg/dL and 210.8 mg/dL respectively. Lipid profile like HDL, LDL, total cholesterol and triglyceride was 40.2 mg/dL, 160.6 mg/dL, 200.2 mg/dL and 180.4 mg/dL respectively. At the end the study, the mean glycosylated haemoglobin changed to 6.9, FPG and PPPG decreased to 110.2 and 170.2 respectively. HDL concentration was increased to 48.2 mg/dL. LDL, total cholesterol and TG concentrated were decreased and were as follows 168.6 mg/dL, 180.2 mg/dL and 166.2 mg/dL.

| | Repaglinide (Gr. A) | Metformin (Gr. B) |
|------------------|---------------------|-------------------|
| Number | 20 | 20 |
| Sex Male /Female | 12/8 | 14/6 |
| BMI (mean) | 30.4 | 31.2 |
| HbA1c % | 8.1 | 8.4 |
| FPG (mg/dL) | 140.6 | 146.6 |
| PPPG (mg/dL) | 210.8 | 200.4 |
| TG (mg/dL) | 180.4 | 188.4 |
| LDL (mg/dL) | 166.6 | 182.4 |
| HDL (mg/dL) | 40.2 | 38.2 |
| CHol (mg/dL) | 200.2 | 202.4 |

Table 1: Parameters before start of study

| | Repaglinide (Gr. A) | Metformin (Gr. B) |
|--------------|-----------------------|----------------------|
| HbA1c% | (8.1–6.9) 14.81% | 8.4–7.1 (15.5%) |
| FPG (mg/dL) | (140.6–110.2) 21.19% | (146.6–110.2) (24.6) |
| PPPG (mg/dL) | (210.8–170.2) (19.0%) | (200.4–180.2)10% |

Table 2: Percentage change in mean FPG, PPG and HbA1c% from baseline after and of the study

| | Repaglinide (Gr. A) | Metformin (Gr. B) |
|-------------|----------------------|------------------------|
| LDL (mg/dL) | (180.4 to 68.6) 6.4% | (188.4 to 150.2) 20.9% |
| HDL (mg/dL) | (40.2 to 48.2) 19.9% | (38.2 to 42.2) 10% |

| | | |
|--------------|-------------------|---------------------|
| Chol (mg/dL) | (200.2–180.2)10 | (202.2 to 160.2)20% |
| TG (mg/dL) | (180.2–166.2)7.7% | (188.2–160.4)14.8% |

Table 3: Mean percentage change in LDL, HDL, cholesterol and triglyceride from baseline, at the end of study

In group B, out of 20 patients fourteen were male and six were female, mean FPG and PPPG was 146.6 mg/dL and 200.4 mg/dL, mean glycosylated haemoglobin concentration was 8.4. Regarding lipid profile, HDL was 38.2 mg/dL; LDL, total cholesterol and triglyceride concentration was 182.4 mg/dL, 202.4 mg/dL and 188.4 mg/dL respectively. At the end of the treatment, glycosylated haemoglobin decreased to 7.1, FPG and PPPG decreased to 110.2 mg/dL and 180.2 mg/dL respectively HDL concentration was increased to 42.2 mg/dL. LDL, total cholesterol and TG was reduced to 150.2 mg/dL, 160.2 mg/dL and 160.4 mg/dL respectively.

DISCUSSION: Repaglinide and metformin are two drugs whose mechanisms of action are different; one increases the insulin secretion, but other works by better utilisation of insulin and modification of glucose utilisation.⁵ This study was designed to compare the efficacy of these two drugs on type-2 diabetes mellitus patients in our study, it has been found that both the drugs are effective in the treatment of diabetes mellitus.

Regarding effect on glycosylated haemoglobin, there was much difference between percentage change in HbA1c. In group A it was 14.8% and group B it was 15.5 % which is similar to the study of Robert Mose et al.⁶

Fasting plasma glucose was decreased in both the group but percentage reduction in postprandial glucose was significantly higher in group A. Hyperlipidaemia is the major cardiovascular risk factor in type 2 DM. Percentage change in LDL concentration was more in group B than group A that is 26.4% and 20.9% respectively. HDL concentration was increased more in group A than group B. Total cholesterol concentration was decreased more in group B than group A but triglyceride concentration was decreased more in group B, which is similar to the study of Zhang H et al.⁷ Overall change in lipid profile was better in group B than group A.^{8,9}

CONCLUSION: Repaglinide and metformin are two drugs whose mechanisms of action are different; one increases the insulin secretion, but other works by better utilisation of insulin and modification of glucose utilisation. Both the drugs are effective in the treatment of diabetes mellitus. Glycaemic control is better with Repaglinide but overall change in lipid profile is better in metformin group. There are various drugs available for treatment of diabetes mellitus, but awareness about the complication and control is of major importance.

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