

A PROSPECTIVE STUDY OF EFFECT OF NATEGLINIDE VERSUS NATEGLINIDE IN COMBINATION WITH METFORMIN ON GLYCAEMIC CONTROL AND DYSLIPIDAEMIA IN TYPE – 2 DIABETES MELLITUS PATIENTS IN COASTAL DISTRICT OF ANDHRA PRADESH

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ABSTRACT

BACKGROUND

Diabetes mellitus is a clinical syndrome characterised by hyperglycaemia caused by absolute or relative deficiency of insulin. Persistent hyperglycaemia leads to both micro and macrovascular complication, so a treatment goal is recommended. To achieve that various drug either as monotherapy or in combination is used.

MATERIAL AND METHOD

Forty patients having type 2 diabetes mellitus were selected randomly, those who are taking nateglinide alone or metformin in combination with nateglinide. Patients were divided in to two groups, each group having 20 patients, group 1 were taking nateglinide 60 mg and group 2 were taking nateglinide 60 mg plus metformin 500 mg. Metabolic parameters that are FPG, PPPG, Fasting, C- Peptide, HDL level, TG Level, LDL level and serum cholesterol were studied before and at the end of the study that is 16 weeks.

RESULT

There was significant reduction in FPG and PPPG in both the groups having p value <.0001. Fasting C-peptide level change was more significant in group 2 than group 1, that is 19.0% and 14.86% respectively. Change in lipid profile was more in group 2 than group 1.

CONCLUSION

We conclude that nateglinide and its combination both have equal effect on glycaemic control, but reduction in fasting C-peptide level is more when nateglinide in combination with metformin.

KEYWORDS

Nateglinide, Metformin, Glycaemic Control.

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INTRODUCTION: Diabetes mellitus is a clinical syndrome characterised by hyperglycaemia caused by absolute or relative deficiency of insulin. Hyperglycaemia represents an independent risk factor for diseases of both small and large blood vessels. Type-2 diabetes is a more complex condition than type 1 diabetes because there is a combination of resistance to the actions of insulin in liver and muscle together with impaired pancreatic β – cell function leading to relative insulin deficiency.⁽¹⁾ Recently compiled data show that approximately 150 million people have diabetes mellitus worldwide and that this number may well double by the year 2025. Much of this increase will occur in developing countries and will be due to population growth, ageing, unhealthy diets, obesity and sedentary life style.⁽²⁾

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Optimal diabetes therapy involves more than plasma glucose management and medication, so that the term comprehensive diabetes care is used.⁽³⁾ For this, a treatment goal has been recommended by American Diabetes Association.⁽⁴⁾

| | |
|--|-----------------------------------|
| Glycaemic Control | |
| HbA ₁ C | < 7.0% |
| Preprandial capillary plasma glucose | 4.4 – 7.2 mmol/L (80 – 130 mg/dL) |
| Peak postprandial capillary plasma glucose | < 10.00 mmol/L (<180 mg/dL) |
| Glucose | |
| Blood pressure | <140/90 mmHg |
| Lipids | |
| Low-density lipoprotein | <2.6 mmol/L (100 mg/dL) |
| High-density lipoprotein | > 1 mmol/L (40 mg/dL) in men |
| | >1.3 mmol/L (50 mg/dL) in women |
| Triglycerides | <1.7 mmol/L (150 mg/dL) |

Source: American Diabetes Association: Diabetes care 38 (suppl 1):s1, 2015.⁽⁴⁾

To achieve this goal, various drugs are used as mono therapy or as combination of various drugs. Present study is conducted to know the efficacy of nateglinide verses nateglinide and metformin on type 2 diabetes mellitus patients.

MATERIAL AND METHOD: This is a prospective, open labelled, randomised study conducted in the dept. of General medicine Konaseema Institute of Medical Sciences, Amalapuram during Feb 2012 to Dec 2015. The study protocol was approved by the Institutional Ethics Committee, and permission was obtained from the medical supernatant and concern department head.

Selection of the Patient: Forty patients having type 2 diabetes mellitus were selected randomly those who are taking nateglinide alone or metformin in combination with nateglinide. Informed consent was obtained on predesigned consent from before start of the study. Patient was selected as per exclusion and inclusion criteria.

| Inclusion Criteria | Exclusion Criteria |
|----------------------------|--|
| Age 35 to 70 yrs. | <ul style="list-style-type: none"> • Complication like ketoacidosis, CHF, |
| FPG-130 mg/dL to 220 mg/dL | <ul style="list-style-type: none"> • Renal and hepatic dysfunction • hypersensitivity to drugs |

Plan of Study: Patients were divided into two groups, each group having 20 patients, group 1 were taking nateglinide 60 mg and group 2 were taking nateglinide 60 mg plus metformin 500 mg. Metabolic parameters that are FPG, PPPG, Fasting, C-Peptide, HDL level, TG Level, LDL level and serum Cholesterol were studied before and at the end of the study that is 16 weeks. FPG and PPPG were measured every 15 days. Plasma glucose was measured by hexokinase method, c-peptide was measured by radio immunoassay, 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.

Patient was advised to take less carbohydrate diet and regular extensive 45 min. five days in a week. Details of the patient's address and phone number was taken to be in touch. Data was calculated by using paired t- test and P value < 0.05 was considered significant.

RESULT: There was significant change in fasting plasma glucose in both the groups, it was 13.34% in group 1 and 14% in group 2. Postprandial plasma glucose also decreased significantly in both groups, that is 12.21% in group 1 and 12.30% in group 2 which is same in both the groups.

| Parameters | Mean before treatment n=20 | Mean before treatment n=20 | t - value | p - value |
|---------------------------|----------------------------|----------------------------|-----------|-----------|
| FPG (mg/dL) | 145.4 | 126 | 6.341 | <.0001 |
| PPPG (mg/dL) | 207.1 | 181.8 | 9.701 | <0.0001 |
| HbA1c (%) | 8.59 | 7.67 | 8.566 | <0.05 |
| C- peptide level (nmol/L) | 11.32 | 1.2 | 4.56 | <0.05 |
| HDL(mg/dL) | 37.5 | 42.2 | 7.66 | <0.05 |
| LDL(mg/dL) | 140.9 | 112.4 | 10.34 | <0.05 |
| TG (mg/dL) | 170.2 | 146 | 9.47 | <.0001 |
| Tchol (mg/dL) | 209 | 184 | 10.225 | <.0001 |

Table 1: Change in Metabolic Parameters in Group A taking Nateglinide

Glycosylated haemoglobin was decreased in both groups. In group 1, it was 10.71%; and group 2, it was 13.01 %. Fasting C-peptide level change was more significant in group 2 than group 1 that is 19.0% and 14.86% respectively. Serum HDL concentration was significantly increased in both groups, but group 2 has more increase than group 1(26.8%, 12.53% respectively). Regarding LDL concentration, there was decrease in both the groups. Group -1 it is 20.22% and group-2 it is 27.18%. TG concentration was also decreased significantly in both groups, but group 2 has more percentage decreases than group 1, that it is 14.11% in group 1 and 34% in group 2. Total cholesterol was also decreased, that is 11.96% and 14.70 respectively in both group 1 and group 2 respectively.

| Parameters | Mean before treatment | Mean before treatment | t-value | p-value |
|----------------------------|-----------------------|-----------------------|------------|------------------|
| FPG (mg/dL) | 148.4 | 127.6 | 14.8 | <.0001 |
| PPPG (mg/dL) | 196.6 | 172.4 | 9.7 | <0.001 |
| C- peptide | 1.37 | 1.17 | 8.502 | <0.05 |
| HbA1c (%) | 8.5 | 7.47 | 11.7 | <0.0001 |
| HDL(mg/dL) | 37.2 | 47.2 | 7.9 | <0.05 |
| LDL(mg/dL) | 139.27 | 101.36 | 11.4 | <0.0001 |
| TG (mg/dL) | 150.62 | 99.73 | 10.1 | <0.001 |
| Total chol. (mg/dL) | 210.9 | 179.77 | 8.9 | <0.001 |

Table 2: Change in Metabolic Parameters in Group B taking Nateglinide and Metformin

DISCUSSION: Nateglinide is a non-sulfonylureas KATP Channel modulator which promotes a more rapid but less sustained secretion of insulin so its major therapeutic effect is post prandial glycaemic control. It is associated with less episode of hypoglycaemia then other drug. Metformin is a biguanide. It increases the activity of AMP-dependent kinase. It is currently most commonly used drug both as

monotherapy as well as to potentiate the efficacy of other drug.

Effect on Plasma Sugar: There was significant decrease in fasting and postprandial plasma sugar in both the groups having P- value <0.001, that is highly significant. Percentage change in the mean plasma sugar was also almost same in both the groups, which is similar to the study of Edwards Horton et al.⁽⁵⁾ Glycosylated haemoglobin was decreased more in group 2 than group 1 which is similar to the study of various authors.^(5,6) C-peptide level was decreased in both the groups and was statistically significant, but decrease was more in group 2 than group 1, because metformin is an insulin sensitiser which is similar to the work of Nicholas et al.^(7,8)

Changes in Lipid Profile: -There was significant decrease in serum HDL concentration in both groups that is 12.53% and 26.8% respectively. The serum LDL concentration was decreased from mean value 140.9 mg/dL to 112.4 mg/dL in group 1 and 139.27 to 101.38 mg/dL in group 2 which is statistically significant. Serum cholesterol concentration was decreased in both the groups, but in group 2 reduction was more. The serum triglyceride was decreased significantly in both the groups. The percentage change in the mean in group 1 was 14.11% and group 2 was 34% respectively, which is supported by work of various authors.^(9,10)

CONCLUSION: Type 2 diabetes mellitus is difficult to control with a single oral agent and the rate of monotherapy failure is high, so combination therapy with complementary classes of drugs that act on different aspects of glycaemic control would be expected to be an effective strategy. In our study, we found that nateglinide and its combination both have equal effect on glycaemic control but reduction in fasting C-peptide level is more when nateglinide in combination with metformin. Lipid profile is better controlled in group with metformin combination.

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