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Original Research Article.

Comparative Analysis of Metformin and Combination of Metformin and Sitagliptin in Type II Diabetic Mellitus Patients at a Tertiary Care Hospital

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ABSTRACT

Background: The present study was conducted for comparing Metformin and Combination of Metformin and Sitagliptin in Type II Diabetic Mellitus Patients.

Materials & Methods: A total of 40 patients with presence of type 2 diabetic were enrolled. Complete demographic and clinical details of all the patients were obtained. All the patients were divided into two study groups with 20 patients in each group as follows: Group A: Patients receiving Metformin alone, and Group B: Patients receiving of combination of Metformin and Sitagliptin. Baseline Fasting (FPG) and post-prandial plasma glucose (PPPG) levels were evaluated. All the patients were regularly monitored. At the end of 1st month and 2nd month of treatment, results were evaluated and compared. All the results were recorded and analyzed using SPSS software.

Results: Mean age of the patients of group A and group B was 49.5 years and 51.7 years. Majority proportion of patients of both the study groups were males. Mean fasting plasma glucose levels among the patients of group A at baseline, 1st month and 2nd month was 153.8 mg/L, 149.7 mg/L, and 129.5 mg/L respectively. Mean fasting plasma glucose levels among the patients of group B at baseline, 1st month and 2nd month was 158.1 mg/L, 133.1 mg/L, and 133.8 mg/L respectively. Mean fasting plasma glucose levels and mean PPPG levels among the patients of group A were significant lower in comparison to patients of group B at one month after therapy.

Conclusion: The results disclosed that patients using metformin monotherapy had insufficient glycemic control. The best strategy for preserving glycemic control is to add one dosage of sitagliptin each day.

Key words: Metformin, Sitagliptin, Diabetic Mellitus.

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INTRODUCTION

Diabetes mellitus (DM) is probably one of the oldest diseases known to man. Type 2 DM (formerly known as non-insulin dependent DM) is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency. Type 2 DM results from interaction between genetic, environmental and behavioral risk factors.[1, 2]

The use of oral agents, such as acarbose, metformin or thiazolidinediones, in people without type 2 diabetes has also led to the suggestion that early pharmacotherapy might prevent diabetes and induce remission. However, discontinuation of pharmacotherapy is not necessarily associated with a sustained improvement in glycaemia. Thiazolidinedione treatment in women with a history of gestational diabetes, decreases the annual incidence of type 2 diabetes (at least compared to the expected rate).[3- 5] Sitagliptin (Januvia, Glactiv(R), Tesavel(R)) is a dipeptidyl peptidase-4 inhibitor indicated for the treatment of type 2 diabetes mellitus.

Oral sitagliptin as monotherapy or combination therapy was generally well tolerated and improved glycaemic control in well-designed clinical trials in patients with type 2 diabetes. Glycosylated haemoglobin (HbA(1c)) levels were significantly reduced with sitagliptin monotherapy relative to voglibose monotherapy or placebo, and with sitagliptin as initial combination therapy with metformin or pioglitazone relative to monotherapy with these agents or placebo.[6]

Hence; the present study was conducted for comparing Metformin and Combination of Metformin and Sitagliptin in Type II Diabetic Mellitus Patients.

MATERIALS & METHODS

The present study was conducted for comparing Metformin and Combination of Metformin and Sitagliptin in Type II Diabetic Mellitus Patients. A total of 40 patients with presence of type 2 diabetic were enrolled. Complete demographic and clinical details of all the patients was obtained. All the patients were divided into two study groups with 20 patients in each group as follows:

Group A: Patients receiving Metformin alone.

Group B: Patients receiving combination of Metformin and Sitagliptin.

Baseline Fasting (FPG) and post-prandial plasma glucose (PPPG) levels were evaluated. All the patients were regularly monitored. At the end of 1st month and 2nd month of treatment, results were evaluated and compared. All the results were recorded and analyzed using SPSS software.

Table 1: Comparison of fasting plasma glucose levels (mg/dL)

Time interval	Group A	Group B	p-value
Baseline (mg/dL)	153.8	158.1	0.127
1st month (mg/dL)	149.7	133.1	0.001 (Significant)
2nd month (mg/dL)	129.5	133.8	0.435

Table 2: Comparison of postprandial plasma glucose levels (mg/dL)

Time interval	Group A	Group B	p-value
Baseline (mg/dL)	218.4	223.5	0.282
1st month (mg/dL)	212.7	195.8	0.001 (Significant)
2nd month (mg/dL)	189.2	191.8	0.395

RESULTS

Mean age of the patients of group A and group B was 49.5 years and 51.7 years. Majority proportion of patients of both the study groups were males. Mean fasting plasma glucose levels among the patients of group A at baseline, 1st month and 2nd month was 153.8 mg/L, 149.7 mg/L, and 129.5 mg/L respectively. Mean fasting plasma glucose levels among the patients of group B at baseline, 1st month and 2nd month was 158.1 mg/L, 133.1 mg/L, and 133.8 mg/L respectively. Mean fasting plasma glucose levels and mean PPPG levels among the patients of group A were significant lower in comparison to patients of group B at one month after therapy.

DISCUSSION

Diabetes is a complex metabolic disorder characterized by chronic hyperglycaemia, which leads to microvascular and macrovascular complications. Hyperglycaemia arises because of relative or absolute insulin deficiency. Broadly speaking, diabetes can be divided into two categories – immune-mediated diabetes (type 1 diabetes) and non-immune-mediated diabetes (type 2 diabetes). In essence, such a definition characterizes type 2 diabetes as something it is not, rather than specifying a particular pathogenesis or another positive definition. The poorly controlled DM can lead to damage to various organs, especially the eyes, kidney, nerves, and cardiovascular system. DM can be of three major types, based on etiology and clinical features.[7-9] These are DM type 1 (T1DM), DM type 2 (T2DM), and gestational DM (GDM). In T1DM, there is absolute insulin deficiency due to the destruction of β cells in the pancreas by a cellular mediated autoimmune process. In T2DM, there is insulin resistance and relative insulin deficiency. GDM is any degree of glucose intolerance that is recognized during pregnancy. DM can arise from other diseases or due to drugs such as genetic syndromes, surgery, malnutrition, infections, and corticosteroids intake.[10,11] Hence; the present study was conducted for comparing Metformin and Combination of Metformin and Sitagliptin in Type II Diabetic Mellitus Patients.

Mean age of the patients of group A and group B was 49.5 years and 51.7 years. Majority proportion of patients of both the study groups were males. Mean fasting plasma glucose levels among the patients of group A at baseline, 1st month and 2nd month was 153.8 mg/L, 149.7 mg/L, and 129.5 mg/L respectively. Mean fasting plasma glucose levels among the patients of group B at baseline, 1st month and 2nd month was 158.1 mg/L, 133.1 mg/L, and 133.8 mg/L respectively. Derosa G et al evaluated the impact on glycemic control, insulin resistance, and insulin secretion of sitagliptin+metformin compared to metformin in type 2 diabetic patients. Patients were instructed to take metformin for 8 ± 2 months, then they were randomly assigned to sitaglipin 100 mg or placebo for 12 months. They evaluated at 3, 6, 9, and 12 months: body mass index (BMI), glycemic control, fasting plasma insulin (FPI), HOMA-IR, HOMA-β, fasting plasma proinsulin (FPPr), proinsulin/fasting plasma insulin ratio (Pr/FPI ratio), C-peptide, glucagon, adiponectin (ADN), and high sensitivity-C reactive protein (Hs-CRP). Before, and after 12 months since the addition of sitagliptin, patients underwent a combined euglycemic hyperinsulinemic and hyperglycemic clamp, with subsequent arginine stimulation. Both treatments similarly decreased body weight, and BMI; on the other hand, they both improved glycemic control, glucagon and HOMA-IR, but sitagliptin+metformin were more effective in reducing these parameters. Sitagliptin+metformin, but not placebo+metformin, decreased FPPr, FPPR/FPI ratio, and increased C-peptide values, even if no differences between the groups were recorded. Sitaglitin+metformin gave also a greater increase of HOMA-β, M value, C-peptide response to arginine and disposition index

compared to placebo+metformin group. Other than improving glycemic control, sitagliptin+metformin also improved β-cell function better than metformin alone.[12]

Mean fasting plasma glucose levels and mean PPPG levels among the patients of group A were significantly lower in comparison to patients of group B at one month after therapy. Tahashildar, J et al evaluated the comparison of clinical outcomes of sitagliptin +metformin and glimepiride in uncomplicated Type-2 diabetics. 299 Type-2 diabetics patients were enrolled and were randomly allocated to two groups viz Group A and Group B. Group A received sitaglitin+metformin (50+500) mg/day and Group B received glimepiride 1mg/day respectively. At the end of six months follow up the patients of Group A who received sitaglitin+metformin (50+500) mg/day had greater reduction in FPG, PPG and HbA1c (all P<0.001) was recorded when compared between zero and six month within group. A significant reduction in FPG, PPG and HbA1c (all P<0.01) also recorded in Group B who received glimepiride 1mg/day when compared between zero and six months within group. A statically significant difference (all P<0.05) was recorded at six months between group. The adverse events like hypoglycemic episodes, gastrointestinal adverse events etc were greater in Group B than Group A. Changes in weight were also noted in both Groups. Weight loss in Group A and weight gain in Group B was recorded.[13]

Lim S et al assessed the predictive parameters for therapeutic efficacy, a multivariate regression analysis was performed with baseline fasting glucose, insulin, C-peptide, and glucagon levels, homoeostasis model assessment-insulin resistance (HOMA-IR) and β-cell function (HOMA-B), insulinogenic index, and area under the curve for glucose, insulin, and C-peptide obtained after 75-g oral glucose tolerance test. After 52 weeks, mean HbA1c levels and fasting and postload 2-h glucose were significantly decreased from 8·7±1·4% to 7·2±1·3%, 9·2±3·0 to 7·2±1·8 mm, and 17·5±5·1 to 10·9±3·6 mm, respectively (P<0·01). HOMA-B and IGI increased significantly from 50·3±33·5 to 75·1±32·8 and from 11·3±1·3 to 35·0±6·3 at 52 weeks, respectively (P<0·01). Multivariate regression analysis indicated that the reduction in HbA1c was significantly associated with high baseline HbA1c, low IGI, and short duration of diabetes after adjusting for age, sex, body mass index, blood pressure, triglycerides, creatinine, high-sensitivity CRP, glucagon, C-peptide, HOMA-B, and HOMA-IR. No severe adverse events were observed. These results suggested that drug-naïve type 2 diabetic patients with low β-cell function would benefit the most from early initial combination therapy of sitagliptin and metformin.[14]

CONCLUSION

The results disclosed that patients using metformin monotherapy had insufficient glycemic control. The best strategy for preserving glycemic control is to add one dosage of sitagliptin each day.

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