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Comparative Study of Metformin and Combination of Metformin and Sitagliptin in Type II Diabetic Mellitus Patients.

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ABSTRACT

Background: Metformin is recommended as initial monotherapy for treatment of type 2 diabetes mellitus because it decreases the higher blood glucose by suppressing hepatic production of glucose, apart from suppression of hepatic glucose production, it also increases sensitivity of insulin, it also enhances the peripheral uptake of glucose (by inducing GLUT4 enhancer factor phosphorylation), and it also decreases the insulin-induced suppression of fatty acid oxidation. The aim of this study, metformin and combination of metformin and sitagliptin in type ii diabetic mellitus patients. **Methods:** Two groups were included in this study. Each group has 50 cases & each case was having diabetic mellitus. This study conducted in the Career Institute of Medical Sciences in the Department of Pharmacology. The duration of study was over a period of six month. **Results:** In our study we were included two groups. Each group has 50 cases, means total 100 cases were included. In group I we were observed 26 male & 24 female out of 50 cases. In group I we found that 13 had vomiting followed by diarrhea, metallic taste, abdominal pain. While in group II we found that 3 had vomiting followed by diarrhea, metallic taste, abdominal pain. **Conclusion:** The foregone discussion revealed that in patients who are on monotherapy with metformin alone having inadequate glycaemic control. The addition of one daily dose of Sitagliptin 100 mg is the most effective way of maintaining glycaemic control.

Keywords: Diabetes Mellitus, Metformin, Sitagliptin.

INTRODUCTION

There are various Oral Hypoglycemic drugs available for glycemic control. Sitagliptin is a DPP-4 (dipeptidyl peptidase 4) inhibitor and it is indicated for the treatment of type 2 diabetes mellitus.1 In various trials it has been shown that sitagliptin as an initial therapy has shown to improve the glycemic control with little hypoglycemic risk, and weight stability. Sitagliptin is very highly selectivity towards DPP-4, and there is no affinity towards other DDP enzymes like DPP-8 and DPP-9. Sitagliptin and various other DPP-4 inhibitors have a multimodal action in Type 2Diabetes Mellitus patients, by preserving stimulated circulating incretin hormones, insulin secretion is stimulated under hyperglycemic conditions and glucagon secretion is suppressed.[1]

Metformin is recommended as initial monotherapy for treatment of type 2 diabetes mellitus because it decreases the higher blood glucose by suppressing hepatic production of glucose, apart from suppression of hepatic glucose production, it also increases sensitivity of insulin, it also enhances the peripheral uptake of glucose (by inducing GLUT4 enhancer factor phosphorylation), and it also decreases the insulin-induced suppression of fatty acid oxidation. It is proved that metformin increases the peripheral utilization of glucose due to improved insulin binding to insulin receptors.[2,3] However, patient on metformin do experience some common side effects like gastrointestinal intolerance and risk of lactic acidosis in poor perfusion states and also in Renal Failure.[3]

Metformin hydrochloride, a biguanide, is the most popular oral glucose-lowering medication in most countries, widely viewed as 'foundation therapy' for individuals with newly diagnosed type 2 diabetes mellitus. This reputation has resulted from its

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effective glucose-lowering abilities, low cost, weight neutrality, overall good safety profile (especially the lack of hypoglycemia as an adverse effect), and modest evidence for cardio protection.[4] A derivative of guanidine, which was initially extracted from the plant Galega officinal or French lilac, metformin was first synthesised in 1922 and introduced as a medication in humans in 1957, after the studies of Jean Sterne.[5] Its popularity increased after eventual approval in the USA in 1994, although it was used extensively in Europe and other regions of the world prior to that.[6] The drug's efficacy has been demonstrated in monotherapy as well as in combination with other glucose lowering medications for type 2 diabetes mellitus.

MATERIALS AND METHODS

Sample Size: Two groups were included in this study. Each group has 50 cases & each case was having diabetic mellitus.

Study Area: This study conducted in the Carrier institute of medical sciences in the department of pharmacology.

Study duration: The duration of study was over a period of six month.

Data collection: Patients were divided to Group I and Group II. The Group I comprised of patients receiving Metformin (500mg orally twice daily), while Group II comprised of patients receiving of combination of Metformin (500mg orally twice daily) and Sitagliptin (100mg orally once in a day). Sitagliptin was added in type II diabetic patients which were inadequately controlled with metformin alone. Baseline Fasting (FPG) and post-prandial plasma glucose (PPPG) levels were measured. Follow up was done at 4, 8 and 12 weeks of therapy. At each visit, FPG Level and PPPG level were measured and safety of drugs was noted.

Data Analysis: Data were analyses by the using mean ± SD & Microsoft excel.

RESULTS

In our study we were included two groups. Each group has 50 cases, means total 100 cases were included. In group I we were observed 26 male & 24 female out of 50 cases .While in group II we were observed 30 male & 20 female out of 50 cases. Comparison of metformin monotherapy and combination of metformin & sitagliptin on Fasting Plasma Glucose level in mg/ dl
at 0,4,8 and 12 weeks showed in table 1. Comparison of metformin monotherapy and combination of metformin & sitagliptin on Postprandial Plasma Glucose level in mg/dl at 0,4,8 and 12weeks showed in table 2.Adverse drug effect were reported by total 33 cases out of 100 cases. In group I we found that 13 had vomiting followed by diarrhea, metallic taste, abdominal pain. While in group II we found that 3 had vomiting followed by diarrhea, metallic taste, abdominal pain which was showed in chart 3.

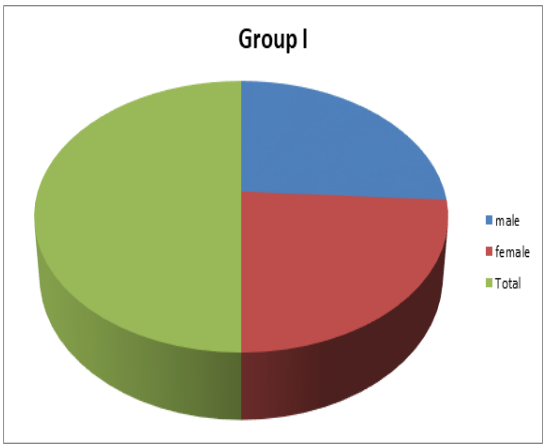

Figure 1: Distribution of cases according to gender in group I

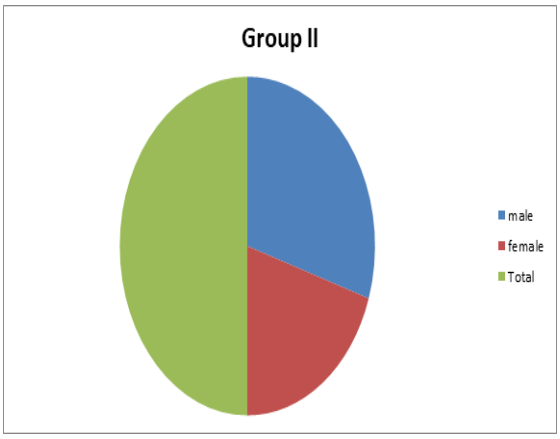

Figure 2: Distribution of cases according to gender in group II

Table 1: Comparison of metformin monotherapy and combination of metformin & sitagliptin on Fasting Plasma Glucose level in mg/ dl at 0,4,8 and 12 weeks

Time interval	Group I Mean ±SD	P value	Group II	P value Mean ±SD
0 week	140.56±55.59		164.70±59.87	
4 week	135.05±45.05	>0.05	156.06±55.94	>0.05
8 week	137.95±38.34	>0.05	141.60±5.29	<0.05
12 week	131.62±44.62	>0.05	118.80±33.92	<0.001

Table 2: Comparison of metformin monotherapy and combination of metformin & sitagliptin on Postprandial Plasma Glucose level in mg/dl at 0,4,8 and 12weeks

Time interval	Group I Mean ±SD	P value	Group II	P value Mean ±SD
0 week	203.84±77.79		224.70±83.18	
4 week	196.02±70.67	>0.05	221.64 ±80.46	>0.05
8 week	195.80±63.02	>0.05	199.28±75.22	>0.05
12 week	186.08±61.24	>0.05	166.98±50.26	>0.05

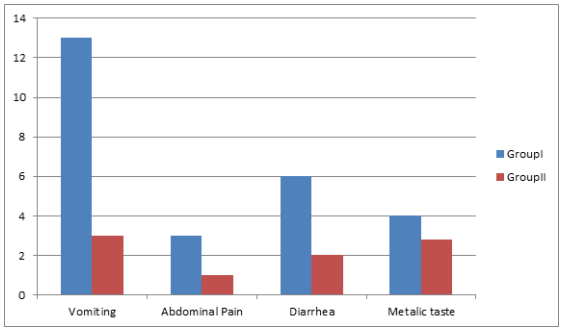

Figure 3: Adverse drug effect in both group

DISCUSSION

It has been reported in 2015 that worldwide, almost 415 million people were affected by type 2 diabetes mellitus.[7] 10% of total health care budget is used to control type II diabetes mellitus which resulted in reduction of rise of complications. Though, it is very difficult to achieve it.[8] As type II diabetes mellitus is characterized by deterioration of glycaemic control and pancreatic function, it is necessary to intensify therapy to maintain appropriate glycaemic target. It has been observed that 60% of diabetic patients who were on monotherapy did not achieve their therapeutic target. To achieve glycaemic control, dual therapy is necessary.[9]

At early stage, combinational therapy was also proposed to delay the glycaemic deterioration in patients with outcome of preservation of functioning of beta cells.[8,10] To improve glycaemic control with their distinct mechanism, the use of two or three drugs in combination is useful. This also helps in overall drug dosing in same setting and minimize adverse effects.[11-13]

This study results showed that the combination of Metformin and Sitagliptin is more effective than Metformin alone in type II diabetics. The decrease in fasting plasma at 4 and 12 weeks was higher in Group II significantly than Group I, but there was no significant decrease at 8 weeks, whereas reduction in postprandial plasma glucose at 4,8 and 12 weeks was significantly ($p<0.05$) more in Group II than Group I. Statistically significant reduction in percentages of mean FPG level at 4,8 and 12 weeks and mean PPPG at 8 and 12 weeks was noted in Group II patients in comparison to Group I patients whereas decrease in mean FPG at 4 week was noted in Group I patients compared to Group II patients. Reasner et al, found that the efficacy of combinational therapy of metformin and sitagliptin with significant reduction in fasting as well as postprandial plasma glucose. Similar results were observed by Perez-monteverde et al and Wanstein et al.[14-16] Benard Charbonel et al in one of their study showed the effectiveness of addition of daily one dose of Sitagliptin 100mg with ongoing Metformin therapy in type II diabetic patients who had insignificant glycaemic control with monotherapy using Metformin.[17]

It is observed that when patients were treated with single antidiabetic drug, they were not able to maintain glycaemic control so many patients required combination of antidiabetic drug.[12]

Results of this study revealed that there was an improvement in glycaemic control after the addition of sitagliptin in patients with metformin monotherapy and inadequate glycaemic control.

This study also showed that the incidence of adverse effects was less in metformin and sitagliptin combination group. The adverse effects in group I were observed to be higher than group II patients. Reasner et al showed that in 20.6% of patients, the combination therapy of metformin and sitagliptin exerted the gastrointestinal side effects and patients on monotherapy exerted the gastrointestinal side effects in 24.6% of patients.[14]

CONCLUSION

The foregone discussion revealed that in patients who are on monotherapy with metformin alone having inadequate glycaemic control. The addition of one daily dose of Sitagliptin 100 mg is the most effective way of maintaining glycaemic control.

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