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Original Research Article.

Evaluation of Metformin and Combination of Metformin and Sitagliptin in Patients with Type 2 Diabetic Mellitus in a Tertiary Care Hospital

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ABSTRACT

Background: For the prevention of diabetes related complications, improvement in glycaemic control is of the prime importance. Thus far, different oral anti-hyperglycemic agents are available to achieve euglycemia. During trial of mono or dual therapy for optimal efficacy, tolerability and safety of the patients is of prime importance. A drug combination which is efficacious and is with less adverse effects should be chosen for the treatment of T2DM.

Materials and Methods: 56 known type 2 diabetic patients were selected and were randomly divided into two groups, group A and group B. The Group A comprised of patients receiving Metformin, while Group B comprised of patients receiving of combination of Metformin and Sitagliptin.

Results: Comparison of metformin monotherapy and combination of metformin & sitagliptin on fasting blood sugar level in mg/ dlat 1,4,8 and 12 weeks.

Conclusion: In conclusion, both sitagliptin or metformin monotherapy as well as in combination with other helped in improving glycemic control in patients with type 2 diabetes mellitus.

Keywords: Diabetes Mellitus, Metformin, Sitagliptin, Combination Therapy.

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INTRODUCTION

For the prevention of diabetes related complications, improvement in glycaemic control is of the prime importance. Thus far, different oral anti-hyperglycemic agents are available to achieve euglycemia. Reports have shown that about 60% of the diabetes patients do not achieve their therapeutic targets when on monotherapy making dual therapy a necessity to achieve glycaemic control.[1] During trial of mono or dual therapy for optimal efficacy, tolerability and safety of the patients is of prime importance. A drug combination which is efficacious and is with less adverse effects should be chosen for the treatment of T2DM.[2]

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. 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 2 diabetes mellitus patients, by preserving stimulated circulating incretin hormones, insulin secretion is stimulated under hyperglycemic conditions and glucagon secretion is suppressed.[3]

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.[4] However, patient on metformin do experience some common side effects like gastrointestinal intolerance and risk of lactic acidosis in poor perfusion states and in renal failure.[5]

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 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.[6] 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.[7] 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.[8] Our aim was to be the drug's efficacy has been demonstrated in monotherapy as well as in combination with other glucose lowering medications for type 2 diabetes mellitus in a tertiary care hospital.

MATERIALS AND METHODS

This present study was conducted in the Department of Pharmacology, in collaboration with department of Medicine of Gauri Devi Institute of Medical Sciences, India, during the period of six months. In the present study,56 known type 2 diabetic patients were selected and were randomly divided into two groups, group A and group B. The Group A comprised of patients receiving Metformin (500mg orally twice daily), while Group B 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 2 diabetic patients which were inadequately controlled with metformin alone. Baseline Fasting (FBS) and post-prandial plasma glucose (PPBS) levels were measured. Follow up was done at 4, 8 and 12 weeks of therapy. At each visit, FBS Level and PPBS level were measured, and safety of drugs was noted. Data were analyses by the using mean & SD & Microsoft excel.

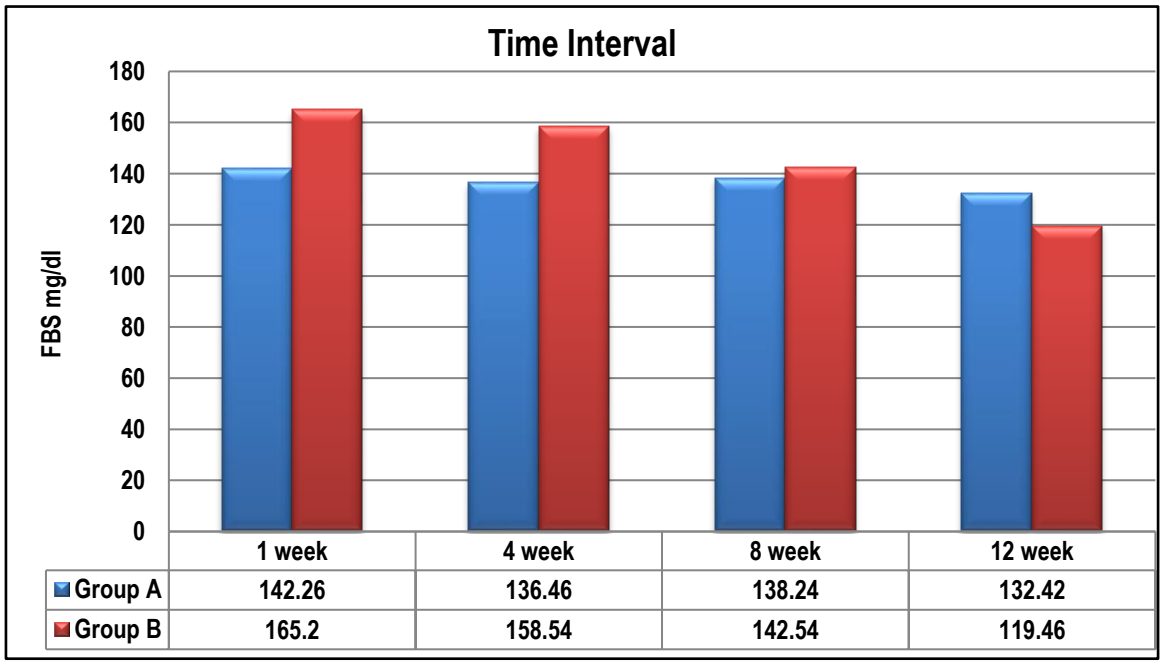

Fig 1: Comparison between group A and group B on FBS level.

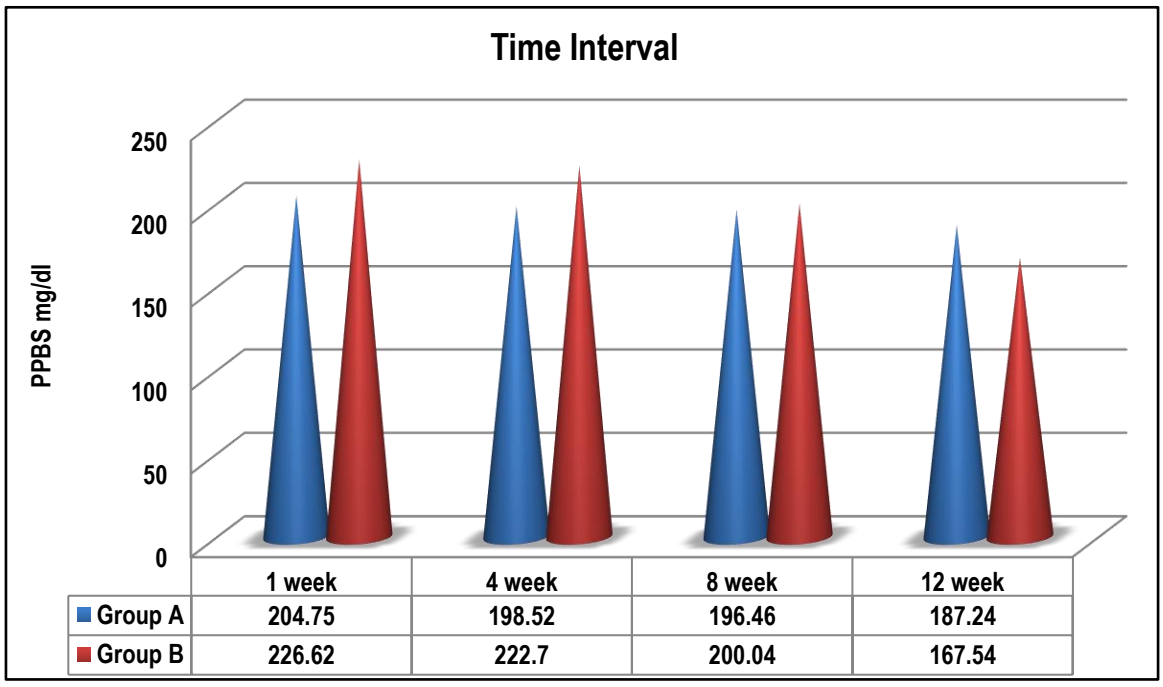

Fig 2: Comparison between group A and group B on PPBS level.

RESULTS AND DISCUSSION

This present study was carried out in the Department of Pharmacology, in collaboration with department of Medicine of Gauri Devi Institute of Medical Sciences, India. Comparison of metformin monotherapy and combination of metformin & sitagliptin on fasting blood sugar level in mg/ dlat 1,4,8 and 12 weeks showed in Fig. 1. Comparison of metformin monotherapy and combination of metformin & sitagliptin on postprandial blood sugar level in mg/dl at 1,4,8 and 12 weeks showed in Fig. 2. Adverse effects were reported by total 17 cases out of 56 cases.

In group A, we found that 12 had vomiting followed by diarrhea, metallic taste, abdominal pain. While in group B, we found that 5 had vomiting followed by diarrhea, metallic taste, abdominal pain.

It has been reported in 2015 that worldwide, almost415 million people were affected by type 2 diabetesmellitus.[9] 10% of total health care budget is used to control type 2 diabetes mellitus which resulted in reduction of rise of complications. Though, it is very difficult to achieve it.[10] As type 2 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.[11] At early stage, combinational therapy was also proposed to delay the glycaemic deterioration in patients with outcome of preservation of functioning of beta cells.[12] 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.[13-15] This study results showed that the combination of Metformin and Sitagliptin is more effective than Metformin alone in type 2 diabetics. The decrease in fasting plasma at 4 and 12 weeks was higher in Group B significantly than Group A, but there was no significant decrease at 8 weeks, whereas reduction in postprandial plasma glucose at 4,8 and 12 weeks was significantly more in Group B than Group A. Statistically significant reduction in percentages of mean FBS level at 4,8 and 12 weeks and mean PPBS at 8 and 12 weeks was noted in Group B patients in comparison to Group A patients whereas decrease in mean FBS at 4 week was noted in Group A patients compared to Group B 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 Perezmonteverde et al and Wanstein et al.[16-18] 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 2 diabetic patients who had insignificant glycaemic control with monotherapy using metformin.[19] 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.[14] 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 A were observed to be higher than group B patients. Reasner et al.[16] 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.

CONCLUSION

In conclusion, both sitagliptin or metformin monotherapy as well as in combination with other helped in improving glycemic control in patients with type 2 diabetes mellitus. 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 very effective way of maintaining glycaemic control.

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