

Sitagliptin Versus Metformin as an Initial Monotherapy in Type 2 Diabetes Mellitus Patients - Observational Study

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ABSTRACT

Introduction: Diabetes mellitus is a chronic metabolic disease. So an Observational study Comparing sitagliptin to metformin as an initial monotherapy in type 2 diabetes mellitus patients. Diabetes mellitus is a chronic, progressive disease and lifestyle modifications alone are inadequate, one or more agents are usually required to attain adequate glycemic control.

Material and methods: In the present study 200 known diabetic patients were selected and these patients were randomly divided into two groups, group A comprised 100 patients whose baseline glycemic parameters were recorded and patients were put on sitagliptin 100 mg per day, whereas Group B comprised of 100 patients and these patients were placed on metformin 500mg – 2000 mg per day to achieve glycemic control and repeat testing for HbA1c was done after 24 weeks, patients were monitored closely for ensuring the compliance to diet, drug and exercise.

Results: These 200 patients were randomly divided into two groups, Group A comprised 100 patients were put on sitagliptin 100 mg per day, Group B comprised 100 patients were selected and were placed on metformin 500mg – 2000mg. Both the groups baseline FBS, PLBS, HbA1C was estimated prior to the study. It was observed that the mean baseline HbA1c in the Group A patients was 7.85% and in Group B was 7.99%, whereas the mean HbA1c after 24 weeks of therapy was 7.49% and 7.80% respectively in the Group A and B. There was a significant decrease in HbA1c in both the groups and it was statically significant.

Conclusion: In this 24 week study sitagliptin was not inferior compared to metformin in controlling the HbA1C in patients with type 2 diabetes mellitus. In summary, both sitagliptin or metformin monotherapy helped in improving glycemic control in patients with type 2 diabetes mellitus. Both the group of the drugs was well tolerated by the patients, and the incidence of gastrointestinal-related adverse effects was there but it lower, whereas the weight loss was low in the sitagliptin group of patients. The result of this study provides the data for the use of sitagliptin as initial monotherapy for type 2 diabetes mellitus patients.

Keyword: Type 2 Diabetes Mellitus, Sitagliptin, Metformin, Glycosylated Hemoglobin, Fasting Blood Glucose, Glycemic Variability

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 DPP 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.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 Our objective was to assess the impact of DPP-4 on glycemic levels if initiated as a first line therapy.

MATERIAL AND METHODS

This Observational study was conducted at MNR Medical College to assess similarity of efficacy of a new agent to a standard treatment. In the present study 200 known diabetic patients were selected from MNR Medical College and Hospital, the patients were randomly divided into two groups, group A comprised 100 patients whose baseline glycemic parameters were recorded and patients were put on sitagliptin 100 mg per day, whereas Group B comprised of 100 patients and these patients were placed on metformin 500mg – 2000 mg per day to achieve glycemic control and repeat testing for HbA1c was done after 24 weeks, patients were monitored closely for ensuring the compliance to diet, drug and exercise.

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Metformin 500 mg was started with once daily dose and up titrated to 500 mg twice daily over a maximum 3-5 week period. Down-titration of metformin was done for patients who were intolerant to maximum dosage and these patients were given minimum dosage of 1000 mg/day. Patients treated with were analyzed as a single group, regardless of final dose. Counseling of all Patients was done in regards to diet and exercise during the study period.

Inclusion Criteria

1. Men and women with type 2 diabetes (17 – 72 years of age),
2. HbA1c 6.5 – 9.1% were eligible to participate in the study.

Exclusion Criteria

1. Type 1 diabetes,
2. Fasting plasma glucose (FPG) <100 mg/dl or >250mg/dl,
3. Coronary Artery disease,
4. Renal impairment (in males if creatinine more than 1.4 mg/dl or ≥ 1.2 mg/dl for females or creatinine clearance less than 60 ml/min),
5. Elevated Hepatic enzymes.

STATISTICAL ANALYSIS

The results were analyzed using SPSS software using paired t test and chi square analysis for patients before and after the therapy.

RESULTS

In the present study 200 patients were selected from MNR Medical college, the patients were randomly divided into two groups, Group A comprised 100 patients were put on sitagliptin 100 mg per day, Group B comprised 100 patients were selected and were placed on metformin 500mg – 2000mg both the groups baseline FBS, PLBS, HbA1c was estimated prior to the study.

It was observed that the mean baseline HbA1c in the Group A patients was 7.85% and in Group B was 7.99%, whereas the mean HbA1c after 24 weeks of therapy was 7.49% and 7.80% respectively in the Group A and B. There was a significant decrease in HbA1c in both the groups and it was statistically significant.

There was a significantly positive correlation ($p < 0.001$) in both the two groups, group A ($r = 0.913$) having higher positive correlation than compared to group B ($r = 0.759$), whereas the mean difference in HbA1c was higher in the group A patients (0.39) than compared to group B patients (0.22) suggesting a greater reduction in HbA1c with sitagliptin arm group of patients when compared to metformin group, as the mean difference was significant the effect size (d) was also calculated. It was observed that in group A patients the effect size was ($d = 1.19$) larger than when compared to the group B ($d = 0.51$).

Occurrence of other symptoms associated to the drugs like nausea, headache and diarrhoea were also seen in both the groups and it was observed that nausea was higher in group A patients i.e. (17%) when compared to Group B patients

i.e.(9%), this increase was non-significant statistically and the p value was = 0.35. Headache was higher in group B (11%) than compared to A (6%), the increase was observed to be non-significant statistically and the p value was = 1.0. Diarrhoea was greater in group B patients (20%) than compared to group A (3%), the increase was observed to be significant statistically and the p value was = 0.016.

DISCUSSION

International Diabetes Federation (IDF) and the American Association of Clinical Endocrinologists (AACEs), suggest that HbA1c less than 6.5% is the prime target in Type 2 diabetes mellitus patients and it is proved that good glycemic control helps in reduction of the macrovascular and microvascular complications.⁴

Metformin lowers hepatic glucose output and it also increases hepatic sensitivity to insulin and decreases hepatic gluconeogenic substrates which results in decreasing gluconeogenesis. In addition, it also helps in increased utilization and uptake of glucose by skeletal muscles. And also reduces glycogenolysis. Apart from glycemic control it also has a potential to induce mild anorexia, which may facilitate glycemic control. Metformin is eliminated by renal tubular secretion, and its half-life is 6.2 hours. Sitagliptin is highly selective DPP-4 inhibitor, its Oral bioavailability is nearly 87% and terminal half-life is about 10 to 12 hours.

Bloomgarden et al, have shown that different oral antihyperglycaemic agents have similar efficacy when the data are corrected for differences in baseline HbA1c values.⁵ Our study has shown that patient with sitagliptin were having lesser side effect and better tolerated, apart from achieving better glycemic control hence it can be used apart from metformin as a initial therapy.

Brazg et al, has done A randomized, double-blind, placebo-controlled study for evaluation of sitagliptin and metformin combination and its impact on glycemic levels. It was shown that patients on combination had better glycemic reduction than compared to placebo group.⁶

Williams-Herman et al. has done a longer-term randomized control trials to establish the safety and efficacy of sitagliptin/metformin in type-2 diabetes patients with poor glycemic control. Patients were divided in various groups who received individual drugs like i) sitagliptin group 50to 100mg, ii) metformin 500 twice a day group, iii) metformin 1000 twice a day, iv) Sitagliptin and metformin combination.⁷ It was shown that Sitagliptin and metformin combination group was having greater HbA1c Reduction than compared to other groups.

Reasner et al. has done 44-week study to compare the efficacy and safety of sitagliptin/metformin with metformin monotherapy in type 2 DM treatment-naive patients. It was shown combination had greater reduction than compared to individual drug.⁸

Miller S 2006 has shown that sitagliptin as a monotherapy can provide greater reduction of glycemic levels and fewer complications in patients who are intolerant to metformin.⁹ Zerilli T, (2007) study has shown that there is greater

reduction of HbA1c with Sitagliptin group and the drug is well tolerated in these groups.¹⁰

In trials (Aschner et al; Raz I et al), it was that patients treatment with once-daily 100mg sitagliptin had significantly reduction of HbA1c when compared with placebo group.¹¹⁻¹²

CONCLUSION

Diabetes mellitus is a chronic, progressive disease and lifestyle modifications alone are inadequate, one or more agents are usually required to attain adequate glycemic control. In summary, both sitagliptin or metformin monotherapy helped in improving glycemic control in patients with type 2 diabetes mellitus. Both the group of the drugs was well tolerated by the patients, and the incidence of gastrointestinal-related adverse effects was there but it lower, whereas the weight loss was low in the sitagliptin group of patients. The result of this study provides the data for the use of sitagliptin as initial monotherapy for type 2 diabetes mellitus patients.

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