Glycemic Impact of Individual Oral hypoglycemic Drugs in Type 2 Diabetes Mellitus- An Observational Study

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ABSTRACT

Introduction: The Incidence and prevalence of type 2 diabetes mellitus around the world is dramatically increasing over the past decades. Study aimed to assess the effectiveness of various Oral Hypoglycemic drugs on glycemic levels in established Type 2 Diabetes Mellitus patients.

Material and Methods: In the present study 300 diabetic patients were selected and randomized into three groups. Group A comprised 100 patients whose baseline glycemic parameters were recorded and patients received Vildagliptin 50 mg twice a day, whereas Group B comprised of 100 patients and these patients received metformin 0.5gm–2gm/day and Group C comprised of 100 patients and these patients received Voglibose 0.2mg thrice a day for 24 weeks. Patients were monitored closely for ensuring the compliance to diet, drug and exercise.

Result: In the present study patients were randomly divided into three groups, Group A on Vildagliptin 50 mg, Group B on metformin 500mg – 2000mg. Group C on Voglibose 0.2mg. These entire three 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 7.83 % and in Group B was 7.92%, Group C was 7.94% whereas the mean HbA1c after 24 weeks of therapy was 7.42%, 7.78% and 7.81% respectively in the Group A, B, and C. There was a significant decrease in HBA1c in all these three groups and it was statically significant.

Conclusion: In summary, all three Oral hypoglycemic agent vildagliptin or metformin or voglibose monotherapy helped in improving glycemic control in patients with type 2 diabetes mellitus.

Keywords: Glycemic Impact, Oral hypoglycemic Drugs, Type 2 Diabetes Mellitus

INTRODUCTION

Trends of Diabetes are increasing Despite many newer oral hypoglycemic agents are available efforts for better management of this disease.[1] Despite so many advances, the blood glucose levels remains uncontrolled and the patients are unsatisfied due to poor glycemic control. Type 2 diabetes mellitus is characterized by insulin resistance, deficiency of insulin and increased hepatic glucose output. Keeping the above things in mind various therapies are aimed to correct these physiologic abnormalities. In type 2 diabetes mellitus American Diabetes Association recommends to initiate first by giving a trial of diet and exercise. If the desired glycemic level is not achieved with diet and exercise then these patients should be initiated on medication to achieve good glycemic control.

Various OHA are available for the management of Diabetes, still biguanides (metformin) holds prime position in management of Diabetes as a first line drug.[2] Metformin has multiple actions and it is used in various other medical conditions. It basically acts by reducing the hepatic glucose output production and, to a very lesser extent it can enhance the sensitivity of insulin in hepatic tissues apart from having an action on peripheral tissues. Metformin has been shown to reduce the glycemic variability.[2-3]

Apart from Metformin, other drugs are available like Alpha-glucosidase inhibitors, which act on enzyme alpha-glucosidase and inhibit it, these enzymes are present at brush border cells in small intestine, it acts by braking more complex carbohydrates into sugars. This helps in achieving better post prandial glycemic levels under control than fasting glycemic levels.[4-5]

Vildagliptin is selective and potent inhibitor of dipeptidyl peptidase-4 (DPP-4). It increases availability of endogenous incretin hormones, GLP-1 (glucagon-like peptide-1) and GIP (glucose-dependent insulinotropic polypeptide) which helps in achieving glycaemic control. Various studies have proved that when Vildagliptin is given along metformin it Complements the pharmacological effect of metformin and helps in better glycemic control. It is well known that vildagliptin suppresses release of glucagon and enhances glucose-dependent insulin secretion, thereby improves the glycaemic control, and superadded it is also weight-neutrality effect and tendencies of hypoglycaemia is very less when compared to other Oral hypoglycemic agents.[6-7]

Study aimed to assess the effectiveness of various Oral Hypoglycemic drugs on glycemic levels in established Type 2 Diabetes Mellitus patients.

MATERIAL AND METHODS

This Observational study was conducted to assess similarity of efficacy of a new agent to a standard treatment. In the present study 300 known diabetic patients were selected, these patients were randomly divided into three groups, Group A comprised 100 patients whose baseline glycemic parameters were recorded and patients were put on Vildagliptin 50 mg

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twice a day, whereas Group B comprised of 100 patients and these patients were placed on metformin 500mg – 2000 mg per day and Group C comprised of 100 patients and these patients were placed on Voglibose 0.2mg thrice a 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.

Inclusion Criteria

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

Exclusion Criteria

1. Type 1 diabetes mellitus,
2. Fasting plasma glucose (FPG) less than 90 mg/dl or more than 260mg/dl,
3. Cardiovascular disease
4. Renal impairment (males if creatinine ≥1.4 mg/dl or ≥1.2 mg/dl for females)
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, 300 established Type 2 diabetes mellitus patients were randomly divided into three groups, Group A comprised 100 patients were put on Vildagliptin 50 mg twice a day, Group B comprised 100 patients were selected and were placed on metformin 500mg – 2000mg. Group C was given Voglibose 0.2mg thrice a day. These entire three 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 7.83% and in Group B was 7.92%, Group C was 7.94% whereas the mean HbA1c after 24 weeks of therapy was 7.42%, 7.78% and 7.81% respectively in the Group A, Band C. There was a significant decrease in HBA1c in all these three groups and it was statically significant.

There was a significantly positive correlation ($p<0.001$) in all the three groups, group A ($r = 0.911$) having higher positive correlation than compared to group B ($r= 0.761$), group C ($r= 0.749$), whereas the mean difference in HbA1c was higher in the group A patients (0.41) than compared to group B patients (0.14) and group c patients (0.13) suggesting an 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 ($d= 0.56$), and group c ($d= 0.49$)

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 C patients i.e. (11%) when compared to Group B patients i.e.(7%), and Group A patients i.e.(7%), 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%) and Group C (2%), the increase was observed to be non-significant statistically and the p value was = 1.0. Diarrhoea was greater in group B patients (18%) than compared to group C (10%) and group A (3%), the increase was observed to be significant statistically and the p value was = 0.014.

DISCUSSION

International Diabetes Federation (IDF) and the American Association of Clinical Endocrinologists (AACEs), suggest that target HbA1c should be less than 6.5% in Type 2 diabetes mellitus patients and it is proved that good glycemic control helps in reduction of the macro and microvascular complications.[8]

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.

Our study has shown that patient with vildagliptin were having lesser side effect and better tolerated, apart from achieving better glycemic control hence it can be used apart from metformin and voglibose as an initial therapy. The Gastrointestinal problem were more with metformin and voglibose group than other group

Williams-Herman et al. has done a longer-term randomized control trails 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.[9]

Reasner et al. has done 44-week study to compare the efficacy and safety of metformin monotherapy versus sitagliptin/metformin in type 2 Diabetes mellitus. This study has shown that patient son combination therapy had better HbA1c reduction than compared to individual monotherapy drug.[10]

Lukashevich V (2014) had done double-blind study for24 weeks and study randomized patients received vildagliptin 50 mg bid (n = 158) or placebo (n = 160). After 24 weeks, the mean haemoglobin A1c (HbA1c) was -1.01% with vildagliptin group and -0.25% with placebo.[11]

Ristic S (2005), had enrolled 279 known type 2 diabetes mellitus patients and these patients received 12-week active treatment phase, these patients were given variable dosage and it was compared with placebo group. These patients received following dosages of vildagliptin: 25 mg twice daily, 25, 50 or 100 mg once a day, or placebo. There was significant reduction of HbA1c in the vildagliptin 50 mg qd and 100 mg qd groups and it was statistically significant when compared to placebo group.[12]

Mori K 2016; has done randomized open-label trials, in which 78 patients were randomized (1:1) and these patients received 5 mg linagliptin once daily for 12-week treatment or 0.2 mg voglibose three times a day. At week 12, the mean HbA1c decreased by −0.60% in linagliptin group whereas in voglibose group the mean HbA1c decreased by −0.20%.[13]
Cai X (2013) has done a study to compare the glycemic control between Asian and Caucasian, with alpha glucosidase inhibitors (AGI) in patients with diagnosed type 2 diabetes. Totally 58 patients were selected. Comparison of Patients on AGI treatment with placebo has shown clearly that there was a significant HbA1c decline favoring AGI treatment in Asian whereas in Caucasian also there was a significant decrease in HbA1c favoring AGI treatment.[14]

CONCLUSION

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

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