Influence of Individual Oral Hypoglycemic drugs on Glycemic Levels in Type 2 Diabetes Mellitus - An Observational Study

Mohd Riyaz[1]

ABSTRACT

Introduction: Trends of Diabetes are increasing at alarming rate despite so many advance in detection and management of diabetes and its allied complication. 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 150 diabetic patients were selected and randomized into three groups. Group A comprised 50 patients whose baseline glycemic parameters were recorded and patients received Linagliptin 5mg once a day, whereas Group B comprised of 50 patients and these patients received metformin 0.5gm–2.5 gm/day and Group C comprised of 50 patients and these patients received Voglibose 0.2mg twice a day for 48 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 received Linagliptin, Group B received metformin. Group C received Voglibose. 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 7.82% and in Group B was 7.92%, Group C was 7.97% whereas the mean HbA1c after 48 weeks of therapy was 7.40%, 7.75% and 7.83% respectively suggesting a greater reduction of HbA1c in linagliptin arm group than other two groups.

Conclusion: In summary, all three Oral hypoglycemic agent Linagliptin or metformin or voglibose monotherapy helped in improving glycemic control in patients with type 2 diabetes mellitus, but linagliptin group patient had better glycemic control than compared to other groups.

Keyword: Type 2 Diabetes Mellitus, Linagliptin, Metformin, Alpha Glucosidase inhibitor, Voglibose, Glycosylated Hemoglobulin, Fasting blood glucose, Glycemic Variability, Oral Hypoglycemic Drugs

INTRODUCTION

Incidence and prevalence of type 2 diabetes mellitus is dramatically increasing all round the world.[1] Despite on best of the treatment there is gross glycemic variability and also there is poor glycemic control which could be due to multiple factors. It is well known and proved that in patients with Type 2 diabetes mellitus there is insulin resistance, deficiency of insulin and increased hepatic glucose output. The main goal of treatment in these patients is targeting all these issues which are discussed above. Various guidelines and recommendation have been formulated by IDF, American Diabetes Association, AACE, EASD in managing the diabetic patients.[2-3] Best initial line of management for all patients is life style modification, diet and exercise. Despite this if the glycemic level are not under controlled these patient should be initiated on medication as per requirement to achieved strict glycemic control.

Despite so many advances and multiple OHA are available for the management of Diabetes, still gold standard is metformin and it holds pivotal role in management of Diabetes as a first line drug. Metformin acts by reducing the hepatic glucose output production and it can also enhances the sensitivity of insulin in hepatic tissues apart from having an action on peripheral tissues.[4-5]

Linagliptin is selective and potent inhibitor of dipeptidyl peptidase-4 (DPP-4) which results in increases endogenous incretin hormones availability like (GLP-1 (glucagon-like peptide-1) and GIP (glucose-dependent insulinotropic polypeptide)leading to stimulation and release of insulin which eventually helps in achieving glycaemic control. Unlike other DPP-4 inhibitors, linagliptin is excreted chiefly via the enterohepatic system, and can be used without dose adjustment in patients with renal or hepatic impairment.[5] Various studies have proved that when linagliptin is given along metformin it Complements the pharmacological effect of metformin and helps in better glycemic control.

Alpha-glucosidase inhibitors (voglibose), acts on enzyme alpha-glucosidase and inhibit it, these enzymes are present at brush border cells in small intestine, and it acts by breaking more complex carbohydrates into sugars. This helps in achieving better post prandial glycemic levels under control than fasting glycemic levels.[6] 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 150 known diabetic patients were selected, these patients were randomly divided into three groups, Group A comprised 50 patients whose baseline glycemic

[1]Professor of Medicine, MNR Medical College and Hospital, Sangareddy, Telangana, India

Corresponding author: Dr. Mohammed Riyaz, H. No:11-5-337/2 Red Hills, Hyderabad- 500004, Telangana, India

How to cite this article: Mohd Riyaz. Influence of individual oral hypoglycemic drugs on glycemic levels in type 2 diabetes mellitus - an observational study. International Journal of Contemporary Medical Research 2018;5(5):E48-E50.

DOI: http://dx.doi.org/10.21276/ijcmr.2018.5.5.34

parameters were recorded and patients were placed on Linagliptin 5 mg once a day, whereas Group B comprised of 50 patients and these patients were placed on metformin 500mg – 2500 mg per day and Group C comprised of 50 patients and these patients were placed on Voglibose 0.2mg twice a day, to achieve glycemic control and repeat testing for HbA1c was done after 24 and 48 weeks, patients were monitored closely for ensuring the compliance to diet, drug and exercise.

Inclusion Criteria

1. Men and women with type 2 diabetes (20 – 69 years of age)
2. HbA1c 6.5 – 8.9% were eligible for the study

Exclusion Criteria:

1. Type 1 diabetes mellitus,
2. Fasting plasma glucose (FPG) less than 80 mg/dl or more than 260mg/dl,
3. Any preexisting Cardiovascular disease
4. Renal impairment (males if creatinine ≥1.4 mg/dl or ≥1.2 mg/dl for females)
5. Elevated Hepatic enzymes

RESULTS

In the present study, 150 established Type 2 diabetes mellitus patients were randomly divided into three groups, Group A comprised 50 patients were put on Linagliptin 5 mg once a day, Group B comprised 50 patients were selected and were placed on metformin 500mg – 2500mg. Group C comprised 50 patients were given Voglibose 0.2mg twice a day. These entire three groups baseline FBS, PLBS, HBa1C was estimated prior to the study.

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

It was observed that the mean baseline HBA1c in the Group A patients was 7.82% and in Group B was 7.92%, Group C was 7.97% whereas the mean HbA1c after 48 weeks of therapy was 7.40%, 7.75% and 7.83% 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 ($r = 0.9$) having higher positive correlation than compared to group B, group C, whereas the mean difference in HbA1c was higher in the group A patients (0.42) than compared to group B patients (0.17) and group c patients (0.14) suggesting an greater reduction in HbA1c with linagliptin arm group of patients when compared to metformin group.

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. (12%) when compared to Group B patients i.e.(9%), and Group A patients i.e.(4%), this increase was non-significant statistically. Incidence of Diarrhoea was greater in group B patients (16%) than compared to group C (11%) and group A (3%), this increase which was observed to be significant statistically.

DISCUSSION

Multiple international associations like American Diabetes association, International Diabetes Federation (IDF) and the American Association of Clinical Endocrinologists (AACEs), suggest HbA1c target should be 6.5 – 7.0% in established case of Type 2 diabetes mellitus patients preferably it is better to keep HbA1c less than 6.5%. It is been proved by various studies that good glycemic control helps in reduced incidence of macro and microvascular complications.[8]

DPP-4 is widely distributed in endothelial cells, pancreas, uterus, liver, salivary glands, lymph node, spleen, and thymus. DPP-4 regulates glucagon-like peptide (GLP)-1, and glucose-dependent insulinotropic peptide (GIP) which leads to glucose homeostasis via enhancing insulin secretion and suppression of glucagon, which results in control of post-prandial and fasting hyperglycemia. Other substrates of DPP-4 are neuropeptide-Y (NPY) and substance P. NPY plays significant role in appetite, control of blood pressure and energy homeostasis, whereas substance P plays a role in pain and inflammation. Linagliptin is a DPP-4 inhibitor which increases the concentrations of active hormones of incretin, which results in stimulation of release of insulin and decreases the glucagon levels

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 linagliptin 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 problems were more with metformin and voglibose group than other group.

Del Prato S1, Barnett AH, et. al. (2011) this study has shown that patient on linagliptin Monotherapy had significant, reduction in glycaemic control and HbA1c of nearly ≥0.5% at 24 weeks.[9]

Taskinen MR et. al. (2011), this study was done for 24-week, it was double blinded randomized, placebo-controlled, parallel-grouped study which was carried out in almost 82 centers in 10 countries. Linagliptin was given as an additional drug to the patients whose glycemic level was not normalized with metformin. Addition of Linagliptin to metformin group showed significant reductions when compared to placebo (mean changes from baseline of HbA1c -0.49 vs. 0.15%).[10]

UKPDS study has shown significant risk reduction of nearly 32% ($p=0.002$) for endpoint related to diabetes, 42% reduction for diabetes-related death ($p=0.017$), and 36% for all-cause mortality ($p=0.011$) in Metformin group of patients when compared to control group.[11] It was clearly demonstrated by UKPDS that metformin was effective in controlling glycemic levels in obese and non-obese type 2 diabetes mellitus patients.

Cai X et. al. (2013) study was done to compare the glycemic control in 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.[12]

T. Haak et. al. (2012) study was done for 24-week, two groups were selected, one group received linagliptin 2.5 mg twice daily with either low metformin dose of 500 mg or high metformin dose of 1000 mg twice a day. It was observed that Mean HbA1c from baseline was −1.7% for the group with high-dose metformin plus Linagliptin, and −1.3% mean HbA1c for low-dose metformin plus linagliptin.[13]

Inagaki N et.al 2013 study was done in Japanese patients for comparison of once daily linagliptin with metformin as an add-on therapy to sulfonylurea or an a-glucosidase inhibitor, it has shown significant reduction of HbA1c and adverse events like hypoglycemia were similar in all the groups.[14]

CONCLUSION

Diabetes is a disease of chronic progressive in nature and life style modifications only is not enough for glycemic control, addition of oral hypoglycemic agents are usually required for achieving good glycemic control. Successful management of type-2 diabetes mellitus involves targeting both glucose and non-glucose goals which eventually help in achieving greater reduction in morbidity and mortality. A variety of pharmacological agents are available for managing hyperglycemia, each molecules have their benefits and risks. Treatment choice and therapeutic targets should be individualized and based on clinical data as well as patient parameters.

In summary, all these three Oral hypoglycemic drugs had a good impact on glycemic control in all the three groups of patients who received monotherapy of linagliptin or metformin or voglibose.

REFERENCES

1. Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract 2011; 94:311–321
2. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B; American Diabetes Association; European Association for Study of Diabetes. "Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2009;32:193-203.
3. Alan J. Garber, Martin J. Abrahamson, Joshua I. Barzilay, Lawrence Blonde, Zachary T. Bloomgarden, Michael A. Bush, Samuel Dagogo-Jack, Ralph A. DeFronzo, Daniel Einhorn, Vivian A. Fonseca, Jeffrey R. Garber, W. Timothy Garvey, George Grunberger, Yehuda Handelsman, Irl B. Hirsch, Paul S. Jellinger, Janet B. McGill, Jeffrey I. Mechanick, Paul D. Rosenblit, and Guillermo E. Umpierrez (2017) Consensus Statement By The American Association Of Clinical Endocrinologists And American College Of Endocrinology On The Comprehensive Type 2 Diabetes Management Algorithm – 2017 Executive Summary. Endocrine Practice: 2017;23:207-238.
4. Bailey CJ, Turner RC: Metformin. N Engl J Med 1996; 334:574–583.
5. DeFronzo RA. Pharmacologic therapy for type 2 diabetes mellitus. Ann Intern Med 1999;131:281-303.
6. Scott LJ. Linagliptin: in type 2 diabetes mellitus. Drugs. 2011;71:611-24.
7. Van de Laar FA, Lucassen PL, Akkermans RP, et al.: Alpha-glucosidase inhibitors for type 2 diabetes mellitus. Cochrane Database Syst Rev 2:CD003639, 2005.
8. Terry T1, Raravikar K, Chokrungvaranon N, Reaven PD."Does aggressive glycemic control benefit macrovascular and microvascular disease in type 2 diabetes? Insights from ACCORD, ADVANCE, and VADT."Curr Cardiol Rep. 2012;14:79-88.
9. Del Prato S1, Barnett AH, Huisman H, Neubacher D, Woerle HJ, Dugi KA. Effect of linagliptin monotherapy on glycaemic control and markers of β-cell function in patients with inadequately controlled type 2 diabetes: a randomized controlled trial. Diabetes Obes Metab. 2011;13:258-67
10. Taskinen MR1, Rosenstock J, Tamminen I, Kubiak R, Patel S, Dugi KA, Woerle HJ, Safety and efficacy of linagliptin as add-on therapy to metformin in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled study, Diabetes Obes Metab. 2011;13:65-74.
11. Prospective Diabetes Study (UKPDS) Group: Effect of intensive blood glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet. 1998, 352: 854-865.
12. Cai X, Han X, Luo Y, Ji L. Comparisons of the Efficacy of Alpha Glucosidase Inhibitors on Type 2 Diabetes Patients between Asian and Caucasian. PLoS ONE 2013 8: e79421.
13. T. Haak, T. Meinicke, R. Jones, S. Weber, M. von Eynatten, H.-J. Woerle. Initial combination of linagliptin and metformin improves glycaemic control in type 2 diabetes: a randomized, double-blind, placebo-controlled study. A journal of pharmacology Volume 2012;14:565–574.
14. Inagaki N, Watada H, Murai M, et al. Linagliptin provides effective, well-tolerated add-on therapy to pre-existing oral antidiabetic therapy over 1 year in Japanese patients with type 2 diabetes. Diabetes Obes Metab 2013; 15: 833–843.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 06-05-2018; **Accepted:** 09-06-2018; **Published:** 17-06-2018