Effect of Sitagliptin on Diabetic Profile of Type 2 Diabetes Mellitus Patients

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ABSTRACT

Introduction: Sitagliptin is a dipeptidyl-peptidase inhibitor (DPP-4 inhibitor) Like other DPP-4 inhibitors its action is mediated by increasing levels of the incretin hormones glucagon-like peptide-1 (GLP-1) and gastric inhibitory polypeptide (GIP). Sitagliptin is effective in lowering HbA1c and fasting as well as postprandial glucose in monotherapy and in combination with other oral antidiabetic agents. The study was aimed to evaluate the effect of sitagliptin on fasting and postprandial blood sugar, fasting plasma insulin levels and HbA1C in patients with type-2 Diabetes Mellitus at 0 level and after 16 weeks of treatment with sitagliptin.

Material and Methods: A prospective study comprising 70 diagnosed cases of type 2 diabetes mellitus was carried out**.** These patients were put on sitagliptin 100 mg OD for 16 weeks and venous blood samples were taken at 0 level and after 16 weeks.

Results The decrease in mean fasting plasma glucose levels at 0 week and 16 weeks was 40.18mg/dl (17.71%) therapy. The change in mean post prandial glucose level was 56.18mg/dl (19.97%). On Statistical analysis, the reduction in mean fasting plasma glucose levels and post prandial blood sugar in total number of patients was highly significant ($p<0.001$). The change in mean glycosylated hemoglobin level was 0.88% (9.75%)and p value was also highly significant $p<0.001$. The change in mean plasma insulin level was 2.50µIU/ml (10.69%). The decrease in values in study group at 4 months was statistically highly significant.

Conclusions: The study concludes that Sitagliptin represents a substantial advance in antidiabetic therapy and it helps in improving the diabetic profile of type 2 diabetes patients.

Key words: Dipeptidyl-peptidase inhibitor (DPP-4 inhibitor), Diabetic Profile, Sitagliptin, Type 2 Diabetes Mellitus

INTRODUCTION

Diabetes mellitus type 2 - formerly called non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes - is a metabolic disorder that is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency.[1] The prevalence of diabetes for all age groups worldwide was estimated to be 2.8% in year 2000 and 4.4% in year 2030. According to the International Diabetes Federation**,** 61.3 million people in India had diabetes in 2011.That figure is projected to rise to 101.2 million by 2030. IDF data reveal that India has more diabetes than the United States.[2]

The β-cell secretion of insulin is greater after the oral administration of glucose than after the intravenous administration of glucose, expressed as C-peptide levels, in subjects without T2DM.[3] This difference in insulin secretion is referred to as the "incretin effect".[4] Regardless of the method of glucose administration, the insulin response is delayed, blunted and prolonged in patients with T2DM, compared with that response in healthy subjects

The two major incretins in humans are Glucagon- like peptide -1 (GLP-1) and glucose-dependent insulinotropic (GIP).[4] They both increase insulin secretion; however, only GLP-1 suppresses glucagon secretion. Both GLP-1 and GIP are rapidly inactivated by the enzyme DPP-IV.[5]

The DPP-IV inactivation process results in greater than 50% inactivation of GLP-1 within 1 to 2 minutes, and greater than 50% inactivation of GIP within 7 minutes.[6]

Dipeptidyl peptidase IV inhibitors suppress the degradation of incretins, thus extending the activity of GLP-1 and GIP. Several DPP-IV inhibitors are either available or in development for patient treatment, these includes-

Sitagliptin phosphate

Vildagliptin[7]

Sitagliptin is rapidly absorbed following oral administration, with an absolute bioavailability of 87%.[8] Drug–drug interactions were not observed under sitagliptin therapy in clinical studies, and especially no such interactions were found with other antihyperglycemic agents in type 2 diabetic patients.[9],[10] The study was aimed to evaluate the effect of sitagliptin on fasting and postprandial blood sugar, fasting plasma insulin levels and HbA1C in patients with type-2 Diabetes Mellitus at 0 level and after 16 weeks of treatment with sitagliptin.

MATERIAL AND METHODS

The present study was conducted in the Department of Biochemistry on 70 diagnosed cases of type-2 DM reporting in the Department of Internal Medicine of a Tertiary Care Center in North India. These patients were put on Sitagliptin 100 mg OD for 16 weeks (4 months).

Approval of Institutional Ethics Committee was procured. A written consent and detailed history of each patient were

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Time Interval (month)	Range (mg/dl)	Mean±SD (mg/dl)	Mean fall (mg/dl)	Mean% fall	T	P	s
0	154-298	227.74±32.77	40.18	17.71	16.74	<0.001	HS
4	114-260	187.51±34.47					
Normal Value : FPG = 60-110mg%; HS-Highly Significant, SD Standard Deviation							

Table-1: Comparison of mean fasting plasma glucose (FPG) in total number of patients at baseline and after 4 months of sitagliptin treatment

Time Interval (month)	Range (mg/dl)	Mean±SD (mg/dl)	Mean fall (mg/dl)	Mean% fall	t	p	s
0	186-380	278.05±44.54	56.18	19.97	15.39	<0.001	HS
4	142-325	221.87±41.38					
N.V - PPG<140mg%							

Table-2: Comparison of mean postprandial plasma glucose (PPG) in total number of patients at baseline and after 4 months of sitagliptin treatment

Time Interval (month)	Range	Mean±SD (%)	Mean fall (%)	Mean% fall	T	P	s
0	7.6-10.8	8.90±0.69	0.88	9.75	14.17	<0.001	HS
4	7.0-10.2	8.02±0.62					
Normal Range : (HbA1c) <7%							

Table-3: Comparison of mean glycosylated hemoglobin (HbA1c) in total number of patients at baseline and after 4 months of sitagliptin therapy

Time Interval (month)	Range (µIU/ml)	Mean±SD (µIU/ml)	Mean fall (µIU/ml)	Mean% fall	T	P	S
0	4.8-52.0	22.87±12.33	2.50	10.69	7.62	<0.001	HS
4	4.2-48.5	20.36±11.29					
N.V Fasting Plasma Insulin = 0.7-25 µIU/ml							

Table-4: Comparison of fasting plasma insulin in total number of patients at baseline and after 4 months of sitagliptin therapy

taken. The cases of clinically confirmed type-2 DM (Age >18 years) were included who were not on sitagliptin. The type 2 DM patients were earlier on sulfonylurea group and metformin and were poorly controlled. Patients with history of renal diseases, pancreatitis, Chronic hepatitis B or C, liver diseases and contraindication to sitagliptin were excluded.

Blood Sugar estimation (Fasting and Postprandial) was done using Glucose Oxidase Peroxidase method, Glycosylate haemoglobin (HbA1C) by Ion Exchange Resin Method[11] and Plasma insulin levels by ELISA technique by kit method.[12] Blood samples were collected under all aseptic conditions. Statistical analysis was performed using t -test and results were analysed accordingly.

RESULT

The mean level of fasting plasma glucose was decreased from 227.74±32.77 mg/dl to 187.51±34.47 mg/dl. The change in mean FPG level was 40.18mg/dl (17.71%). On in Statistical analysis, the reduction mean fasting plasma glucose levels in total number of patients was highly significant (p<0.001) (table-1).

The mean postprandial plasma glucose levels also dropped from 278.05±44.54 mg/dl to 221.87±41.38 mg/dl at 4 months. On Statistical analysis, the reduction in mean postprandial plasma glucose levels in study group was highly significant (p<0.001) (table-2).

The mean glycosylated value was also improved in patients on sitagliptin therapy and p value was also highly significant p<0.001 (table-3).

The mean plasma Insulin levels decreased from 22.87±12.33 µIU/ml to 20.36±11.29 µIU/ml at 4 months. On Statistical analysis, the reduction in mean Plasma Insulin levels was highly significant (p<0.001) (table-4).

DISCUSSION

Type 2 diabetic patients have raised levels of Fasting Plasma Glucose, Postprandial Glucose, Glycosylated Haemoglobin and Fasting Plasma Insulin levels.

When people with type 2 diabetes are treated with Sitagliptin 100 mg once daily for 16 weeks (a DPP-IV inhibitor), we see enhancement of glucose-dependent insulin secretion, and suppression of glucagon secretion, and hence lowering of blood glucose.[13] Both fasting and postprandial glucose contribute to HbA1c. So sitagliptin decreases HbA1c by lowering both fasting and postprandial blood glucose.[14] The possible mechanism for reduction in fasting plasma Insulin levels is by increasing insulin sensitivity.[15,16] Improvement in the fasting proinsulin- to- insulin ratio, consistent with improved β-cell function, was also observed with sitagliptin treatment.

So, Sitagliptin represents a substantial advance in antidiabetic therapy, combining several advantages over other insulin secretagogues (i.e. sulphonylureas and glinides). Blood glucose control is achieved by stimulating insulin release in a glucose-dependent way. Therefore, patients treated with gliptins are at lower risk of hypoglycaemia compared to those using other insulin secretagogues.[17]

Thus, orally administered DPP-IV inhibitors have emerged as a new class of anti-hyperglycaemic agents with the ability for extending the biological effects of incretin hormones

through the inhibition of their degradatinon with the advantage of higher stability and bioavailability.

CONCLUSION

The mean decrease in Fasting Plasma Glucose, Postprandial Glucose, Glycosylated Haemoglobin and Fasting Plasma Insulin levels were statistically highly significant in patients of type 2 DM after sitagliptin treatment. for 16 weeks. Thus Sitagliptin represents a substantial advance in antidiabetic therapy, it can be used as a monotherapy or an adjuvant therapy with other antidiabetic drugs and can delay the patients for insulin therapy and prevent subsequent problems of insulin therapy like needle prick and low chance of hypoglycaemia etc. So, it can be an alternative mode to manage such patients. So more studies should be done in future with longer duration of sitagliptin treatment and on larger population of same ethnic group to evaluate the effects of sitagliptin on parameters like fasting plasma insulin, insulin resistance index, Beta-cell function index, body mass index and lipid profile and to define the role of sitagliptin in the management and prevention of progression of disease in type 2 diabetic patients.

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