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Research Article

A STUDY ON THE CURRENT PRESCRIBING PATTERNS OF DIPEPTIDYL PEPTIDASE 4 INHIBITORS IN A MULTI SPECIALITY HOSPITAL OUTPATIENT SETTING

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ABSTRACT

Objective: To evaluate the current prescribing pattern of dipeptidyl peptidase 4 inhibitors in a multi specialty hospital outpatient setting.

Method: The study was a retrospective descriptive analysis of consecutive patients prescribed with DPP4 inhibitors and attending the diabetic clinic of the tertiary care hospital. Patient data was collected in relation to drugs prescribed, lab parameters, co morbid conditions and diabetic complications. The prescribing pattern of DPP4 inhibitors was studied and evaluated.

Results: During the study, prescription of 74 patients who were initiated with dipeptidyl peptidase 4 inhibitors was reviewed. Sitagliptin (51%) was the most prescribed drug. The most commonly prescribed combinations were Metformin and DPP4 inhibitor (62%) as 2nd line agent, Metformin + Sulphonylureas + DPP4 inhibitor (44%) as 3rd line agents. In our study DPP4 inhibitors were initiated in patients with higher body mass index and Glycated hemoglobin greater than 9%.

Conclusion: Our evaluation revealed the most commonly prescribed DPP4 inhibitor to be Sitagliptin. Initiation of DPP4 inhibitor was more commonly seen as a 3rd line agent. As DPP4 inhibitors are recently approved drugs educational intervention regarding their appropriate use is required.

Keywords: Diabetes mellitus, Dipeptidyl peptidase 4 inhibitors, Sitagliptin, prescribing patterns, Hyperglycemia.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. [1] Various agents are available which are used as monotherapy, or in combinations for the treatment of diabetes mellitus. Several of these agents are also associated with adverse effects that include weight gain, hypoglycaemia and gastrointestinal distress. There is a need therefore, for alternative therapies that can overcome the limitations associated with conventional anti-hyperglycaemic medications. DPP-4 inhibitors are relatively new oral hypoglycaemic drugs that have a role in effectively reducing blood glucose levels. DPP-4 inhibitors increase Glucagon-like peptide-1 (GLP-1) and Gastric inhibitory polypeptide (GIP) levels, which inhibit glucagon release, which in turn increases insulin secretion and there by decrease blood glucose levels.[14] The American Diabetes Association (ADA), American Association of Clinical Endocrinologists (AACE) and National Institute for Health and Clinical Excellence (NICE) guidelines suggests adding a DPP-4 inhibitor as a second line treatment to Metformin if there is a considerable risk for hypoglycaemia or if a sulfonylurea is contraindicated or-not-tolerated.[2] DPP4 inhibitors possess weight neutral effect without causing hypoglycaemia. They are more expensive when compared to other agents.The main objective of this study is to review the prescribing pattern of DPP -4 inhibitors in the treatment of Diabetes mellitus in a tertiary care outpatient centre.

METHODS

A Single-center, retrospective observational study was conducted for duration of 6 months with the approval of Institutional Ethics Committee (protocol no: SVCP/2012/01). All Adult Outpatients in the diabetic Clinic with a new initiation of DPP -4 inhibitors were included in the study. All in-patients, pediatric patients, pregnant women, and patients who were already on DPP-4 inhibitors were excluded from the study.

Data from Patient data forms (PD) of the diabetic clinic were reviewed from June 2010 to July 2012, for the patients with newly prescribed DPP-4 Inhibitors. The PD forms were reviewed for the newly initiated DPP- 4 inhibitors, dose, frequency, patient's demographics such as age, sex, height, weight, body mass index (BMI), family history, duration of DM, co-morbid conditions, diabetic complications, lab parameters such as Glycated hemoglobin (HbA1C), Serum Creatinine (S.Cr), Micro albumin (MicrAL), Fasting plasma glucose (FPG), Postprandial glucose (PPG), Serum Glutamic-Oxaloacetic Transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT) and Self monitoring blood glucose (SMBG). Descriptive statistics were used to report the prescribing patterns of DPP4 inhibitors.

RESULTS In our study of 74 patients, 54 (72.9%) were males and 20 (27.1%) were females. A majority of our study population belonged to the age group of 41-65years (68%). Co morbidities associated with our study population were hypertension (HTN) in 54% patients, coronary artery disease (CAD) in 3% patients and Dyslipidemia in 6% patients. The average HbA1C was recorded between the range 6.5-7.5% in 8(10.8%) patients, 22 (29.7%) patients between 7.6-9% and 44 (59.4%) patients >9.1% (Table 1). Diabetic complications such as neuropathy were found in 34 patients (54%), retinopathy in 5 patients (8%); Gastro paresis in 1 patient (2%), and 23 patients (36%) had no complications. Pre prandial glucose of the patients in our study with <130 mg/dl and >130 mg/dl were 16% and 84% respectively. The post prandial

glucose was found to be <180 mg/dl in 5 % and 180-250 mg/dl in 33 % and >251 mg/dl 62 %.

Table 1: Patient characteristics

S. No	Parameters	Ranges	Averages
1	BMI (kg/m^2)	21.36 - 44.08	29.24 ± 4.75
2	Duration (years)	1 week - 30years	9.74 ± 7.48
3	HbA1c	7 - 13.9	9.54 ± 1.68
4	Creatinine (mg/dl)	0.6 - 1.8	0.93 ± 0.24
5	MicrAL (mg/dl)	2 - 95	22 ± 3.56
6	FPG (mg/dl)	101 – 339	182.5 ± 54.26
7	PPG (mg/dl)	168 - 478	279 ± 69.78
8	SGOT (U/L)	11 - 45	22.8 ± 9.47
9	SGPT (U/L)	21 - 108	43.6 ± 17.47

BMI-Body mass index, HbA1C-Glycated hemoglobin, MicrAL-Micro albumin FPG-Fasting plasma glucose, PPG-Postprandial glucose, SGOT-Serum Glutamic-Oxaloacetic Transaminase, SGPT-Serum Glutamic Pyruvic Transaminase

From our study we could observe that the most commonly prescribed DPP4 inhibitor is Sitagliptin (51 %) followed by Vildagliptin (32%), Saxagliptin (12%), and Linagliptin (5%). Only one patient was found to be on DPP4 I monotherapy with Saxagliptin. Most commonly prescribed total daily dose of Sitagliptin/Metformin was 50mg/1000 mg (34.4%) followed by 100mg/1000 mg (34.4%). Similarly, prescribed total daily dose of Vildagliptin/Metformin was 100mg/1000 mg (42.8%). Different combinations of DPP4 I with other oral hypoglycemics are represented in Table 2.

Table 2: Comparison of DPP4 Inhibitors as 1stLine, 2nd Line, 3rd Line agents

S.No	DPP4I initiated as	No. Patients (%) (n=74)
1	***1st Line agent***	***1 (1.35)***
2	***2nd Line agent***	***21(28.4)***
	Metformin+ DPP4 I	13(17.6)
	SU+ DPP4 I	04(5.4)
	Pioglitazone+ DPP4 I	01(1.35)
	Insulin+ DPP4 I	03(4)
3	***3rd Line agent***	***43* (58.05)**
	Metformin+insulin+DPP4 I	10(13.5)
	Metformin+ SU+ DPP4 I	23(31)
	AGI+Insulin+ DPP4 I	01(1.35)
	SU+Insulin+ DPP4 I	02(2.8)
	Metformin+AGI+ DPP4 I	04(5.4)
	Metformin +Pioglitazone+ DPP4 I	03(4)
4	***4th Line agent***	***9(12.2)***
	Metformin +Pioglitazone +AGI+ DPP4 I	01(1.35)
	Metformin+AGI+Insulin+DPP4 I	01(1.35)
	Metformin+SU+AGI+DPP4 I	01(1.35)
	Metformin+SU+Insulin+DPP4 I	03(4)
	Metformin+Pioglitazone+Insulin+DPP4I	01(1.35)
	Metformin+SU+Pioglitazone+DPP4 I	02(2.8)

SU-sulphonyl ureas, AGI-Alpha Glucosidase Inhibitors

DISCUSSION

In our study majority of the population were males. Higher percentage of our study population belonged to the age group of 41-65 years as it is known that the risk of Diabetes is significantly higher in this age group. DPP4 inhibitors were initiated for majority of the overweight and obese patients, as it has an advantage of weight neutral effect. [4, 5, 6]

About half of our study population had hypertension with lower incidence of coronary artery disease (CAD) and dyslipidemia. Initiation of DPP 4 inhibitors in Cardiac patients may be influenced by their cardio-renal protective effects of these drugs, which are still under study in various ongoing trials. [3, 5, 7] Family history with Diabetes Mellitus (DM) was found in majority of the patients. Initiation of DPP4 I was influenced by higher post prandial glucose, when compared with their pre prandial glucose levels, as it reduces the Post prandial glucose (PPG) primarily. [8, 9, 5, 10]

In our study DPP4 inhibitors were initiated in patients with longer duration of diabetes, HbA1C >9% and in whom complications had already begun but as per the ADA and AACE guidelines DPP4I must be initiated at an early HbA1c level of <9%, reflecting inertia towards these newer agents. They may also be used as a rescue drug in patients with longer duration of Diabetes, prior to the use of insulin.

DPP4I can be used in renal/hepatic impaired patients; with appropriate dosage adjustments. In one patient appropriate dose adjustment for Sitagliptin was done. Commonly used other anti-diabetic drugs are Metformin, sulphonylureas, insulin, Pioglitazone and Alpha Glucosidase Inhibitors. From our study we could observe that the most commonly prescribed gliptin was Sitagliptin. This can be attributed to the fact that it is the first approved DPP4 inhibitor in the market and also to the Asian study (China India Korea study), which suggests that sitagliptin was more effective in the Indian population with greater HbA1c reductions. Linagliptin is a comparatively recently approved drug and its use in future is expected to increase in due course of time, as it's hepatic clearance is an added advantage over the other DPP4 inhibitors[9]

DPP4 inhibitors are known to reduce blood glucose as effective as other oral anti diabetics when prescribed as monotherapy when HbA1c levels are between 6.5-7.5%, with minimal risk of hypoglycemia. [4, 11, 12, 13]

CONCLUSION

From our study it was observed that the most commonly prescribed gliptin is sitagliptin. Most of our study population initiated on DPP4 I, have their HbA1c greater than 9%, potentially influenced by the BMI levels. However, the duration of DM has no effect on the prescriptions of Gliptins. They are initiated as a 3rd line agent in patients with higher post prandial glucose as they effectively reduce it. The most commonly prescribed anti diabetic agents along with Gliptins is Metformin, followed by Sulphonylureas, as a combination pill, use of Metformin and Sitagliptin is common. Maximum benefit of the gliptins can be achieved when initiated in the earlier stages of DM, but it is not being followed so. The compliance of the gliptin use may be affected by its cost. Awareness among clinicians is needed regarding the time of initiation of DPP4 I in type 2 DM.

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