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Original Article

A Quantitative Analytical Study of the Prevailing Prescriptions of Dipeptidyl Peptidase 4 Inhibitors, Sitagliptin and Gemigliptin, among Type II Diabetes Mellitus Patients of Tertiary Care Hospitals

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Abstract

Introduction: Diabetes mellitus type II is globally very common, yet neglected. Inhibition of dipeptidyl peptidase-4 by DPP-4 inhibitors enhances hormonal activity of incretins (GLP-1, GIP, and GRP), stimulates insulin release, and reduces glucagon secretion, thus producing anti-hyperglycemic activity in type II diabetes mellitus patients.

Objective: The objective is a quantitative analytical study of the prevailing prescriptions of dipeptidyl peptidase 4 inhibitors, sitagliptin and gemigliptin, among type II diabetes mellitus patients of tertiary care hospitals.

Materials and Methods: A total of 250 new early moderate grade type II diabetes mellitus patients were prescribed oral sitagliptin 25 mg once daily or gemigliptin 25 mg once daily for 3 months, in monotherapy, or in combination therapy, or in a mixed regimen of monotherapy and combination therapy, with another oral hypoglycemic drug. The safety and efficacy assessments, with blood sugar and HbA1c levels and urine routine examination, at subsequent intervals and follow-up, were recorded and statistically analyzed. The number of prescriptions for each drug was recorded, and the corresponding prescription rates were statistically analyzed in percentages.

Results: Sitagliptin was most commonly prescribed (200 prescriptions, 80%) followed by gemigliptin (50 prescriptions, 20%).

Conclusions: Prescription frequency of sitagliptin was followed by gemigliptin.

Key words: Dipeptidyl peptidase-4 inhibitors, Sitagliptin, Gemigliptin, Prescribing patterns

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INTRODUCTION

Diabetes mellitus type II is one of the universally prevalent common, yet often neglected, disease that the world has witnessed in the recent times. The incidence and prevalence of type 2 diabetes mellitus (T2DM) are increasing globally, with about one in 11 adults having

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diabetes mellitus and 90% of them having T2DM. According to the International Diabetes Federation, 425 million people worldwide have diabetes mellitus, accounting for two-thirds of adults aged 20–64 years, and the proportion of deaths due to diabetes mellitus before the age of 60 years ranges from 36 to 73%. The 10 countries with the highest prevalence of diabetes mellitus account for almost 60% of the global disease burden, with China (114 million people), India (73 million people), and the USA (30 million people) contributing to most of this. Therefore, the management of diabetes mellitus through effective treatment interventions is of the utmost importance in the field of clinical research.[1,2]

Inhibition of dipeptidyl peptidase-4 by dipeptidyl peptidase-4 inhibitors enhances the hormone activity of incretins, such as glucagon like peptide-1 and other bioactive peptides (glucose-dependent insulinotropic polypeptide and gastrin-releasing peptide), thus stimulating the release of insulin and reducing the secretion of glucagon, when given in monotherapy or in combination with metformin. This effect decreases the blood glucose levels as well as HbA1c levels in type II diabetes mellitus patients, without causing severe hypoglycemia.[3,4]

Objective

The objective is a quantitative analytical study of the prevailing prescriptions of dipeptidyl peptidase 4 inhibitors, sitagliptin and gemigliptin, among type II diabetes mellitus patients of tertiary care hospitals.

MATERIALS AND METHODS

Ethical Approval

At first, the Institutional Ethics Committee clearance and approval was taken. The study was conducted in accordance with the ethical principles of Declaration of Helsinki and Good Clinical Practices contained within the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH-E6) and in compliance with the regulatory requirements. An informed consent was obtained from each patient.

Inclusion Criteria

The inclusion criteria were as follows: (i) Patients of any gender, (ii) patients within 35 and 60 years, (iii) patients presenting with new type II diabetes mellitus, of early moderate grade, (iv) type II diabetes mellitus American Diabetes Association diagnosis criteria, (v) cooperative and conscious patients, (vi) patients willing to undergo all pre- and post-treatment investigations and willing to complete the entire course of treatment, (vii) patients who have given consent and are willing to go for a follow-up, (viii) patients not taking any previous antidiabetic drug, and (ix) patients not taking any concomitant medication.

Exclusion Criteria

The exclusion criteria were as follows: (i) Uncooperative or unconscious patients, (ii) patients below 35 and above 60 years, (iii) patients presenting with any grade other than early moderate grade of diabetes, (iv) patients with a history of hypersensitivity to any of the study drugs, (v) patients with high-risk diseases or comorbidities, (vi) cardiac, renal, or any other associated complications or comorbidities, (vii) any chronic disease intervening with the study data, (x) pregnant or lactating women, (xi) pediatric or geriatric patients, (xii) other associated medical illness or disorders, having impact on study results, and (xiii) female patients using hormonal contraceptives.

Study Design

A global, multicenter, retrospective, observational, and analytical study of the clinical prescriptions was performed.

Study Population

The study population consisted of 250 treated new type II diabetes mellitus patients, of early moderate grade.

Study Period

The study period, comprising the periods for the research study and the compilation of the study literature, was 5 months, from June 2021 to October 2021.

Place of Study

The research study and the compilation of the study literature were done in the Departments of Pharmacology, Clinical Pharmacology, Molecular Pharmacology, Pharmacovigilance, Clinical Medicine, Endocrinology, Pathology, and Clinical Pathology, in Dr. Moumita Hazra's Polyclinic and Diagnostic Centre, Dr. Moumita Hazra's Academic Centre, Dr. Moumita Hazra's Educational Centre, Hazra Nursing Home, Mamata Medical College and Hospitals, Rama Medical College Hospital and Research Centre, Hi-Tech College of Nursing, Shri Ramkrishna Institute of Medical Sciences and Sanaka Hospitals, Raipur Institute of Medical Sciences, Fortis Hospitals, and GIOSTAR IRM Institutes, Hospitals, and Laboratories.

Study Procedure

A total of 250 new early moderate grade type II diabetes mellitus patients were prescribed oral sitagliptin 25 mg once daily or gemigliptin 25 mg once daily for 3 months, in monotherapy, or in combination therapy, or in a mixed regimen of monotherapy and combination therapy, with another oral hypoglycemic agent.

The patients' characteristics, diabetic symptoms assessment, patients' disease, and disease-related history were recorded with a pro forma. Then, thorough general physical examination and systemic examination were performed on the patients under study. The relevant blood, urine, and other investigations were done to confirm the progressing health status of the patients being treated.

The efficacy assessment was done, by recording the fasting and the postprandial blood sugar level, HbA1c level, and urine routine examination findings including sugar and albumin levels and microscopy, at subsequent intervals, and follow-up.

The safety assessment was done by the monitoring of adverse drug reactions, at subsequent intervals, and follow-up.

The prescription patterns of both the drugs were analyzed. The number of prescriptions of 250 patients treated with sitagliptin and gemigliptin was recorded; and the percentage of prescriptions for either drug was calculated.

Statistical Analysis

The respective prescription rates were statistically analyzed by percentages.

RESULTS

The demographic characteristics of the patients were comparable.

Figure 1 depicts that sitagliptin was most commonly prescribed (200 prescriptions, 80%) followed by gemigliptin (50 prescriptions, 20%).

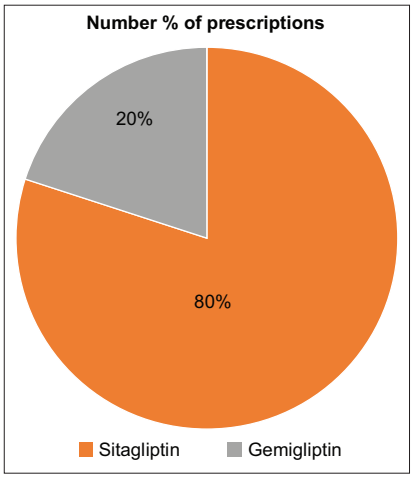

Figure 1: The prescription rates of different anti-diabetic drugs in percentages

The prescription rates of the dipeptidyl peptidase 4 inhibitors were as follows: Sitagliptin > gemigliptin.

The monotherapy, or combination therapy, or mixed regimen of monotherapy and combination therapy of sitagliptin or gemigliptin, with another oral hypoglycemic drug, was observed to be quite efficacious, which had controlled type II diabetes mellitus among new patients, with significant decrease in the blood sugar levels and the HbA1c levels, in the successive 3 months. The adverse effects observed with monotherapy, or combination therapy, or mixed regimen of monotherapy and combination therapy, were statistically non-significant. Therefore, the monotherapy, or combination therapy, or mixed regimen of monotherapy and combination therapy, was safe and tolerable.

DISCUSSION

Diabetes, which is a chronic metabolic disorder, has recently sharply increased on a global scale. According to the International Diabetes Federation (IDF), there were 415 million patients diagnosed with T2D. Diabetes among Asian populations has some distinguishing characteristics from other races in the world, namely, the early decrease in beta-cell function resulting in high postprandial blood glucose and the development to chronic diabetic complications occurs at an early stage of the disease. Hence, a therapeutic agent which increases beta-cell function plays an important role in antihyperglycemic protocols.

Nowadays, anti-DPP4 antihyperglycemic agents have been widely used for patients with T2D under guidelines of diabetes associations and proved to be effective in the enhancement of beta-cell function through ameliorating serum incretin hormone concentrations (two major incretins, GLP-1 and glucose-dependent insulinotropic polypeptide, GIP) – an anti-beta-cell apoptosis agent. There have been two incretin-related therapies for patients with T2D, namely, glucagon-like peptide-1 agonists, exedin-4 and dipeptidyl peptidase-IV inhibitor, sitagliptin. In 2009, the American Association of Clinical Endocrinologists (AACE/ACE) issued the guideline for antihyperglycemic treatment protocol which mentioned about the usage of incretin therapies as the first-line drug for newly diagnosed patients with T2D (i.e., incretin therapies could be monotherapy or in combination with other antidiabetic drugs such as biguanide, sulfonylurea, or insulin). These days, incretin therapies regarding treatment for patients with T2D have been developed on a global scale and shown positive effects on not only glycemic control but also prevention from chronic diabetic

complications as well. While anti-DPP4 agents have many effects on antihyperglycemic conditions, there have been little researches on the Asian population to investigate the role of these drugs on beta-cell function, peripheral insulin sensitivity, insulin resistance, and serum GLP-1 concentrations in comparison to healthy subjects but results were controversial.

In a study, drug choice was based on the guidelines of the American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE 2009). Patients with T2D had low HbA1C concentrations, so sitagliptin was selected as the first choice for treatment therapy in adjunct to lifestyle modification and exercises. The primary endpoint was the change from baseline in GLP-1, HOMA2-B, HOMA2-IR, and HOMA2-S after 3 months of treatment with sitagliptin. Other variables of interest consisted of FPG, lipid profile, safety laboratory measurements (urea, creatinine, ALT, and AST) after 3 months of treatment with sitagliptin. After 3 months of treatment with 100 mg/day sitagliptin, patients illustrated higher HOMA2-B, HOMA2-S, and lower HOMA2-IR to those before interventions. Sitagliptin, one of the anti-DPP4 agents, has been consistently demonstrated to have effects on beta-cell and insulin concentrations indirectly prolonging active incretins and this exhibits L-cells to secrete more GLP-1. Recently, this group of agents was approved to be a second-line therapy for patients with type 2 diabetes mellitus internationally but as recommended by AACE/ACE (2009), the anti-DPP4 agents may be used to start monotherapy for type 2 diabetes patients. One model-based analysis (a placebo-controlled clinical study) found that sitagliptin improved beta-cell function relative to placebo in both fasting and postprandial states in patients with T2D. Although sitagliptin has been shown numerous efficacies in antidiabetic therapy overall, these effects varied from different races. A meta-analysis showed that, among patients with T2D in Asia, sitagliptin had increased insulin sensitivity and weight much higher in comparison to that in the Caucasian population and the between-group (Asia-Caucasian) different in HOMA2-B was - 4.97 (95% CI, - 9.86 to - 0.09, $P < 0.05$). One suggestion for these differences could be due to Asian anthropometric indices including low BMI and high blood glucose due to insulin resistance rather than insulin deficiency. DPP4 inhibitors might induce beta-cell regeneration, prevention from pancreas islet hypertrophy and insulin synthesis *in vitro* studies. DPP4-inhibitors also improved beta-cell function both inside and outside the setting of food consumption, but some studies found that there was no change in the incretin effect. Moreover, DPP-4 inhibitors would allow beta-cells to adapt to the degree of insulin resistance and have a better response to glucose overload and as the result, they decrease the overall insulin exposure and the pro-insulin-to-insulin ratio.[4]

In this study, the demographic characteristics of the patients were comparable. Sitagliptin was most commonly prescribed (200 prescriptions, 80%) followed by gemigliptin (50 prescriptions, 20%). The prescription rates of the antidiabetic drugs were as follows: Sitagliptin > gemigliptin.

The monotherapy, or combination therapy, or mixed regimen of monotherapy and combination therapy of sitagliptin or gemigliptin, was observed to be quite efficacious, which had controlled type II diabetes mellitus among new patients, with significant decrease in the blood sugar levels and the HbA1c levels, in the successive 3 months. The adverse effects observed with monotherapy, or combination therapy, or mixed regimen of monotherapy and combination therapy, were statistically non-significant. Therefore, the monotherapy, or combination therapy, or mixed regimen of monotherapy and combination therapy, was safe and tolerable.[1]

CONCLUSIONS

The prescription frequency of sitagliptin was followed by gemigliptin.

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