A Study of Prescription Pattern of Anti-Diabetic Drugs and Usage of Teneligliptin for Type II Diabetis Mellitus

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Abstract **Background:** Prescription pattern studies are a tool for assessing the prescribing, dispensing and distribution of medicines. Diabetes mellitus (DM) is a spectrum of metabolic disorders as a consequence of different pathogenic mechanisms resulting in hyperglycemia. A genetic predisposition to develop β-cell dysfunction synergizes with insulin resistance to lead to type 2 DM. Adequate management of type 2 DM requires institution of non- pharmacological management followed by pharmacological management. Currently trending anti diabetic drugs, Teneligliptin a magic drug which is recently developed oral dipeptidyl-peptidase-4 inhibitor indicated for the management of uncontrolled type 2 diabetes mellitus (T2DM) in adults along with diet and exercise. **Methods:** This cross-sectional study was conducted in the Department of Pharmacology in collaboration with Department of General Medicine. A total of 518 patients were enrolled in study based on inclusion and exclusion criteria after taking written informed consent. A structured case recording form was used to record demographic details and prescription details. The rationality of prescriptions was assessed using American Diabetes Association guidelines (ADA) 2015. **Results:** Majority of the patients were prescribed combination therapy (54%) followed by monotherapy (46%). Oral anti-diabetic agents used as monotherapy other than metformin were appropriate. Among the patients receiving combination therapy majority were receiving a fixed dose combination which were appropriate. Among the recent anti- diabetic drug Teneligliptin was the most commonly prescribed drug and Teneligliptin has been found to be well accepted and tolerated, and the safety profile is similar to other dipeptidyl peptidase-4 inhibitors. Teneligliptin was used as monotherapy, add-on to metformin or add-on to metformin plus sulfonylureas combination for better glycaemic control. **Conclusion:** Upon overall analysis this study indicates that rational prescribing of drugs in tertiary care hospital has to be improved by prescribing current trends, Prescribing drugs from Essential drug list (EDL) and the use of combination therapy was significant. The study of drug prescribing pattern showed that antidiabetic drugs were prescribed according to American Diabetes Association guidelines. The trends in prescribing newer anti diabetic drugs shows the acceptance of teneligliptin and updated skills in physicians to promote better glycaemic control.

Key Words diabetes mellitus, prescription pattern, oral anti-diabetic agents, teneligliptin

1. Introduction

The term diabetes mellitus describes a metabolic disorder with heterogeneous etiologies which is characterized by chronic hyperglycaemia and disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both [1]–[3]. The long–term relatively specific effects of diabetes include development of retinopathy, nephropathy and neuropathy [4]. People with diabetes are also at increased risk of cardiac, peripheral arterial and cerebrovascular disease [5].

Globally, an estimated 422 million adults are living with diabetes mellitus, according to the Global report on diabetes launched in 2016 data from the World Health Organization (WHO) and 1.6 million deaths are directly attributed to diabetes each year [6]. The first WHO Global report on diabetes demonstrates that the number of adults living with diabetes

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has almost quadrupled since 1980 to 422 million adults [7]. This dramatic rise is largely due to the rise in type 2 diabetes and factors driving it include overweight and obesity [8].

Diabetes therapy is characterized by individual influence factors, such as differences in the characteristics of the subcutaneous tissue, and also specific eating habits, physical activities, and many others besides [9]. The immediate objective and subjective effects include hyper- or hypoglycemia, and macro-and micro-angiopathy, neuropathy, bephropathy, and retinopathy [10]. Besides pure delayed action insulin, so-called intermediate acting insulin's have above all proven to be preparations which are optimally suited to the requirements of the patient [11].

Despite the early discovery of insulin and the later discovery and use of sulfonylureas (e.g., chlorpropamide, tolbutamide, acetohexamide, tolazamide, and biguanides such as phenformin) as oral hypoglycemic agents, the treatment of diabetes is less than satisfactory [12]. Several current treatments for T2DM have already been tested concerning their effects in reducing Glucose variability, considering that metformin, the first choice of drug for the treatment of T2DM, usually cannot provide a long term glucose control, other anti-diabetic drugs should be added as second agents, such as dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors) and sulphonylureas, sodium glucose co-transporter 2 inhibitors (SGLT-2 inhibitors) and thiazolidinedione's (TZDs) [13].

In addition, non- pharmacological interventions are very important like life style modifications including exercises and diet control [14]. The role of specific anti-diabetics in changing glucose variability is still a controversy [15]. OHAs still dominate the prescribing pattern, but there was a shifting trend toward the use of insulin preparations in the management of Type 2 diabetes mellitus [16].

Numerous therapies have come into sight in the past decade, such as incretin-based therapies and SGLT-2 inhibitors and Gliptins, making the choice of suitable antidiabetic regimens challenging. Gliptins or dipeptidyl peptidase-4 (DPP-4) inhibitors have revolutionized the management of T2DM. These agents have formerly been reviewed as first-line treatment options by the WHO Expert Committee on the Selection and Use of Essential Medicines. Despite better glucose control is seen with suphonylureas in many previous studies, they induce more hypoglycemias and weight gain as compared to DPP-4 inhibitors [17].

Therefore, drug utilization studies, which evaluate the current trends are more meaningful, and observe the prescribing attitude of physicians with the aim to provide drugs rationally. This study attempts to analyze the use of evidence based medicine, fulfill the drug information needs of the physician and also give feedback to the prescribers in maintaining adequate glycemic control in diabetic patients, so as to improve quality of healthcare. The results of this study will enable us to compare the data with other studies done at different levels and throw light on emerging trends. This would also aid in the process of planning, supply and distribution of drugs in the hospital.

2. Materials and Methods

This is a Non-interventional, observational, Descriptive study was conducted in the Department of Pharmacology at Tertiary Care Teaching Hospital over a period of 1 year.

A. Study Setting

Prescriptions of 518 patients diagnosed with type II diabetes mellitus attending medicine OPD for a period of 18 months. The data was collected once in a week on every Wednesday at geriatric OPD.

B. Study Criteria

Patients will be enrolled into the study by considering the following criteria:

C. Inclusion criteria

Patients presenting to Out Patient Department, diagnosed with Type 2 Diabetes mellitus irrespective of the co-morbid conditions. Patients of age 30-60 years irrespective of gender. Patients on anti-diabetic drugs. Patients willing to consent.

D. Exclusion criteria

Age less than 30 years and more than 60 years. 4.8.B2. Type I diabetes mellitus. Pregnant women and lactating women. Patients with diabetes mellitus due to secondary causes. Patients with any complications of Type II diabetes mellitus and also under ICU care. Any patient not willing to take part in the study.

E. Methodology

Patients will be enrolled in study based on inclusion and exclusion criteria. Informed consent will be obtained from the patient at the time of enrolment. All the data regarding demographics, treatment and other medical details will be collected in a specially designed Patient Data Collection Form. Prescribing pattern and usage of teneligliptin will be assessed for anti-diabetic drugs in type 2 diabetes mellitus.

Prescription given by the physician to such patients were collected, and details like name of the drug, dosage, route of administration, duration and number of drugs prescribed were noted. The details of the data collected were transferred in to MS Office Excel worksheet. The study included only one prescription per patient during that particular hospital visit.

3. Results

Total 518 case records were collected and were analyzed for epidemiologic profile, disease spectrum and drug prescription patterns.

Table 1 shows the age wise distribution of patients having type-2 diabetes mellitus. The mean age of the study population was 49.56±7.4years.

Table 2 shows the gender wise distribution in the study population. Out of 518 patients studied, 51.3% were male and 48.8% were female.

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Age in years	Number of patients	%
30-34	28	5.4
35-40	56	10.81
41-45	83	16.02
46-50	83	16.02
51-55	104	20.07
56-60	164	31.6
TOTAL	518	100

Table 1: Age distribution of patients studied

Gender	Number of patients	%
Male	287	55.4
Female	231	44.5
Total	518	100

Table 2: Gender distribution of patients studied

Table 3 shows the different antidiabetic class of drugs prescribed in the study population in the descending order Biguanides (40.58%), Sulfonylureas (32.80%), DPP4 Inhibitor's(18.71%), Alpha glucosidase inhibitors (5.10%) and Thiazolidinedione's (2.79%).

Table 4 shows the individual antidiabetic drugs prescribed in the study population in the descending order, Metformin (30.88%), Glimepiride (26.64%), Teneligliptin (9.45%), Pioglitazone (4.44% each), Voglibose (3.66%), Glipizide (3.47%), Acarbose (1.93%).and least common prescribed was Glibenclamide (1.73%).

Apart from metformin and glimepiride, tenegliptin was the most common drug used individually among recent oral antidiabetic drugs.

Table 5 shows the double combination antidiabetic drugs prescribed in the study population in the descending order, Metformin+Teneligliptin (12.54%), Metformin+glimepiride (12.16%), Glimepiride+Teneligliptin (3.47%), Metformin+Acarbose (3.38%), Glimepiride+ Acarbose (2.5%), Metformin+pioglitazone (1.35%), Glimepiride+Pioz (0.96%)

Newer drug teneligliptin was seen to be trending and was seen to be more commonly prescribed with metformin and

Class of Antidiabetic drugs prescribed	Number of prescriptions (823)	%
Sulfonylureas	270	32.80
Biguanides	334	40.58
Thiazolidinedione's	23	2.79
Alpha-glucosidase inhibitors	42	5.10
DPP4 Inhibitors	154	18.71

Table 3: Antidiabetic class of drugs prescribed

Antidiabetic drugs	Number of patients (n=518)	%
Metformin	160	30.88
Glimepiride	138	26.64
Glipizide	18	3.47
Glibenclamide	9	1.73
Acarbose	10	1.93
Voglibose	19	3.66
Pioglitazone	23	4.44
Teneligliptin	49	9.45

Table 4: Individual antidiabetic drugs prescribed

Antidiabetic drugs	Number of patients (n=518)	%
Metformin+glimepiride	63	12.16
Metformin+pioglitazone	7	1.35
Metformin+Teneligliptin	65	12.54
Metformin+Acarbose	17	3.28
Glimepiride+ Acarbose	13	2.5
Glimepiride+Teneligliptin	18	3.47
Glimepiride+Pioz	5	0.96

Table 5: Double combination antidiabetic drugs prescribed

Antidiabetic drugs	Number of patients (n=518)	%
M+G+P	10	2.12
M+G+A	4	0.77
G+A+T	7	1.35
G+M+T	50	9.6
G+P+A	1	0.19

Table 6: Triple combination antidiabetic drugs prescribed

glimepiride other than the standard combination of metformin and glimepiride.

Table 6 shows the triple combination antidiabetic drugs prescribed in the study population in the descending order, G+M+T (9.6%), M+G+P (2.12%), G+A+T (1.35%), M+G+A (0.77%), G+P+A (0.19%). In triple combination also the usage of teneligliptin was seen to be prescribed with metformin and glimepiride

Table 7 shows the triple combination anti-diabetic drugs prescribed in the study population in the descending order, G+M+A+T (10.42%), G+M+P+T (2.5%). Among 4-drug combination also teneligliptin was more commonly added with metformin, glimepiride and acarbose.

Table 8 shows the oral antidiabetic drugs prescribed as a single and combination drug formulation. In the study population of 757 prescriptions, 56.27% of oral antidiabetic drugs were prescribed as a single drug formulation and where as 43.72% were prescribed as combination drug formulation.

4. Discussion

In our study population the most common antidiabetic class of drug prescribed was biguanides (40.58%), followed by sulfonylureas (32.80%), DPP4 Inhibitors (18.71%) and the least common being Alpha-glucosidase inhibitors (5.10%) and also Thiazolidinediones (2.79%). Among biguanides,

Antidiabetic drugs	Number of patients(n=518)	%
G+M+A+T	54	10.42
G+M+P+T	13	2.5

Table 7: Four combination antidiabetic drugs prescribed

	No	%
Total number of oral antidiabetic agents prescribed	757	100.0
Number of oral antidiabeticdrugs prescribed as single drug formulation	426	56.27
Number of prescribed formulation oral as antidiabetic combination drugs drug	331	43.72

Table 8: Oral antidiabetic drugs prescribed as single and combination drug therapy

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metformin was the only biguanide prescribed and among sulfonylureas, glimepiride was the most common drug prescribed and in the class of DPP4 Inhibitors, teneligliptin was the most commonly prescribed drug. These results are consistent with findings in previous study by Cheng SF et al [18] and Sudha Vengurlekar et al [19] which showed that metformin was the most common antidiabetic agent prescribed followed by glibenclamide, but in this study most commonly used drug was glimepiride. This could be because metformin, glimepiride and teneligliptin has beneficial effects like effective glycaemic control, weight reduction, less risk of hypoglycemia and it is economical.

Previous study done by Chu W et al [20] showed that there is rational justification for the use of combination drug formulations because blood glucose control tends to be better and the risk of side effects owing to use of maximal dose of monotherapeutic agent is reduced. Combination of metformin (which reduces hepatic glucose production and improves insulin resistance) with a sulfonylurea (which stimulates insulin secretion) is the rational combination for counteracting the two defects seen in type-2 diabetes mellitus. In our study, among the prescribed oral antidiabetic agents, 56.27% were single drug formulations and 43.72% were combination drug formulations. Among the combination it was metformin with teneligliptin (12.54%) followed by glimepiride with metformin (12.16%) was most commonly prescribed. There is need to promote this rational combined drug formulation for above mentioned reasons.

In the study population among the 3 drug combination most efficacious combination was metformin, glimepiride and teneligliptin (9.6%), for its very good glycaemic control. Also noted that in the 4 drug combination metformin, glimepiride teneligliptin and acarbose (10.42%), was seen to be useful before starting on insulin therapy.

In our study it was seen that the physicians are well aware of the newly available anti-diabetic drugs and teneligliptin being a wonder drug among current trends among anti-diabetic medications. In our study also it is noted that teneligliptin has been used as a single drug showed significant reductions in glycaemic parameters which was inadequately controlled with diet and exercise and other anti-diabetic drugs.

Study showed similar results as Maladkar M et al, [21] that is, addition of teneligliptin in patients with T2DM not controlled with metformin therapy in a combined form that is 2 drug (metformin with teneligliptin) was believed to be effective in controlling blood glucose and well tolerated in patients with T2DM and in 3 drug combination (metformin, glimepiride and tenegliptin) and 4 drug (metformin, glimepiride teneligliptin and acarbose) for tight glycaemic control [22].

Also a recent study by Sharma M et al. [23] showed the acceptance of teneligliptin by the physicians which were also prescribed as alternate add-on therapy options, however were rarely used for first-line treatment in T2DM, but in our study it was seen that the drug was also used as monotherapy, as the glycemic control was comparatively good in the population.

5. Conclusion

We can conclude that most of the prescriptions were rational with the current trends, but further improvement in prescribing indicators is necessary because of more usage of brand names prescribing practices. Usage of tenegliptin was significant as a monotherapy, and as a double/triple combination therapy as well as four combination. It shows the acceptance of newer drugs and it can be a help in updating the physicians for helping the patients in controlling better glycaemic control. Teneligliptin has been used as a single agent as teneligliptin 10 mg, 20 mg, 40 mg and Addition of teneligliptin in patients with T2DM not controlled with metformin therapy in a combined form that is 2 drug was believed to be effective in controlling blood glucose and well tolerated in patients with T2DM and in 3 drug combination and 4 drug as mentioned above for tight glycaemic control which is a recent and promising evolving trend in anti-diabetic prescriptions.

Conflict of interest

The authors declare no conflict of interests. All authors read and approved final version of the paper.

Authors Contribution

All authors contributed equally in this paper.

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