

DRUG UTILIZATION PATTERN OF ANTI-DIABETIC DRUGS AMONG DIABETIC OUTPATIENTS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: The aim was to evaluate the drug utilization pattern of anti-diabetic drugs in diabetic outpatients and monitor the adverse drug reactions (ADRs) associated with anti-diabetic therapy.

Methods: A prospective observational study was carried out in adult diabetic patients visiting the outpatient Departments of General Medicine and Endocrinology of a tertiary care hospital. Demographic data, drug utilization pattern and ADRs due to anti-diabetic drugs were summarized.

Results: In the present study, 99 (50.3%) of the 197 diabetic patients were males. Majority of patients were in the age group of 51-60 years (39.6%) and most of the patients (36.5%) had a diabetic history of <5 years. Metformin was the most commonly prescribed drug (68%), followed by sulfonylurea class of drugs (49.7%). Nearly, 42% patients were using insulin preparations with 30.4% using biphasic isophane human insulin. Majority of the patients (58.4%) were on multidrug therapy with two drug therapies being received by nearly 40%. Metformin was the most commonly prescribed drug in monotherapy (18.8%) and glimepiride + metformin was the most common two drug therapy (13.2%). Co-morbid condition was found in 172 patients (87.3%) with hypertension (68.5%) being the most common co-morbid condition. 17 ADRs were observed with hypoglycemia being the most common ADR reported.

Conclusions: Metformin was the most commonly used drug. The prescribing trend also appears to be moving towards combination therapy particularly two drug therapies.

Keywords: Drug utilization, Anti-diabetic drug, Adverse drug reaction.

INTRODUCTION

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels [1].

According to International Diabetes Federation (IDF), the number of people with diabetes in the world in 2013 was 382 million, which is going to increase to almost 592 million by 2035. India has the dubious distinction of being home to a large number of people suffering from diabetes. According to IDF, 65.1 million of adults in India suffered from diabetes in the year 2013 [2]. It has been predicted that the prevalence of diabetes in the adult population in India will be 6% by the year 2025 [3].

Modern principles of management of diabetes focus on disease prevention, screening high risk individuals and aggressive treatment of individuals in the pre-diabetic state. The current pharmacotherapy of diabetes mellitus includes treatment with drugs such as insulin and oral hypoglycemic agents. Oral hypoglycemic agents are heterogeneous in their modes of action, safety profiles and tolerability. The main classes include agents that stimulate insulin secretion (sulfonylureas and rapid acting secretagogues), reduce hepatic glucose production (biguanides), delay digestion and absorption of intestinal carbohydrate (α -glucosidase inhibitors), improve insulin action (thiazolidinediones) and incretin based therapies like dipeptidyl peptidase-4 inhibitors [4-6].

According to World Health Organization, drug utilization is defined as the marketing, distribution, prescription and use of drugs in a society with special emphasis on the resulting medical, social and economic

consequences [7]. Several drug utilization studies on anti-diabetic agents are available across the world, including India [8-19].

Drug utilization studies provide useful insights into the current prescribing practices and also identify irrational prescribing. The consequences of irrational prescribing include non-adherence to medications, which can result in complications due to uncontrolled blood glucose levels and also escalate drug costs and health care costs. In view of this, the present study was designed to evaluate the prescribing pattern of anti-diabetic drugs among diabetic outpatients in a tertiary care teaching hospital.

METHODS

This prospective observational study was conducted over a period of 3 months (January-March 2013) in the outpatient departments of General Medicine and Endocrinology at Amrita Institute of Medical Sciences and Research Centre, a tertiary care, teaching and super-specialty referral hospital. The study was approved by the Institutional Ethics Committee.

Adult diabetic patients (either newly diagnosed or known cases) of either sex were included in the study. Patients with any malignancy; pregnant and lactating females were excluded. Patient data relevant to the study were obtained by examination of patient's medical records, direct interview of the patient or his/her caregivers and the hospital information system. The data were recorded in a standard data collection form. Details about demography, medical history, duration of diabetes, family history of diabetes, co-morbid conditions, and anti-diabetic drug utilization, were collected.

The adverse drug reactions (ADRs) related to anti-diabetic drugs were monitored and documented in suitably designed ADR monitoring

forms. The severity and causality of the ADR were also assessed. The severity of ADR was categorized as mild, moderate or severe as per standard definitions. The causality assessment of ADRs was done as per Naranjo scale.

RESULTS AND DISCUSSION

Diabetes mellitus is a chronic lifelong disease affecting a large spectrum of population in the developing countries including India. In the initial stages, single oral agents can be used to control the glucose level, but in later stages combination therapy may be needed for better glycaemic control and prevention of micro and macro vascular complications. Hence, the present study aimed to evaluate the prescription trend of anti-diabetic drugs in diabetic outpatients.

A total of 197 diabetic patients were evaluated during the study period. In the present study, neither male nor female preponderance was seen (males 50.3%; females 49.7%) (Table 1). Similar results were obtained in other studies conducted in Kerala and Ahmedabad [13,15]. However, the results are in contrast to a few studies conducted in India and other countries which have reported either male or female preponderance [8,10,12,17,18].

Majority of our patients were in the age group of 51-60 years (39.6%) which is in concordance with the earlier published literature [8,12,13,16]. The mean age of the patients in the present study was 57.6 years (age range: 18-79 years), a finding similar to that obtained in studies conducted in Nepal and Ahmedabad, which have reported the mean age of patients as 56.9 and 56.8 years, respectively [8,17]. However, a study from Tenali, Andhra Pradesh reported the mean age of patients as 53.4 years [16]. The age distribution of patients is presented in Table 2.

In the present study, 194 patients had Type 2 diabetes mellitus, whereas three patients suffered from Type 1 diabetes mellitus. Among the Type 2 diabetic patients, 103 patients had a family history of diabetes, 69 patients had no family history while the details for 22 patients was not available. Among the three Type 1 diabetic patients, two had a positive family history.

Duration of diabetes has a significant role in its management. Patients who have diabetes for <5 years could usually be managed with single drug therapy while combination therapy is required in patients having diabetes for more than this period. In the present study, most of the patients (36.5%) had a diabetic history of <5 years, a finding consistent with that of other studies [8,13,15].

Co-morbidity has been shown to intensify health care utilization and to increase medical care costs for patients with diabetes. In the present study, co-morbid condition was found in 172 patients (87.3%). 44 patients (22.3%) were suffering from a single co-morbid condition, and 128 (65%) were suffering from more than one co-morbid condition.

Table 1: Gender wise distribution of patients

Gender	Number of patients	Percentage
Male	99	50.3
Female	98	49.7

Table 2: Age wise distribution of patients

Age (years)	Number of patients	Percentage
18-30	4	2.0
31-40	7	3.6
41-50	30	15.2
51-60	78	39.6
61-70	62	31.5
71-80	16	8.1

Majority of the patients (30.4%) were suffering from two co-morbid conditions. Twenty-five patients had no other diseases apart from diabetes. Hypertension (68.5%) was the most common co-morbid condition, followed by dyslipidemia (39.6%). Different studies from India and other countries have reported a similar observation with regard to the co-morbidity in patients with diabetes. However, the prevalence of hypertension has ranged from 31 to 70% [11,17,19]. The combination of hypertension and diabetes is clinically important since it magnifies the risk of diabetic complications. Diabetic neuropathy, nephropathy, and retinopathy were found in 34 patients (17.2%), 19 patients (9.6%) and 15 patients (7.6%), respectively. Diabetic foot complication was present in only one patient.

As diabetes progresses, functional decline in beta cells is usually apparent, and the need for combination therapy is unavoidable. Therefore, combination modalities have become an integral part of diabetes management. The basic rationale for combination therapy is to provide additive effects with different mechanisms of action and to allow lower doses for disease management. Consistent with the same, in the present study, majority (58.4%) of the patients were on combination therapy with two drug therapies being received by nearly 40% patients. In a study conducted in rural areas of Tamil Nadu, monotherapy, and two drug combination therapies were prescribed in 21.7% and 78.3% patients, respectively [18]. The average number of anti-diabetic drugs prescribed in the present study was 1.81, a finding similar to that obtained in another study from Kerala [13].

Unlike sulfonylureas, thiazolidinediones, and insulin, metformin is weight neutral, which makes it an attractive choice for obese patients. Furthermore, the management of Type 2 diabetes can be complicated by hypoglycemia, which can seriously limit the pursuit of glycaemic control. Here, too, metformin has advantages over insulin and some types of insulin secretagogues; by decreasing excess hepatic gluconeogenesis without raising insulin levels, it rarely leads to significant hypoglycemia when used as a monotherapy. As a result, metformin is widely considered an ideal first-line agent for the treatment of Type 2 diabetes. In addition, the cost of metformin is very low, thus making it affordable by the patients in economically weak countries like India. Our study also supported the same conclusion; 68% of patients studied received metformin alone and/or in combination followed by sulfonylureas (49.7%). Our results are in concordance with the results of some other studies [8,12,17-19]. Among the sulfonylureas, glimepiride was the most frequently prescribed (32.5%) followed by glibenclamide (9.1%) (Table 3).

Table 3: Drug utilization pattern of anti-diabetic drugs

Class	Drug	Number of patients (%)	
Biguanides	Metformin	134 (68.0)	
	Sulfonylureas	Glimepiride	64 (32.5)
		Glibenclamide	18 (9.1)
		Glipizide	12 (6.1)
		Gliclazide	4 (2.0)
Total	98 (49.7)		
Insulin	Insulin	83 (42.1)	
	α-glucosidase inhibitors	Voglibose	11 (5.6)
		Acarbose	8 (4.1)
Total	19 (9.6)		
DPP-4 inhibitors	Sitagliptin	7 (3.6)	
	Vildagliptin	5 (2.5)	
	Linagliptin	1 (0.5)	
	Total	13 (6.6)	
Thiazolidinediones	Pioglitazone	8 (4.1)	
	Rosiglitazone	1 (0.5)	
	Total	9 (4.6)	
Glucagon like peptide 1 agonist	Exenatide	1 (0.5)	

DPP-4: Dipeptidyl peptidase-4

Table 4: ADRs

ADR	Number of patients	Percentage
Hypoglycemia	8	4.1
Nausea	3	1.5
Gastric irritation	3	1.5
Diarrhea	2	1.0
Abdominal discomfort	1	0.5

ADR: Adverse drug reactions

Eighty of the 194 Type 2 diabetic patients were on insulin therapy. Among these, nearly 50% had a diabetic history of more than 10 years and the majority of the patients were above the age of 50 years. Among the 83 patients on insulin treatment, 66 patients were using only one insulin formulation while the remaining were using two insulin formulations. Majority of the patients (30.4%) were using biphasic isophane human insulin followed by human neutral soluble insulin (8.1%), insulin glargine and isophane human insulin (4.6% each).

In the present study, the most commonly used anti-diabetic medications in monotherapy were metformin (18.8%) followed by insulin (14.2%), glimepiride (3.6%) and glibenclamide (2.5%). Among two drug combination therapy, glimepiride + metformin (13.2%) was the most commonly prescribed followed by metformin + insulin (12.2%). In the studies by Vengurlekar et al. [12] and Patel et al. [17], glimepiride + metformin was the most commonly prescribed combination. In the study by Kumar et al. [16], insulin + metformin (16.6%) was the most prescribed anti-diabetic combination followed by glimepiride + metformin (10%). However, the most prescribed three drug combination was insulin + glimepiride + metformin (8.3%) which is consistent with our results. Four and five drug combination therapy was received by 4.6% and 0.5% patients, respectively. Sulfonylureas and metformin were part of majority of the four and five drug combinations. Two patients were not on anti-diabetic drugs.

17 ADRs were reported during the study (Table 4). Hypoglycemia was the most common ADR observed in eight patients (moderate intensity in seven patients and mild in one patient). Seven hypoglycemic episodes were probably related to the study medication.

CONCLUSIONS

Metformin was the most commonly used drug. The prescribing trend also appears to be moving towards combination therapy particularly two drug therapy. This study contributes to the growing body of literature on drug utilization research. However, the study has its own limitations since follow-up of the patients was not possible and hence the effectiveness of the anti-diabetic agents could not be assessed. In the future one can investigate the appropriateness of prescriptions and adherence to evidence based recommendations.

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