

## A STUDY ON DRUG UTILIZATION OF ORAL HYPOGLYCEMIC AGENTS IN TYPE-2 DIABETIC PATIENTS

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Received: 6 Aug 2011, Revised and Accepted: 30 Aug 2011

### ABSTRACT

**Objective:** To evaluate drug utilization pattern of oral hypoglycemic agents in Type-2 diabetic outpatients.

**Materials and Methods:** A prospective study was carried out in 202 out patients for a period of 9 months in a tertiary care hospital. Patients treated with oral hypoglycemic agents were used for the study. The demographic data, disease data and utilization of different classes of oral hypoglycemic agents as well as individual drugs were analyzed.

**Results:** The study found that 51.98% patients were males. The greatest number of patients (38.61%) were in the age group of 51-60 years. Sulfonylurea and biguanide combination (57.09%) was the most common class of drug used among the various oral antidiabetics prescribed. The average number of drugs per prescription was 4 and the average number of antidiabetic drugs per prescription was 1.4. Average cost of oral hypoglycemic agents per prescription for 1 month was found to be INR 275.35.

**Conclusion:** Glimepiride and metformin combination drugs were the most commonly used drugs. Overall polypharmacy was high even though polypharmacy among antidiabetic drugs were low. The cost of drugs per prescription was found to be very high.

**Keywords:** Oral Hypoglycemic agents, Drug Utilization.

### INTRODUCTION

Type-2 diabetes is a disease marked by high levels of blood glucose due to the action of insulin and insufficient insulin production. Type-2 diabetes accounts for approximately 90% to 95% of all diagnosed cases of diabetes [1]. Diabetes is a chronic disease affecting almost 6% of world population [2]. It is associated with abnormal carbohydrate, protein and lipid metabolism [3]. Diabetes if uncontrolled can lead to several acute and chronic complications [4]. Chronic complications of diabetes make it needed to prescribe drugs for these patients lifelong [3].

India has the largest population of diabetes in the world. The international diabetes federation (IDF) estimates the number of people with diabetes in India will reach 80million by the year 2025. A survey depicts that 4% of adults in India suffered from diabetes in the year 2000 and is expected to increase to 6% by the year 2025 [5]. The world health organization (WHO) has projected that the global prevalence of type-2 diabetes mellitus will more than double from 5 million in 1995 to 300 million by 2025. Between 1995 and 2025, there will be a 35% increase in worldwide prevalence of diabetes mellitus, from 4 to 5.4% [6].

Type-2 diabetes mellitus is one of the most common chronic conditions in the elderly [7]. It is a metabolic disorder that results from complex interactions of multiple factors and is characterized by 2 major defects: decreased secretion of insulin by the pancreas and resistance to the action of insulin in various tissues (muscle, liver and adipose) which results in impaired glucose uptake [8]. In India 20% of the elderly has type-2 diabetes mellitus [9]. It is the more common of disease engulfing around 90% of all the diabetic cases worldwide [10]. This is due to many socio demographic factors such as increased life expectancy, high rates of obesity and changes in dietary habits [11].

Since 1995, a dozen orally administered diabetes medications or combination of medications for the management of type-2 diabetes mellitus have been approved by FDA [12]. They play a primary defense function against hyperglycemic events in comparison to insulin therapy [13]. Traditionally in oral hypoglycemic agent therapy,

sulphonyl ureases have always been the agents of first choice, while biguanides and alpha-glucosidase inhibitors were unpopular [14]. Metformin is approved for use in pediatrics [12].

A good number of diabetes patients suffer from cardiovascular disease such as hypertension, hyperlipidaemia and ischemic heart disease [3]. Owing to the presence of comorbid conditions, geriatric patients are usually on more than one drug (polymedication).

Several problems in drug use patterns have been reported. This includes use of irrational combinations, excessive prescription of multivitamins, use of antibiotics in viral infections, etc [15]. Often, the chronically ill patients like the diabetic patients suffer from multiple diseases and hence are prescribed multiple drugs. Moreover irrational prescribing can lead to an increase in the cost of drug therapy [16].

Drug utilization is defined as the marketing distribution prescription, and use of drugs in a society, with emphasis on the resulting medical and social consequences [17]. Drug utilization studies create a sound sociomedical and health economic basis for healthcare decision-making. They help to ascertain the role of drugs in a society [18]. The ultimate aim of drug utilization research must be to assess whether drug therapy is rational or not [19].

### MATERIAL AND METHODS

A prospective study was conducted over a period of 9 months (from may 2010 to jan 2011) in the outpatient department of a tertiary care hospital at Kottakkal, Kerala, India. The study was approved by the institutional ethics committee.

A suitable data collection form was designed to collect and document the data. Data collection form included the provision for collection of information related to demographic details of the patient, occupation, social status, past medical history, family history, duration of diabetes mellitus, category of the drug prescribed, dose, dosage form, frequency, duration, total number of drug prescribed, number of anti diabetic drug prescribed, number of antibiotics prescribed, number of injections prescribed, drugs prescribed by generic name, patients knowledge about the drugs, clinical data, class of anti diabetic drugs prescribed and coexisting illness. All the necessary and relevant information were collected from prescription and interviewing the patients.

Only Type-2 DM outpatients more than 18 or equal to 18 years were included in the study. If the diabetic patients had not taken medicines from hospital outpatient pharmacy, those patients were excluded. Also, patients with serious medical conditions requiring

subsequent medical admission were excluded. Prescriptions from patients receiving oral hypoglycemic agents in diabetology department were reviewed. Information was collected from outpatients after they had visited the physician.

## RESULTS

Out of the 202 patients enrolled in the study, 105(51.98%) were males and 97(48.02%) were females. Among the study population, the greatest number of patients were in the age group of 51-60 years [78 (38.61%) of the total]. Demographic details of enrolled patients are presented in the Table 1 and Table 2 respectively.

Among the study population, 11 (5.44%) had their father alone suffering from diabetes, 17 (8.42%) had their mother alone suffering from diabetes, 103 (50.99%) had their other family members suffering from diabetes, 9 (4.45%) had both their father and mother suffering from diabetes and 62 (30.69%) patients had no family members with diabetes.

Among the 202 patients studied there were a total of 306 co-existing illnesses such as hypertension, hyperlipidemia, rheumatoid arthritis, asthma, gastritis, cirrhosis, coronary artery disease (CAD), angina pectoris, thyroid problem, migraine, renal failure, psychiatric illness, depression, chronic obstructive pulmonary disease (COPD), epilepsy, prostatic hyperplasia and infectious diseases. The coexisting illness of enrolled patients is summarized in Table 3.

Out of the total, 141 patients (69.80%) were on single oral hypoglycemic agent or a combination of oral hypoglycemic agents. Remaining 61 patients (30.20%) were on a combination of insulin and oral hypoglycemic agents. Out of the 141 patients on Oral hypoglycemic Agents (OHA), 136(67.33%) were on polytherapy and 5(2.47%) were on monotherapy. Out of 136 on polytherapy, 115 (56.93%) were on two drug therapy, 19 (9.41%) were on three drug therapy, and 2(0.99%) were on four drug therapy. The details of anti diabetic therapy of patients are presented in Table 4.

Among 282 antidiabetic drugs prescribed, 12 patients (4.26%) were prescribed with Glimepiride, 9 patients (3.19%) with Gliclazide, 13 patients (4.61%) with Pioglitazone, 132 patients (46.81%) with

Glimepiride and Metformin, 3 patients (1.06%) with Metformin and Pioglitazone, 29 patients (10.28%) with Glibenclamide and Metformin, 13 patients (4.61%) with

Glibenclamide, Metformin and Rosiglitazone, 2 patients (0.71%) with Glimepiride, Metformin and Pioglitazone and 8 patients (2.84%) with Glibenclamide, Metformin and Pioglitazone and 61 patients (21.63%) with insulin.

Among the various antidiabetics, sulfonylurea and Biguanide combination drug was the common class of drug used accounting for 161 (57.09%) of the total antidiabetics. Details of the class of antidiabetic drugs prescribed for enrolled patients are presented in Table 5.

Out of 202 prescriptions prescribed, 122 prescriptions (60.40%) contained one antidiabetic drug, and 80 prescriptions (38.61%) contained 2 antidiabetic drugs. Average number of antidiabetic drugs per prescription was 1.4 Average numbers of drugs per prescription was 4.

Out of the 202 patients, 66 patients (32.67%) had knowledge about the uses of drug and the remaining 136 patients (67.33%) were ignorant about the drugs they used.

Total cost of the drugs prescribed in 202 prescriptions for one month amounted to INR.158280. The average cost per prescription for one month was found to be INR.783.55. Out of the 202 prescriptions 79 prescriptions (39.11%) were found to be of cost less than 600 Rs., 99 (49.00%) of 601-1200 Rs., 19 (9.41%) of 1201-1800Rs., 4(1.98%) of 1801-2400 Rs. and 1 (0.50%) of more than 2401 Rs. The details of cost of therapy are presented in Table 6.

Out of the total cost (INR.158280) for one month, oral hypoglycemic agents accounted for Rs.55620 (35.14%), insulin Rs.15810 (9.99%) and other drug Rs.86850 (54.87%). Out of the total cost, 71430 Rs. (45.13%) were amounted for antidiabetic drugs. Average cost of antidiabetic drugs per prescription for one month was found to be INR.353.61. The average cost of oral hypoglycemic agents per prescription for month was found to be INR 275.35. The details of cost distribution of drugs prescribed for one month are presented in Table 7.

**Table 1: Sex Wise Distribution of Patients**

Sex	Number of patients (n=202)	Percentage (%)
Male	105	51.98
Female	97	48.02

**Table 2: Age Distribution of Patients**

Age group in year	Total no.of patients (n=202)	No.of male	No.of female	% distribution	% of male	% of female
< 20	0	0	0	0	0	0
21-30	2	2	0	0.99	0.99	0
31-40	17	9	8	8.42	4.45	3.96
41-50	51	19	32	25.25	9.41	15.84
51-60	78	49	29	38.61	24.26	14.36
61-70	43	21	22	21.29	10.39	10.89
> 70	11	5	6	5.44	2.48	2.97

**Table 3: Co-Existing Illness**

Co existing illness	Number of patients (n=306)	Percentage (%)
Hypertension	102	33.33
Hyperlipidemia	75	24.51
Rheumatoid arthritis	9	2.94
Asthma	19	6.21
Gastritis	14	4.58
Cirrhosis	2	0.65
CAD	18	5.88
Angina pectoris	3	0.98
Thyroid problem	13	4.25
Migraine	4	1.31
Renal failure	11	3.59
psychiatric illness	9	2.94
Depression	7	2.29
COPD	3	0.98
Epilepsy	4	1.31
Prostatic Hyperplasia	7	2.29
Infectious Diseases	6	1.96

Table 4: Anti Diabetic Therapy

Therapy	Number of patients (n=202)	Percentage (%)
Mono therapy	5	2.47
Dual drug therapy	115	56.93
Triple drug therapy	19	9.41
Quadruple drug therapy	2	0.99
Insulin+ mono therapy	14	6.93
Insulin+ Dual drug therapy	31	15.35
Insulin+ Triple drug therapy	16	7.92

Table 5: Class of Antidiabetics

Class	Number of patients (n=282)	Percentage (%)
Sulfonyl ureas	21	7.45
Thiazolidonediones	13	4.61
Sulfonyl urea and Biguanides	161	57.09
Thiazolidonediones and Biguanides	3	1.06
Sulfonyl urea, Biguanides and Thiazolidonediones	23	8.16
Insulin	61	21.63

Table 6: Cost of Therapy during the Study

Cost in rupees (INR per month)	Number of prescription (n=202)	Percentage (%)
1-600 Rs.	79	39.11
601-1200 Rs.	99	49
1201-1800 Rs.	19	9.41
1801-2400 Rs.	4	1.98
>2401 Rs.	1	0.50

Table 7: Cost Distribution of the Drugs Prescribed

Drugs	Cost (Total cost/1 month=INR.158280)	Percentage (%)
Oral hypoglycemic agents	55620	35.14
Insulin	15810	9.99
Other drugs	86850	54.87

## DISCUSSION

Type-2 diabetes is a chronic disease requiring lifelong treatment. Although lifestyle modifications play an important role in diabetes management drugs become unavoidable in many patients. A prescription based study is considered to be one of the most effective methods to assess and evaluate drug utilization of medication. Prescription by the clinician may be taken as a reflection of his/her attitude to the disease and role of the drug in treatment. It also provides insight in to the nature of healthcare delivery system. This study analyzed the drug utilization pattern in type-2 diabetic outpatients.

All together a total of 202 prescriptions were collected in the study period of 9 months. This study showed that diabetes mellitus is more prevalent in males than in females.

The study also found a higher incidence of diabetes was among elderly patients, with a high incidence in the age group of 51-60 years [i.e., 38.61% of the total]. Similar results were obtained in the study conducted by Upadhyay D K et al.<sup>[16]</sup>, and Sahoo Subhasish et al.<sup>[20]</sup>. A study from Netherland had reported an average age of 67 years [21] and another study from Spain reported an average age of  $60.5 \pm 12.8$  years<sup>[22]</sup>, which is higher compared to this study. In general elderly patients are at a greater risk of developing type 2 diabetes mellitus. This study showed that 140 (69.31%) patients suffered from T2DM due to genetical reasons and the remaining due to unknown causes.

The duration of diabetes plays an important role in management of diabetes. This study showed that most of the patients had a diabetic history of 1-5 years. Similar result was obtained by the study conducted by upadhyay D K et al. A study from Spain reported the mean duration of diabetes as  $11.8 \pm 8.0$  years<sup>[22]</sup>.

In elderly patients with type-2 diabetes treatment may be initiated with monotherapy followed by early intervention with a combination of oral agents, including a sulfonylurea as a foundation insulin secretagogue in addition to a supplemental insulin sensitizer<sup>[23]</sup>. Several studies showed that a combination of sulfonylurea with metformin has been most widely used<sup>[24]</sup>. The present study also showed that a combination of sulfonylurea with metformin was most frequently prescribed 57.09%. Metformin does not promote weight gain and has beneficial effects on several cardio vascular risk factors. Accordingly, metformin is widely regarded as the first drug of choice for most patients with type-2 diabetes mellitus<sup>[25]</sup>. Our study also supports the same; 66.31% received metformin combination with other oral antidiabetic drugs.

At present, glibenclamide and glimepiride are the second generation sulfonylurea most widely used in the United States<sup>[26]</sup>. In this study among the second generation sulfonylureas, glimepiride and glibenclamide were most commonly prescribed. Adding a second agent is usually better than increasing the dosage of an agent that has already been given in a nearly maximum dosage. In some patients three drug combinations may be useful<sup>[27]</sup>. In this study 56.93% patients received two drugs, 9.41% patients received three drug and 0.99% patients received four drug combination of only OAD.

In most patients, the failure of three oral agents used together calls for the use of insulin alone or in addition to an oral agent. Numerous studies have shown that a combination of insulin and sulfonylurea is more effective than insulin alone in the treatment of patients with type-2 diabetes mellitus after secondary failure to oral drugs, leading to better glucose profiles and/or decreased insulin needs<sup>[28]</sup>. This study shows that 30.2% patients received insulin in combination with OAD. The choice of antidiabetic depends on the

type of patients, their current illness, cost factors, as well as the availability of medicine.

A good number of patients with a long duration of diabetes are at a high risk of developing complications. Among the various complications including hypertension, Hyperlipidemia, Ischemic heart disease, cardiovascular complications cause a major threat. In this study there were a total of 306 co-existing illness in 202 patients. Hypertension was accounted for 33.33% of the total complications in diabetes patients, denoting the highest percentage of the complications. This study showed that hypertension was usually the most common co-existing illness seen with diabetes mellitus (DM). Similar results were obtained by Upadhyay D K et al<sup>[16]</sup> and Sahoo Subhasish et al<sup>[20]</sup>.

Poly pharmacy is associated with higher cost increase the risk of side effects, drug interactions and non compliance <sup>[29]</sup>. In general diabetic patients are at higher risk of developing depression. Studies suggest that diabetes doubles the risk of depression <sup>[30]</sup>. In this study doctors prescribed antidepressants almost 11% of the total drugs prescribed. These patients are more vulnerable to miss their medications, and the possibility of non adherence is very high <sup>[31]</sup>. Doctors should be careful while prescribing Tri cyclic antidepressants [TCAs] to these patients. According to one study, the use of higher dose of Tri cyclic antidepressants [TCAs] was associated with an increased risk of sudden cardiac death <sup>[32]</sup>. Over use of vitamins were also observed <sup>[33]</sup>. In the present study, vitamins accounted only for 2.72% of the total drugs. This is low compared to other studies. This is a positive effect. Analgesics and anti-inflammatory drugs accounted for 0.25% of the total drugs. The prescriber should be aware of the interaction between OHA and Non-steroidal anti inflammatory drugs (NSAIDs). Concurrent use of NSAIDs and sulfonylurea may result in an increased risk of hypoglycemia <sup>[34]</sup>.

The average number of drugs per prescription was 4, when compared to other previous studies of Sutharson L, et al<sup>(1.95)</sup>, Adibe MO, et al<sup>(1.9)</sup>(2.6) and Upadhyay DK, et al<sup>(1.6)</sup>(3.76) this value is high. The high average number of drugs prescribed to patients with diabetes is not surprising. It is recognized that patients with diabetes mellitus are generally prescribed more drugs than other patients <sup>[35]</sup>. In general, due to the multiple diseases, diabetes patients are at a greater risk of polypharmacy. In this study 61.39% prescription contains two or more drugs. It shows that poly pharmacy is high.

The study found that 91.58% of the drugs were prescribed in oral dosage form. The study conducted by upadhyay DK et al<sup>[16]</sup> was found that 94.89% of the drugs were prescribed in oral dosage form. This is a good prescribing habit. Oral dosage forms can definitely play an important role in improving patient adherence to treatment. In this study Patients knowledge about the drugs is less (67.33%) compared to study conducted by Sutharson L et al, (i.e. 47.24%). So proper awareness about the drug should be given.

Cost of drug therapy is a cause for non adherence. In this study average prescription cost for one month was INR.783.55. We found that antidiabetic drugs accounted for 45.13% of the total prescription cost for one month and oral hypoglycemic agents accounted 35.14%. In a study by Wu SYB et al;1998<sup>[36]</sup>, Antidiabetic drugs accounted for 45% of the total drug cost. Cost of prescription is important in chronic diseases like diabetes. One of the better approaches to decrease the prescription cost is to prescribe cheaper brands. A study from Nepal reported a huge variation in cost among brands of a particular drug <sup>[37]</sup>. Also in India, huge variations in cost of antidiabetic medications have been documented <sup>[38]</sup>. A similar finding has been seen in other developing countries <sup>[39]</sup>. Thus there is a huge scope in reducing the prescription cost by prescribing cheaper alternatives. However, while choosing cheaper brands, one should keep in mind the quality of the brands.

## CONCLUSION

A total of 221 oral anti diabetic drugs (OADs) were prescribed in 202 patients giving an average 1.09 OADs per prescription. In this study Males were found to be more affected by Type-2 Diabetes

mellitus than females. Elderly patients were at higher risk of developing Type-2 Diabetes. Patients with a long duration of T2DM were at a higher risk of developing complications. Among the various complications, cardio vascular complications caused major threat and among cardiovascular complications, hypertension was the major one.

This study shows the cause of Type-2 diabetes mellitus in most of the patients is heredity. The study found that the incidence of polypharmacy in Type-2 diabetes patients was high compared to other studies. In this study it was found that combination therapy was more used than monotherapy. Sulfonylurea and Biguanide combination drugs were commonly used. In these Glimperide and metformin combination drugs were used commonly followed by Glibenclamide and metformin. Out of the total drugs most were prescribed in oral dosage form. This is a good prescribing habit.

This study shows that patient knowledge about the drugs is low. In this study cost of drugs per prescription was found to be very high. The cost of prescription can be reduced by choosing most economic drugs without changing its quality.

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