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PHARMACY INFOPEDIA
PRINT ISSN: 2394-6679 | E-ISSN: 2347-7881

A Study on Drug Utilization Pattern and Effectiveness of Oral Hypoglycemic Agents in Diabetes Mellitus

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ABSTRACT

Introduction: Diabetes mellitus is on alarming rise in India. Drug utilization studies help to identify the adherence to standard guidelines and extent of drug use and to evaluate the rational drug usage.
Aims and objectives: To determine the drug utilization pattern and effectiveness of oral hypoglycemic agents among diabetes mellitus patients.
Materials and methods: It is a prospective observational study carried out for a period of six months at RIMS kadapa, and two others diabetic centers. The diabetic patients who visited the medicine outpatient department were included. After obtaining approval from institutional ethical committee, a structured data collection form was used to collect demographic data, complete prescription details and other relevant information required for the study. The drug utilization pattern was determined. The drugs were categorized by Anatomical therapeutic classification (ATC) and DDD/1000 inhabitants/day was calculated by using WHO guidelines. Among all oral hypoglycemic agents the most effective drug/combination in this region was identified.
RESULTS: 716 prescriptions were assessed out of which,401(56.0%) were females and 315(43.9%) were males, most of the patients were in the age group of 40-60 for males 175(55%) and females 205(51.1%). Hypertension was the most common co-morbid seen. The average number of drugs per prescription was 4.26 and anti-diabetics per prescription was 1.79. DDD/1000 inhabitants/day for metformin (A10BA02) was 10.5, glimiperide (A10BB12) was 9.3, glibenclamide (A10BB01) was 7.91, pioglitazone (A10BG03) was 7.25. Out of 716 patients 311(45.25%) patients were on Monotherapy, and 405 (56.5%) were on Combination therapy. A total of 200 newly diagnosed patients of diabetes mellitus were enrolled in the study out of which only 128 members were followed up successfully. The combinations of Metformin +Sulfonyl Ureas + Others showed a good control of fasting blood sugar when compared with only Metformin, only Sulfonyl Ureas or Metformin +Sulfonyl Ureas, Sulfonyl Ureas + Others.
Conclusion: Metformin was the most utilized drug followed by glimiperide. Combination therapy was most frequent when compared to monotherapy in which metformin+glimiperide was commonly prescribed one. so by understanding the current prescribing patterns attempts can be made to improve rational prescribing. The combination of Metformin+Sulfonyl Ureas+Others is more effective combination.

Keywords: Drug Utilization Pattern, Effectiveness, Oral hypoglycemic Agents, Diabetes Mellitus

INTRODUCTION

Diabetes represents a spectrum of metabolic disorders, which has become a major health challenge worldwide [1]. By the year 2030, over 85 percent of the world's diabetic patients will be in developing countries. In India alone, the prevalence of diabetes is expected to increase from 31.7 million in 2000 to 79.4 million in 2030 [2]. The prevalence of Type 2 diabetes is 4-6 times higher in the urban areas as compared to rural areas [3]. The prevalence of impaired glucose

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PRINT ISSN: 2394-6679 | E-ISSN: 2347-7881

tolerance (IGT) in the rural population is also high at 7-8%, which indicates presence of a genetic basis for Type 2 diabetes in ethnic Indian population [4]. The Diabetes Control and Complications Trial (DCCT) demonstrated that good metabolic control, resulting from intensive insulin therapy, reduced the risk of progression or development of retinopathy, nephropathy and neuropathy in type 1 diabetes [5]. The United Kingdom Prospective Diabetes Study (UKPDS) showed that intensive glycemic control in type 2 diabetes significantly reduced the risk of development and deterioration of microvascular complications [6]. The target for good glycemic control recommended by the American Diabetes Association (ADA) is glycated hemoglobin A1c (HbA1c) < 7.0%. The primary goal of the management of diabetes mellitus is the attainment of near normal glycemia [7,8].

According to WHO, Diabetes mellitus is defined as a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, protein and fat metabolism resulting from defects in insulin secretion, insulin action, or both[10]. Drug utilization research can increase our understanding of how drugs are being used. It can be used to estimate the numbers of patients exposed to specified drugs within a given time period. It can describe the extent of use at a certain moment and/or in a certain area (e.g. in a country, region, community or hospital). Researchers can estimate to what extent drugs are properly used, overused or underused .It can determine the pattern or profile of drug use and the extent to which alternative drugs are being used to treat particular conditions. It can be used to compare the observed patterns of drug use for the treatment of a certain disease with current recommendations or guidelines. It can be used in the application of quality indicators to patterns of drug utilization. To obtain a rough estimation of quality of prescribing, Drug utilization data can be fed back to prescribers. This is particularly useful when the drug prescribing by a particular individual can be compared with some form of gold standard or best practice, and with the average prescriptions in the relevant country, region or area. For uniformity ATC system of classification is used throughout the world. Example of ATC classification A10B B01- Glibenclamide .The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults, which is used to determine the drug use. Effectiveness studies are used to analyze the most effective drug among the existing drug therapies [9].So this study was held with following objectives

1.To determine demographic details such as age, gender etc of diabetic patients under the study.

2. To study the Drug utilization pattern.

3. To analyze effectiveness of different existing drug therapies.

MATERIALS AND METHODS

The study was conducted at Rajiv Gandhi Institute of Medical Sciences(RIMS) and two other diabetic hospitals located at Kadapa. It was prospective observational follow up study carried out over a period of six months from December-2014 to june-2015 in patients attending outpatient department. The study protocol was approved by the Institutional Review/Ethical committee of RIMS. The data was collected from prescriptions, patient record books and patient interview. All necessary and relevant baseline information was collected on a standard patient data collection proforma, which contains demographic data, social history, diagnosis data, laboratory investigations , treatment chart. For drug utilization pattern, we have analyzed 716 of DM patients. For effectiveness, the tentative sample size fixed was 200 patients. Among 200 patients only 128 members are successfully followed up and 72 cases were excluded due to lack of follow up data. The patients were followed up for 3 months by comparing the glucose levels through our study period. Once the data was collected, then oral hypoglycemic drugs were classified according to ATC classification system and DDD of individual drugs were calculated. Effectiveness of the existing oral hypoglycemic drug therapy was determined, DDD was calculated by using the formula

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PRINT ISSN: 2394-6679 | E-ISSN: 2347-7881

$$\text{Total number of dosage Strength of each 1000 inhabitants/day} = \frac{\text{Units prescribed X dosage unit X 1000 DDD}}{\text{DDD X Duration of study X Total sample size}}$$

Hence obtained data was interpreted in Excel sheet and the statistical methods used for this study were Descriptive analysis and Wilcoxon Signed-Rank test.

RESULTS

Out of 716 patients, 401(56.0%) were females who were more when compared to males 315(43.9%).The majority of patients were found in between the age group 40-60yearsin which 175(55%) are males, 205(51.1%) are females, in between the age group of 20-40years50(15.87%%) are males, 106(26.4%) are females and finally 90(28.5%) are males, 94(23.4%) are females of <60years of age were tabulated in table-1.

Table 1 Distribution based on Age group

Age group	No. of male patients	No. of Female patients	Total No. of patients
20-40	50(15.87%)	102(25.5%)	152(21.2%)
40-60	175(55%)	205(51.1%)	380(53.0%)
>60	90(28.5%)	94(23.4%)	184(25.6%)
Total	315(43.9%)	401(56.0%)	716(100%)

Among all patients, 311(45.25%) were treated with monotherapy and 405(56.5%) were treated with combination therapy. In combination therapy 249 (34.7%) patients were treated with two-drug combination,139 (19.4%) with three-drug combination and 17(2.3%) with four-drug combination, the same is given in table 2.

Table 2 Distribution Based on Mono and Combination Therapy

Type of therapy	No. of Males	No. of Females	Total
Monotherapy	148(47.5%)	163(52.4%)	311(45.25%)
Combination	195(48.6%)	210(51.6%)	405(56.5%)

Table 3 represents the list of oral hypoglycemic agents which were classified according to WHO ATC system of classification and consumption of individual drug was shown in DDD. The drug consumption in DDD/1000 inhabitants/day states that metformin was the most consumed drug with 10.5 DDD/1000 inhabitants.

Table 3 List of the OHA along with the ATC and DDD

Sno.	Name of the Drug	ATC code	DDD assigned by WHO(mg)	DDD/1000 inhabitants/day
1.	Metformin	A10BA02	2000	10.5
2.	Glimiperide	A10BB12	2	9.3
3.	Glibenclamide	A10BB01	10	7.91
4.	Pioglitazone	A10BG03	30	7.25
5.	Vildagliptin	A10BH02	50	5.5
6.	Voglibose	A10BF03	0.3	5.9
7.	Glipizide	A10BB07	10	4.3

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PRINT ISSN: 2394-6679 | E-ISSN: 2347-7881

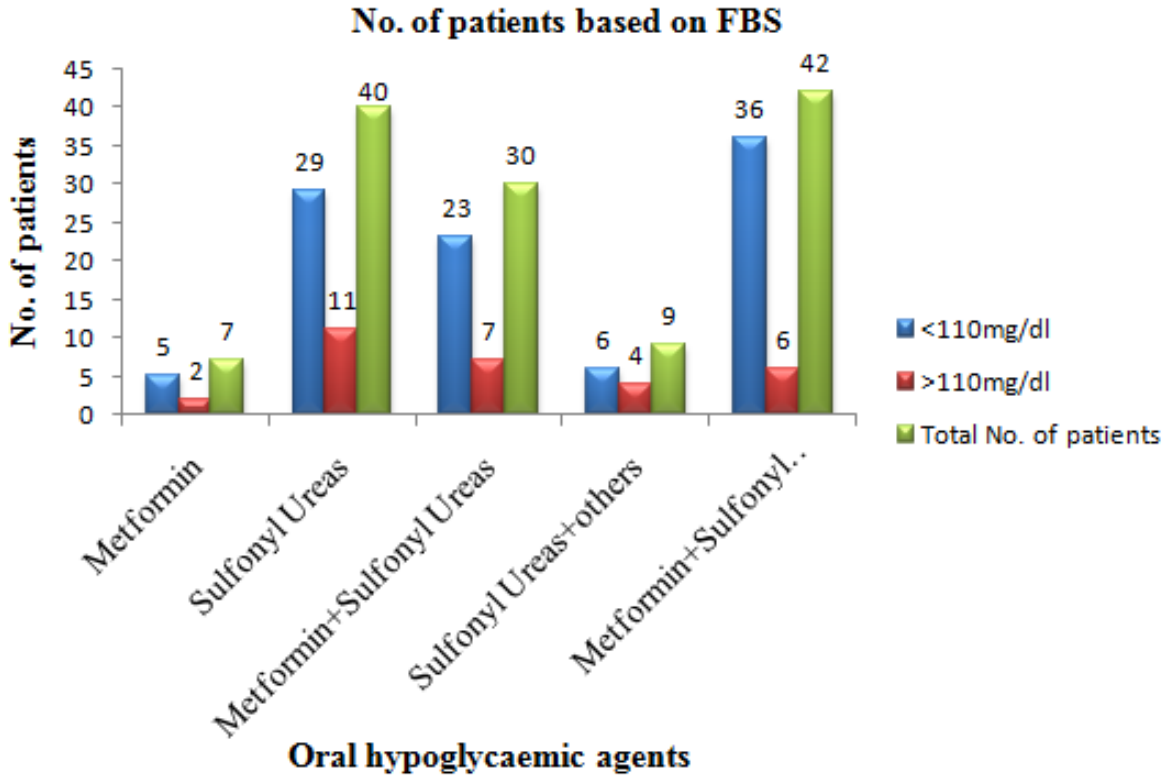
Table 4 represents the percentage distribution of patients based on co-morbid conditions and complications where Diabetic Neuropathy and Gastro Intestinal Disorders are reported more in number then comes to Hypertension and Cardio Vascular Diseases.

Table 4 Percentage distribution of Patients Based on Co-morbidities and complications

Co-morbidities and complications	No. of Male patients	No. of Female patients	Total No. of patients
HTN	125(44.8%)	154(55.1%)	279(38.9%)
Diabetic Neuropathy	37(31.3%)	81(68.6%)	118(16.4%)
CVD	28(56%)	22(44%)	50(6.9%)
GI disorders	37(67.27%)	18(32.7%)	55(7.68%)
UTI	0	3(0.4%)	3(0.4%)
Hypothyroidism	0	11(1.5%)	11(1.5%)

For effectiveness a total of 200 patients were recruited among them 128 patients were followed up successfully. Effectiveness of various available anti-diabetic agents calculated based on the FBS levels in the blood that are noted pre and post usage of respective drug and the data was represented as follows

Figure 1 Effectiveness of oral hypoglycemic agents



The median and P values of oral hypoglycemic agents were presented in the preceding tabular format

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PRINT ISSN: 2394-6679 | E-ISSN: 2347-7881

Table 5 Median and P values of oral hypoglycemic agents

S. no	Name of the Drug	Median values for base line	Median values for follow up	Difference of median values of base line and follow up	Percentage decrease in FBS	P-value
1.	Metformin	152	107	45	29.6%	0.0152
2.	Sulfonylureas	168	108	60	35.7%	0.0001
3.	Metformin + sulfonylureas	206	104	102	49.5%	0.0001*
4.	Sulfonylureas + others	185	110	75	40.5%	0.0001
5.	Metformin + sulfonylureas + others	233	98	135	57.9%	0.0001***

DISCUSSION

Diabetes mellitus is a metabolic disorder as stated by WHO which requires the chronic treatment[10]. Besides the life-style modifications and dietary changes, the pharmacological treatment an integral component in the management of diabetes[9].A drug utilization study is considered to be one the most effective methods to assess and evaluate the prescribing attitude of physician and help to promote rational use of drugs.

In our study, the prevalence of diabetes mellitus is more in females(56%) than males(43%). The middle aged group people(40-60yrs) are more prevalence to the diabetes mellitus similar results were obtained in study the of drug utilization pattern and effectiveness analysis in diabetes mellitus conducted by Premalatha Das.

The average number of antibiotic drugs per prescription is an important index of the scope for review and educational intervention in prescribing practices. It is important to maintain average or required number of drugs for patients in the prescription in order to decrease the risk of drug interactions, poly pharmacy, prescribing errors, higher cost, side effects and non-compliance.

The average number of drugs per prescription in our study was 4.26 and the average number of anti diabetic drugs per prescription was 1.79 which is similar to the results (4.76, 1.53) that obtained in a study conducted by Dr. Zeyad on assessment of drug use by diabetics, this is higher than (2.6) a study conducted by Adibe M.O [11] on outpatient utilization of anti-diabetic drugs in south eastern Nigeria. Lower than (7.58+-2.49)a study conducted by Bela Patel on pattern of anti-diabetic drugs in type-2 diabetic patients(12). The average number of drugs prescribed to the outpatient diabetic population was high mainly because of co-morbidities of patients with diabetes mellitus which is not surprising. It is recognized that patients with diabetes are generally prescribed more drugs than other patients.

This study determines that DDD/1000 inhabitants/day for Metformin was more which is more utilized anti diabetic drug than others and Glimeperide was more utilized drug in Sulfonyl Ureas. Similar results were obtained in a study conducted by Adibe M.O on Outpatient Utilization Of Anti-diabetic Drugs[11].Metformin alone and Metformin combination (anti-diabetic drugs) was commonly prescribed anti-diabetic drug observed in the present study, similar to the results obtained in the study conducted by Bela Patel on pattern of anti-diabetic drugs in type-2 diabetic patients[12].

The combination therapy(56.5%) is more in use in the current study area setting and is more preferred in order to control the FBS of the patients, a common finding observed with early study of V. Sivasankari et.al [13] on drug utilization pattern of anti-diabetic drugs and Khushali et.al [14] on evaluation of anti-diabetic prescriptions which also suggests that combination of biguanides and sulfonylureas were most frequently used combination and are most effective. Our study states

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PRINT ISSN: 2394-6679 | E-ISSN: 2347-7881

that 2-drug combination is more in use. In 2-drug combination Metformin+Glimeperide was most commonly prescribed than other combinations like Metformin+Glibenclamide, Metformin+ Pioglitagone, Metformin+Glipizide, a common finding identified with early study of Bela Patel et.al on patterns of anti-diabetic drugs use but which is in contrast with a study conducted by V.Sivasankari on drug utilization pattern of anti-diabetic drugs states that glibenclamide+metformin was most commonly prescribed drug. In3-drug combination Metformin+Glimeperide+Pioglitazone was most commonly prescribed than other combinations.

It was observed that comorbidities are more in diabetic patients among them hypertension(38.9%), diabetic neuropathy(16.4%), cardio vascular disorders(6.9%), hypothyroidism (1.5%) , gastrointestinal disorders (7.68) are commonly reported in the current study area setting, which is similar to a study conducted by Dr. P.Sharma [15] on screening of prescriptions in patients of type 2 diabetes mellitus.

A total of 200 newly diagnosed patients of diabetes mellitus were enrolled in the study out of which only 128 members were followed up successfully. The effectiveness of different oral hypoglycemic agents were done by comparing the difference of fasting blood sugar between base line and follow up. Metformin +Sulfonyl Ureas + Others can decrease the fasting blood sugar levels effectively when compared to other combination of drugs, this is similar to the study conducted by Premalatha Das on drug utilization pattern and effectiveness analysis in diabetes mellitus. The level of significance (p value) calculated for metformin was 0.0152,Sulfonyl Ureas was 0.0001, Metformin + Sulfonyl Ureas< 0.0001*, Sulfonyl Ureas+ Others was 0.0001, Metformin + Sulfonyl Ureas+ Others was < 0.0001***.

LIMITATIONS

- Glycated haemoglobin is more reliable to assess glycemic control over a period of 3 months. But this was not used in this study because of less time period for our follow up and all patients included for effectiveness were newly diagnosed cases. So only FBS levels are compared before and after therapy for effectiveness of OHA.
- The effectiveness of different OHA were not able to compare with each other effectively because of the different sample size for each type of drug treatment.
- The patients who are included in our study might be followed life style modifications, dietary changes, physical exercises etc that may affect the precise evaluation of effectiveness of OHA.

CONCLUSION

Among all patients females are more in number when compared to males. The middle aged group people (40-60yrs) are more prone to the diabetes mellitus. It was recognized that patients with diabetes are generally prescribed for a long period than other patients. Metformin was most commonly utilized anti diabetic drug than others and Glimeperide was most utilized drug in Sulfonyl Ureas. Metformin alone and Metformin combinations (with other anti-diabetic drugs) were commonly prescribed to diabetic patients in current scenario. Combination therapy is preferred more in the current setting in order to control the FBS of the patients, in which 2-drug combination is more in use, in 3-drug combination Metformin+ Glimeperide+Pioglitazone was the most commonly prescribed than other combinations.200 patients were analyzed for effectiveness of OHA. Combinations of Metformin +Sulfonyl Ureas + Others showed a good control of fasting blood sugar when compared with only Metformin, only Sulfonyl Ureas or Metformin +Sulfonyl Ureas, Sulfonyl Ureas + Others.

Therefore through a thorough understanding of the existing prescribing patterns, attempts can be made to improve the quality and efficacy of drug therapy. Besides setting standards and assessing the quality of care.

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PRINT ISSN: 2394-6679 | E-ISSN: 2347-7881

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