Drug utilization study of drugs used in treatment of diabetes mellitus in medicine OPD of a tertiary care hospital in northern India

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Abstract

Introduction: Diabetes is a metabolic disorder with prevalence among adults being approximately 8% and is expected to rise to 11.4% by the year 2045. The current pharmacotherapy of diabetes mellitus includes treatment with drugs such as insulin and oral antidiabetic agents. The drug utilization data from diabetic patients can provide data for determining pattern of prescription, rationalize drug therapy and ascertain adherence to standard recommendations for treatment of diabetes.

Materials and Methods: The study was conducted in the OPD of department of medicine, KGMU for 8 months. 89 patients with diabetes were analysed for their prescription pattern and the data was recorded on a case record form (CRF). Data for drug utilization as per the core prescribing indicators of WHO for drug utilization studies and data for evaluating drug consumption was calculated in terms of defined daily dose (DDD).

Result: Drug utilization pattern of diabetic patients showed an average of 5 drugs per prescription out of which on an average 2.18 drugs were for diabetes. The average daily prescribed dose of antidiabetics was under the define daily dose (DDD) range prescribed by WHO which is indicative of a rational drug prescription pattern. Among the antidiabetic drugs prescribed, metformin 500mg was the most commonly prescribed drug in monotherapy while in combination therapy glimepiride 2mg + metformin 500mg was most commonly prescribed.

Conclusion: Our study revealed that drug prescription in diabetic patients are quite rational in terms of prescribed dose and number of drugs being prescribed for each patient. Though certain drugs were being prescribed out of the essential medicine list but fell well within the international guidelines for diabetic pharmacotherapy. The results point towards the need of a frequent and thorough revision of the essential medicine list and strict adherence to it.

Keywords: Drug utilization study, Antidiabetic, Essential medicine list, Defined daily dose, Prescription pattern.

Introduction

Diabetes is a metabolic disorder characterized by hyperglycaemia and associated with a high risk of numerous complications. People living with type 2 DM are more vulnerable to various forms of both short- and long-term complications. It remains as one challenging and serious health problems in today's world. The prevalence of diabetes among adults has reached approximately 8% and is expected to rise to 11.4% by the year 2045.[1,2] It is a group of metabolic syndromes which consists of elevated blood sugar which is attributed to inadequate secretion of insulin or insulin resistance or both. Being a multifactorial aetiology, it is complexed with genetic and environmental factors. The tendency of increased morbidity and mortality is seen in patients with type 2 DM because of the commonness of this type of DM, its insidious onset and late recognition. The current pharmacotherapy of diabetes mellitus includes treatment with drugs such as insulin and oral antidiabetic agents. With the exceptions of insulin, exenatide, liraglutide and pramlintide, all are administered orally and are thus also called oral antidiabetic agents.

WHO and various other international, national medical authorities have taken steps to rationalize and standardize drug therapy[3].One initiative was the implementation of essential medicine list, with a separate list for all countries. The national essential list gives names, dosage forms of all drugs that are

supposed to be present at all time and accessible to the patients of that country.[4] Clinicians are encouraged to prescribe drugs from the national essential medicine list to ensure rational and accessible drugs as per the international recommendations. National essential list of India 2015 mentions glimepiride and metformin as only oral hypoglycemic for diabetes mellitus treatment.[5]

The concept of drug utilization research holds its importance in rationalizing and increasing access to available medicine and to achieve health by all. For the same purpose it is essential to validate information about use of drug for assessing patterns of drug use, identification of hurdles, access, interventions, and outcome monitoring for the rational use of drugs. Patterns of drug therapy vary for the disease course in different hospital settings. The drug utilization data from diabetic patients can provide data for determining pattern of prescription.

Material and Methods

The study was conducted in the OPD of department of medicine, KGMU for 8 months. 89 patients with diabetes were analysed for their prescription pattern and the data was recorded on a case record form (CRF). Data for drug utilization as per the core prescribing indicators of WHO for drug utilization studies and data for evaluating drug consumption was calculated in terms of defined daily dose (DDD).

Drug utilization studies as per the prescribing parameters:
1. Average number of drugs per encounter
2. Percentage of drugs prescribed by generic name
3. Percentage of encounters with an antibiotic prescribed
4. Percentage of encounters with an injection prescribed
5. Percentage of drugs prescribed from the Essential medicine drug list (WHO/National)
6. Patient care indicators include:
7. Average consultation time

World Health Organization (WHO) has defined the unit of drug utilization research as measure of defined daily dose (DDD) which uses anatomical therapeutic

chemical [ATC] classification. Thus, the drug utilization was expressed as average dose prescribed per day and DDD/1000 patients /day. DDD/1000 patients /day was calculated by applying the following formula.

$$\frac{Total\ amount\ of\ drug\ consumed\ during\ the\ study\ period}{WHO\ recommended\ DDD\ of\ a\ drug\ x\ duration\ of\ treatment\ x\ sample\ size} \times 1000$$

Results

Amongst the 89 patients' studies for diabetes 59.5% of the patients were male and most commonly affected age group was 51 to 60 years of age followed by 41-50 years of age.

Drug utilization pattern
Drug use indictors

The average number of drugs encountered per prescription were 5. Whereas prescriptions with generic name were 46% and drugs from essential drug list were found to be 83%. During the study, indicators of patient care such as mean consulting time was found to be 6.3 min and availability of key drugs in the hospital was scarce.

Table 1: Drug use indicators for antidiabetic medications

| Core indicator	Number and percentage
Average no. of drugs per prescription	5
Average no. of hypoglycemic drugs per prescription	2.18
Prescription by generic name	46%
Drugs in essential drug list	83%
Facility Indicators	
Availability of essential drug list	Yes
Availability of key drugs	80%
Patient Care Indicators	
Average consulting time	6.3 min

Pattern of drug therapy of oral antidiabetic medication

Out of a total of 89 patients with diabetes mellitus type 2, 27 prescriptions (30.33%) were found with just one drug (monotherapy) whereas 62(69.65%) of the

patients were prescribed either dual therapy or more than 2 drugs. The utilization pattern of different antidiabetic drugs according to the type of therapy i.e., monotherapy, dual therapy and triple therapy is shown in the table below.

Table 2: Pattern of drug therapy in diabetic patients

| Drug therapy	n (%)
Monotherapy	27(30.33)
Dual Therapy	41(46.06)
Triple therapy	21(23.59)
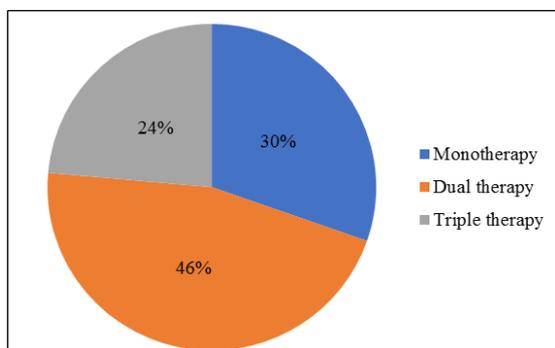
Fig. 1: Distribution as per number of oral hypoglycemics drugs per prescription

Types of oral antidiabetic medications prescribed according to their classes

 Most commonly prescribed antidiabetic group was biguanides (44.4%) in monotherapy followed by thiazolidinediones (40.97%) and dipeptidyl transferase and alpha glucosidase inhibitors with similar prescriptions (7.4%). In combination therapy, most common prescribed combination was found to be thiazolidinediones + biguanides (66%) followed by dipeptidyl peptidase-4 (DPP-4) inhibitors + biguanides, (33.8%).

Table 3: Types of antidiabetic medications prescribed according to their classes

Classes of Therapy	n (%)
Single antidiabetic drugs used in order of their frequency	
Biguanides	12(44.4)
Thiazolidinediones	11(40.97)
Dipeptidyl peptidase-4 (DPP-4) inhibitors	2(7.4)
Alpha glucosidase inhibitor	2(7.4)
Antidiabetic drug combinations used in order of their frequency	
Thiazolidinediones + Biguanides	41(66)
Dipeptidyl peptidase-4 (DPP-4) inhibitors + Biguanides	21(33.8)
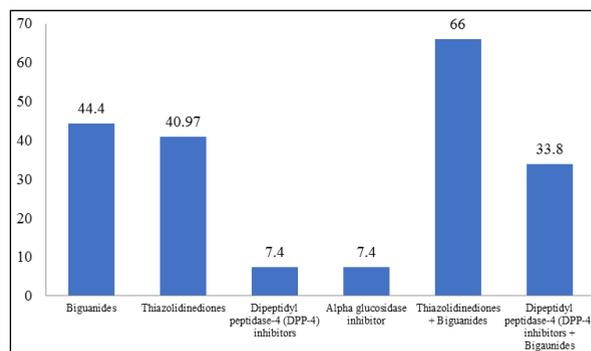
Fig. 2: Types of antidiabetic medications prescribed according to their classes

Antidiabetic drugs according to frequency of prescription encountered, their ATC classification code and most commonly prescribed drug in monotherapy and combination therapy are mentioned in the table below. Metformin 44.44% was most commonly prescribed in monotherapy and glimepiride + metformin in 33.8% of the patients in combination therapy was most common prescribed drug in combination therapy.

Table 4: Commonly used antidiabetic medications

Drug Therapy	n (%)	ATC classification	Most commonly used drug
Monotherapy			
Metformin 500 mg	12(44.4)	A10BA02	**Metformin 500 mg**
Glimepiride 2 mg	8(29.86)	A10BB12	**(44.44% of the**

Glipizide 5 mg	3(11.11)	A10BB07	**patients)**
Teneligliptin 20 mg	2(7.4)	NA	
Acarbose 25 mg	1(3.7)	A10BF01	
Voglibose 0.2 mg	1(3.7)	A10BF03	
Dual Therapy			
Glimepiride 2 mg + Metformin 850 mg	8(12.9)	A10BD02	**Glimepiride 2 mg +**
Glimepiride 2 mg + Metformin 500 mg	21(33.8)	A10BD02	**Metformin 500 mg**
Glimepiride 1 mg + Metformin 500 mg	12(19.3)	A10BD02	**(33.8% of the patients)**
Sitagliptin 50 mg + Metformin 500 mg	11(17.7)	A10BD07	
Teneligliptin 20 mg + Metformin 500 mg	10(16.1)	NA	

 Utilization of various antidiabetic medications on the basis of their average daily dose prescribed and DDD/1000 patients/day has been presented in the table below. According to our study all drugs were prescribed in doses either equal to or less than the WHO DDD prescribed except telmisartan which was prescribed in a higher dose.

While comparing the average daily dose of oral antidiabetics with WHO/ATC defined daily dose it was found that all antidiabetic drugs were less than their DDD. Teneligliptin could not be compared as the DDD and the WHO ATC code is not available.

Table 5: Defined Daily Dose of antidiabetic medications

Drug Therapy	Number of encounters	ATC classification	Average dose	WHO DDD (mg)	DDD/1000 patients/day
Metformin	74(83%)	A10BA02	537.83mg	2000 mg	2.48
Glimepiride	49(55.05%)	A10BB12	1.76 mg	2 mg	5.36
Glipizide	3(3.4%)	A10BB07	5 mg	10 mg	0.187
Teneligliptin	12(13.4%)	NA	20 mg	NA	-
Sitagliptin	11(12.36%)	A10BH01	50 mg	100 mg	1.37
Acarbose	1(1.1%)	A10BF01	25 mg	300 mg	0.0103
Voglibose	1(1.1%)	A10BF03	0.2mg	0.6 mg	0.0415

 Among the antidiabetic drugs prescribed metformin was the most commonly prescribed drug with a frequency of 74 (83%), followed by glimepiride with a frequency of 49(55.05%). The least commonly prescribed antidiabetics was acarbose and voglibose with only 1(0.7%) encounter.

Discussion

Amongst the 89 patients' studies for diabetes 59.5% of the patients were male and most commonly affected age group was 51 to 60 years of age followed by 41-50 years of age. Similar findings were reported by Mandal S et al[6] which showed male being predominantly affected 61.33% and the most common age group was found to be 50 -59 years of age. Study done by Mittal et al [7] most common age was 40.5±17.6 years and males were more affected than females. Abidi et al[8] also showed the similar finding in a study done in north Indian population where the most commonly affected age group was 50-60 years and with a pre dominance of male population (53.82%).

Assessment of drug utilization indicators of oral antidiabetics

83% of the AHA prescribed in this study was as per national essential drug list 2015.The values of our study as compared to various other studies are high for instance study performed by Khan[9] where it ranges from 34.18% to 43.24%, thus indicating rational prescribing in the present study. All prescription medications were not from essential medicine list the

reason of which could be availability of better options and classes of drugs still not mentioned in the national list of essential medicine (NLEM). This points out a need for modification of NLEM according to the current standard recommendations and local requirements of the country.

To determine an estimate of drug consumption, defined daily dose of various all antidiabetic drugs as per the WHO were calculated. The average DDD of metformin was 537 mg/day. Concomitant vitamin B complex was prescribed along with metformin based on rationale that metformin is known to be associated with lower levels of vitamin B12. Similar studies to determine the drug utilization of antidiabetic s have been done in different regions with varied results like Lahiry et al [10] other studies also performed drug utilization with DDD/100 bed days was calculated by Abidi et al.[8]

Assessment of drug utilization based on pattern and class of antidiabetics

From the prescription pattern analysis of our study dual therapy was most common reported in 46% of the patients followed by monotherapy in 30% of the patients and more than 2 drugs were prescribed in 24%. Satpathy et al [11] performed similar study and results showed that combination antidiabetic drug therapy was more common than monotherapy. Polypharmacy in patients was reported by 67.17% of the patients by Abidi et al[8] and even higher polypharmacy of 85.3% by Gnanasegaran et al.[12] It is evident that the reason for polypharmacy in diabetes is for a better glycaemic control and combination therapy help in improving patient compliance.

Oral antidiabetic drugs use according to classes in our study showed biguanides to be the most common used antidiabetic group in 44.4% of monotherapy followed by biguanides + thiazolidinediones combination therapy which were encountered in 66% of the prescriptions. Overall utilization of metformin was the maximum in 83% prescriptions followed by glimepiride in 55.05% prescriptions.

The use of glimepiride as a common drug utilized amongst the sulfonylureas may be because of its long t1/2, stronger extra pancreatic action, lesser hyperinsulinemia and lower incidence of hypoglycaemia.[13] Drug utilization patterns of our study were similar to findings of other studies, Satpathy et al[11] according to which 48% of all patients were prescribed metformin and sulfonylureas, similar findings were found in Sultana G et al.[14] and Mandal et al.[15] This reflects that sulfonylurea and biguanides are still the choice of physicians for achieving adequate glycaemic control and are in line with the recommendations of the American Diabetes Association Standard of care guidelines 2019[16]

Conclusion

Drug utilization pattern of diabetic patients showed results similar to that of hypertensive patients with an average 5 drugs per prescription out of which on an average 2.18 drugs were for diabetes. The average daily prescribed dose of antidiabetics was under the defined daily dose (DDD) range prescribed by WHO which is indicative of a rational drug prescription pattern. Among the antidiabetic drugs prescribed, metformin 500mg was the most commonly prescribed drug in monotherapy while in combination therapy glimepiride 2mg + metformin 500mg was most commonly prescribed. The prescription showed adherence to most of the parameters of rational drug utilization. But lesser prescription drugs from the essential medicine list points towards the need to revise and update the national essential drug list. Another approach that could be considered is development of a personalized hospital essential medicine list and such data can be a significant contributor to determine the hospital requirements. This study also forms a base for a larger multicentric study and cater data from a larger population and throw light on current patterns of antidiabetic medication prescription.

Ethical Approval
The study was approved by the Institutional Ethics Committee

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