<u>Original Article</u>

A drug utilisation study of antihyperglycaemic agents in a rural tertiary care hospital

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ABSTRACT

Background: Diabetes mellitus is an emerging non communicable, life style disease. 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.

Materials and methods: A prospective observational study was carried out in adult diabetic patients from the Department of General Medicine of a rural tertiary care hospital in October 2013- December 2014 after obtaining written informed consent from the patient and approval from institutional ethics committee. Demographic data, drug utilization pattern, cost of the antidiabetic drugs along with defined daily dose was calculated. ADRs due to anti-diabetic drugs were summarized.

Results: A total of 450 patients were enrolled in the study of which there was male preponderance and majority belong to geriatric age. The most common comorbidity was hypertension. Insulin was most commonly prescribed drug during hospital stay and metformin at the time of discharge. Of the combination therapy dual therapy of metformin and glimipiride was most preferred. The total anti-hyperglycaemic drug consumption was 15.65 DDD/ 100 bed days. 67 ADR were reported of which the most common was hypoglycaemia.

Conclusions: The study showed insulin and metformin were the most commonly used drugs. The prescribing trend also appears to be moving towards combination therapy particularly two drug therapies. The most commonly reported ADR was hypoglycaemia.

Keywords: Drug utilization, anti-diabetic drugs, adverse drug reactions, DDD

Introduction

Diabetes is a chronic disorder defined as metabolic cum vascular syndrome of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both leading to changes in both small blood vessels (Microangiopathy) and large blood vessels (Macroangiopathy). Diabetes mellitus is the most common metabolic disorder in the world. According to the International Diabetes Federation 387 million people in the world live with diabetes as of 2014. [1] In most countries the number of individuals with diabetes is steadily increasing. According to WHO, around 31.7 million Indians are effected by diabetes by 2000 and it is estimated that it may increase to 79.4 million by 2030. [2]

Management of diabetes includes both pharmacological treatments like insulins and oral hypoglycaemic agents as well as non-pharmacological management like diet modification and life-style changes. The oral hypoglycaemic agents include sulfonylureas (glibenclamide), biguanides (metformin), thiazolidinediones (pioglitazone), alpha glucosidase inhibitors (acarbose), meglitinides (repaglinide), GLP-1 analogues (exenitide), DPP 4 inhibitors (sitagliptin), SGLT 2 inhibitors (dapaglifozin). [3] Drug utilisition is defined by WHO as "the marketing, distribution, prescription

and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences" (WHO, 1977). [4] These studies play a crucial role in making essential drug list, understanding current drug prescribing practices and also identifying irrational prescribing of drugs.

In this context the present study was undertaken to analyse the prescription pattern of antidiabetic agents during the hospital stay and at the time of discharge with relevance to economic burden and adverse drug monitoring in a tertiary care teaching hospital.

Material and methods

This prospective observational study was conducted over a period of 6 months in the inpatient department of General Medicine at Kamineni Institute of Medical Sciences, a tertiary care teaching hospital. The study was approved by the Institutional Ethics Committee. Informed consent was taken from the subjects prior to the study.

Patients of both sex and age ranging from 16 to 65 years were included in the study. Newly diagnosed and known cases of diabetes with co morbidities were also included in the study. Patients with gestational diabetes mellitus and type 1 diabetes mellitus were excluded from the study. Patient data was recorded in the standard case record form.

Cost of therapy was assessed using total cost of the antidiabetic drug per patient and expressed as mean ± SEM. Defined daily dose was calculated using the formula

DDD/100 bed days   =   Drug consumed(mg) during study period x 100
DDD(mg) x period of study x bed strength x average occupancy

Average occupancy was calculated by dividing number of occupied beds by total number of beds in medicine ward. 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, severe or lethal as per modified Hartwig scale. The causality assessment of ADRs was done as per Naranjo scale into definite, possible, probable and doubtful.

Results

Total enrolled patients were 450 of which 261(58%) are male and 189 (42%) are female. (Fig 1) Mean age of the patients was 62.8± 2.3 years. Comorbid conditions were found in 369 patients of which hypertension was most common. Other co-morbid conditions include diabetic nephropathy, diabetic neuropathy, acute urinary tract infections, respiratory tract infections, frozen shoulder and thyroid disorders (Fig 2). Average number of antidiabetic medicines per prescription according to WHO core drug prescribing indicators was 1.8 (Table 1). Drugs prescribed by generic name were only 12.2% and percentage of drugs prescribed from essential drug list was 78.3%.
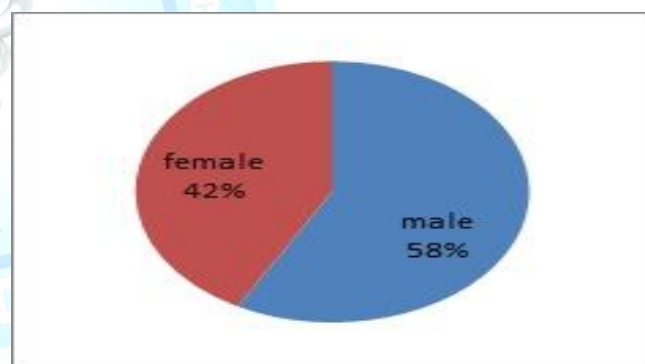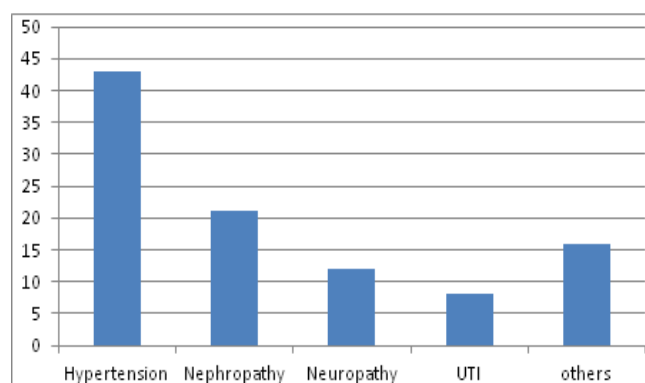

Fig 1: Sex distribution of the patients

Fig 2: Incidence of co-morbidities

Insulin was most commonly prescribed anti hyperglycaemic agent during the stay (76%) and

metformin was the most common at the time of discharge (82%) (Fig 3). Usuage of insulin was reduced by around 30% from hospital stay to the time of discharge and use of metformin has increased by 12% followed by glimipiride (8%). Of the insulins the most common prescribed form was combination of basal insulin and human insulin both during hospital stay and at discharge. Combination therapy of 2 drugs was most commonly prescribed of which metformin with glimiperide is more often given. Triple therapy was less preferred and most commonly added 3rd drug was insulin. 4 drug regimen was given to only 1 patient during hospital stay and to 6 patients while discharge. The drug added to 4 drug regimen was voglibose during hospital stay and sitagliptin during discharge.

The average cost, as expressed in mean ± SD, of anti-diabetic drugs during the hospital stay was Rs. 112.80 ± 34.58 and at the time of discharge was Rs.95.76 ± 54.32. Drug consumption was calculated in defined daily dose (DDD) per 100 bed days. The total drug consumption for anti hyperglycaemic agents was 15.65 DDD/100 bed days (Table 2). The highest DDD was for insulin which was 10.65 and the lowest was for sitagliptin which was not prescribed during hospital stay. The drugs were classified according to Anatomical therapeutic chemical classification and their DDD/100 bed days are tabulated below. During the study period, 67 subjects had adverse drug reaction of which the most common being hypoglycaemia(64). 1 developed loose stools and

2 patients developed flatulence. More females developed hypoglycaemia than males and is observed often in the age group of more than 65 years. Incidence was highest among diabetics with more than one co-morbidity. All reactions were mild/ moderate according to Hartwig scale. In the causality assessment according to Naranjo scale, all belong to probable category.

Table 1: WHO core prescribing indicators applicable to the study

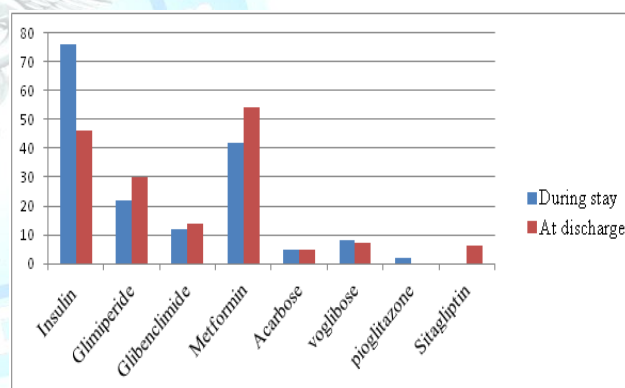| S.no.	Indicator	Value
1	Average number of anti diabetic drugs per encounter	1.8
2	Percentage of drugs prescribed by generic name	21.2%
3	Percentage of encounters with injection	80.8%
4	Percentage of drugs prescribed from essential drug list	78.3%.

Fig. 3 Prescription pattern of drugs at hospital stay and at discharge

Table 2: ATC classification and DDD of the drugs

S.No.	Drug	ATC classification	DDD/100 bed days
1	Insulin(regular)	A10AD01	10.65
2	Insulin(basal)		3.89
3	Metformin	A10BA02	0.87
4	Glimiperide	A10B12	0.54
5	Glibenclimide	A10BB01	0.21
6	Acarbose	A10BF01	0.06
7	Voglibose		0.12
8	Pioglitazone	A10BG03	0.01
9	Sitagliptin		0.00

Table 3: ADR relation with sex, age, co-morbid conditions and duration of diabetes

Characteristics	Number of patients	Patients with ADR
Sex		
Male	261	24
Female	189	43
Age		
More than 65 years	285	52
Less than 65 years	165	15
Co-morbidities		
1 co-morbidity	323	23
More than 1 co-morbidity	127	44
Duration of Diabetes		
Less than 5 years	221	18
More than 5 years	229	49

Discussion

Out of the 450 patients who are enrolled the majority are male and belong to geriatric age group showing male preponderance in diabetes. This is in comparison to other studies done in India. [5,6] The most common co-morbid condition was hypertension which is similar to study done by Abdi SH etal,2012 and Arauz-Pacheco etal,2002. [6,7]

The present study revealed that the most common drug to be prescribed at the time of discharge was metformin but during the stay was insulin. Average number of anti-Diabetic drugs 1.8 which is less than study done by Sultana G etal, 2010. [8] The percentage of diabetics receiving insulin during the hospital stay was higher than the study done by Sultana G etal, 2010[8] but less than Abdi SH etal, 2012. [6] The combination of metformin with glimipiride was most commonly used dual therapy according to the present study which was comparable to other studies. [9] In the study by Kumar et al, insulin + metformin (16.6%) was the most prescribed anti-diabetic combination followed by glimepiride + metformin (10%). [10] Though there were multiple newer drugs their use was restricted mainly due to higher cost and lack of data on prolonged usage.

The average cost of anti diabetic drugs during the hospital stay was Rs. 112.80 ± 34.58 and at the time of discharge was Rs.95.76 ± 54.32 for 450 patients according to DDD concept. DDD is assumed average maintenance dose per day for a drug used for its main indication in adults. Highest DDD was for regular insulin which was 10.65 and overall anti hyperglycaemic drugs was 15.65 DDD/ 100 beds.

During the present study, 67 adverse effects were reported in which there was female preponderance. Adverse effects were more common among geriatric age group and in subjects with multiple comorbidities. Duration of diabetes played a significant role in development of ADR as subjects having diabetes or more than 5 years are most commonly treated with dual or triple regimen leading to the adverse reaction of hypoglycaemia (Table 3).

Metformin was the most commonly used drug at discharge and insulin was the most common during the hospital stay. The trend towards dual therapy was increasing showing strict control of glycaemic status. The use of newer drugs was highly restricted. Incidence of ADR particularly hypoglycaemia was high among geriatrics and combination therapy patients.

References

1. IDF Diabetes Atlas. 6th ed. International Diabetes Federation, 2013. Available from: http://www.idf.org. Accessed on 10 october 2016.

2. Anjana RM, Pradeepa R, Deepa M, Datta M, Sudha V, Unnikrishnan R, et al. Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: phase I results of the Indian Council of Medical Research-India Diabetes (ICMR-INDIAB) study. Diabetologia 2011;54:3022-27.

3. Unger J. Current strategies for evaluating, monitoring, and treating type 2 diabetes mellitus. Am J Med 2008;121(6 Suppl):S3-8.

4. Lee D, Bergman U. Studies of drug utilization. In: Strom BL, editor. Pharmacoepidemiology. 4 ed. New York: John Wiley & Sons; 2005.p. 401.

5. Vengurlekar S, Shukhla P, Patidar P, Bafna R, Jain S. Prescribing pattern of anti-diabetic drugs in Indore city hospital. Indian J Pharm sci 2008;70:637-40.

6. Abdi SH, Churi S, Ravi Kumar YS. Study of drug utilization pattern of antihyperglycaemic agents in South Indian tertiary care teaching hospital. Indian J Pharmacol Sci 2102;44:210-14.

7. Arauz-Pacheco, Parrott MA, Raskin P. Treatment of hypertension in patients with diabetes. Diabetes care 2002;25:134-7.

8. Sultana G, Kapur P, Aqil M, Alam MS, Pillai KK. Drug utilisation of oral hypoglycaemic agents in university teaching hospitals in India. J Clin Pharm Ther 2010;35:267-77.

9. Lau GS, Chan JS, Chu PL, Tse DC, Critchely JA. Use of antidiabetic and anti hypertensive drugs in hospital and outpatient settings in Hong kong. Ann Pharmacother 1996;30:232-7.

10. Kumar KS, Sreeramya G, Krishna KM, Nalini K, Kiranmai N, Vasavi P. Drug use pattern study of antidiabetics in type 2 diabetes mellitus at a tertiary care hospital in Tenali, Andhra Pradesh. Int J Inv Pharm Sci 2013;1:162-6.