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Original Research Article

Pattern of anti-diabetic drugs prescribed for type 2 diabetes mellitus patients in a tertiary care hospital of India: an observational study

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a leading cause of significant morbidity and mortality in developing countries. Evaluation of anti-diabetic drug use pattern guides the healthcare professionals to identify early signals of irrational prescribing and to plan interventions to optimize the benefits of pharmacotherapy.
Methods: Observational descriptive study was conducted on 500 prescriptions of T2DM patients collected from Outpatient department of a tertiary care hospital. Prescriptions were analysed for type, number, generic/brand names, fixed dose combinations (FDCs) of anti-diabetic drugs and anti-diabetic drugs prescribed from within National List of Essential Medicines (NLEM) 2015.
Results: Average number of anti-diabetic drugs per prescription was 2.5. Of these 49% were from within NLEM and only 39% were prescribed by their generic names. Among all the anti-diabetic groups of drugs used, biguanide (32.85%) was the most frequently prescribed followed by insulins (25.4%) and DPP-4 inhibitors (13.75%). Combined drug therapy was more prevalent than monotherapy (70% versus 30%). Metformin+sitagliptin and metformin+linagliptin were most commonly prescribed fixed dose combinations.
Conclusions: Recent trend of anti-diabetic drug use included newer anti-diabetic drugs in combination with metformin to achieve better euglycemia and to minimize complications of T2DM.

Keywords: Diabetes mellitus type 2, Drug utilization, Prescription study

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the leading cause of significant morbidity and mortality in developing countries mainly due to its associated complications viz. coronary artery disease, peripheral vascular disease, stroke, retinopathy and nephropathy.[1] India has the largest number of diabetic patients amongst all the countries.[2] During the year 2000, around 31.7 million individuals were affected by diabetes which may further rise to 79.4 million by the year 2030 probably due to increased susceptibility to diabetes and increasing urbanization in India.[3] Lifestyle modification along with use of appropriate anti-diabetic drugs have pivotal role in achieving euglycemia and preventing complications.

Evaluation of anti-diabetic drug use pattern guides the healthcare professionals to identify early signals of the irrational prescribing and to plan interventions to optimize the benefits of pharmacotherapy.[4,5] Previous studies conducted in India reported that the use of metformin (27%-44%) and glimepiride (13%-24%) was frequent and

combination of multiple anti-diabetic drugs was more prevalent than monotherapy.[6,7] On the other hand, in developed countries the use of metformin (25%-32.8%) or sulfonylurea (18.9%-44%) was more prevalent as monotherapy; suggesting trend of using more combinations of anti-diabetic drugs in India.[8,9] An insight into the existing drug use pattern will help optimize the benefits of hypoglycemic agents by promoting rational prescribing including the use of generic medicines and prescribing from within the hospital drug formulary and National list of essential medicine (NLEM). Hence, this study was planned to find the pattern of anti-diabetic drugs prescribed for T2DM patients in tertiary care hospital.

METHODS

An observational cross-sectional study was conducted on 500 prescriptions of T2DM patients collected from Outpatient Department (OPD) of Internal Medicine, Lady Hardinge Medical College and associated Smt. Sucheta Kriplani Hospital. The study period was one year (from March 2014 to March 2015). The principal investigator visited the OPD on alternate days and collected prescription of every fourth diabetic patient. The inclusion criteria was the prescriptions of T2DM patients containing anti-diabetic medication with age above 18years. Prescriptions of patients not prescribed anti-diabetic drugs and pregnant patients were excluded from the study. Prescriptions were scrutinized for type, number, generic/brand names, fixed dose combinations (FDCs) of anti-diabetic drugs and anti-diabetic drugs prescribed from within National List of Essential Medicines (NLEM) 2015.[10] Individual drugs of fixed dose combinations were considered in their respective drug classes for the purpose of analysis. The relevant prescribing information was translated into customized data collection sheet. Study was done after the approval of Institutional Ethical Committee for Humans. The statistical package for Social Sciences® (SPSS, version 21) was used to analyse the data.

RESULTS

A total of 500 patients were recruited from Medicine OPD. Average age of the patients was 52.69±10.25 years (range 28 years-78 years) and mean duration of anti-diabetic treatment was 59.78±72.40 months (range 15 days-21 years) (Table 1). Median age of the patients was 53 (60-45) years and median duration of anti-diabetic treatment was 24 (96-4.25) months.

A total of 1236 anti-diabetic drugs with an average of 2.47±1.34 anti-diabetic drugs per prescription were prescribed. Almost half (48.7%) of all the anti-diabetic medicines were from within the NLEM, 482 (39%) medicines were prescribed by their generic names, 29.13% drugs were FDCs and 27.18% were administered as injectables.

A total of 178 FDCs were prescribed, 82 FDCs were for oral use and 96 FDCs were for parenteral use. Among the oral FDCs, metformin with sitagliptin was most commonly prescribed FDC (51%) followed by metformin and linagliptin (27%) and metformin and glimepiride (10%). Among the FDCs for parenteral administration, all contained insulins. FDCs of regular+NPH insulin and aspart+protamine aspart insulin were present in 52 and 44 prescriptions respectively.

Table 1: Demographic profile and biochemical parameters of the patients.

Parameters		No. (%)
Gender; N (%)	Females	318 (63.6)
	Males	182 (36.4)
Age in years (Mean±SD)		52.69±10.254
Smokers, N (%)		74 (14.8)
Duration of T2DM (Mean±SD); in months		59.78±72.40
FPG (Mean±SD); mg/dl		155.32±71.51
PPPG (Mean±SD); mg/dl		205.62±87.35
HbA1C (Mean±SD); %		08.39±2.42
SBP (Mean±SD); mmHg		132±19.99
DBP (Mean±SD); mmHg		81.8±10.36

Table 2: Description of classes of anti-diabetic drugs prescribed (N=1250).

Classes of anti-diabetic drugs	Anti-diabetic drugs	N (%)
Biguanide	Metformin	406 (32.85)
Insulins		318 (25.73)
	Regular insulin	136 (11.00)
	NPH insulin	54 (4.37)
	Aspart insulin	46 (3.72)
	protamine aspart insulin	44 (3.56)
	Degludec	30 (2.43)
	Detemir insulin	08 (0.65)
Dipeptidyl peptidase 4 inhibitors		170 (13.75)
	Sitagliptin	60 (4.85)
	Linagliptin	88 (7.12)
	Vildaglptin	22 (1.78)
Alpha glucosidase inhibitors	Voglibose	134 (10.84)
Thiazolidinediones	Pioglitazone	90 (7.28)
Sulphonylureas		84 (6.80)
	Glimepiride	78 (6.31)
	Gliclazide	4 (0.32)
	Glibenclamide	2 (0.16)
PPARα+γ agonists	Saroglitazar	18 (1.29)
GLP-1 receptor agonists	Liraglutide	6 (0.48)

Among all the anti-diabetic groups of drugs used, biguanide was the most frequently (32.85%) prescribed group of drugs followed by insulins (25.4%). Whereas, GLP-1 receptor agonists were least prescribed (Table 2).

The average dose of metformin and voglibose was 1618.23±498.33mg and 0.85±0.14 mg respectively (Table 3).

Table 3: Average daily doses of anti-diabetic drugs (Mean±SD).

Anti-diabetic drugs	Dose (mg)
Metformin	1618.23±498.33
Glimepiride	2.23±1.29
Glibenclamide	5± 0
Gliclazide	120±56.57
Pioglitazone	29.33±7.12
Sitagliptin	96.67±26.04
Vildagliptin	86.36±23.35
Linagliptin	4.94±0.38
Voglibose	0.85±0.14
Liraglutide	1.2±0
Saroglitazar	4±0

Table 4: Description of drugs prescribed in multiple drug therapies (N=350).

Drug combinations of anti-diabetics	N (%)
Two drug therapy	128 (36.57)
Metformin+Glimepiride	50 (39.06)
Regular insulin+NPH insulin	20 (15.62)
Others	58 (45.31)
Three drug therapy	112 (32.00)
Metformin+Linagliptin+ Voglibose	14 (12.50)
Metformin+Regular insulin+NPH insulin	14 (12.50)
Others	84 (75)
Four drug therapy	70 (20.00)
Metformin+Pioglitazone+Voglibose+Sitagliptin	12 (17.14)
Metformin+Voglibose+Linagliptin+ regular Insulin	10 (14.29)
Others	48 (68.57)
Five drug therapy	28 (8.00)
Metformin+Linagliptin+Voglibose+ Pioglitazone+Regular insulin	06 (21.43)
Others	22 (78.57)
Six drug therapy	10 (2.86)
Metformin+Pioglitazone+ Voglibose+Linagliptin+Insulin aspart+Insulin protamine aspart	04 (40.00)
Others	06 (60.00)
Seven drug therapy	02 (0.57)
Pioglitazone+Voglibose+Metformin+Sitagliptin+Insulin aspart+Insulin protamine aspart+Regular insulin	02 (100)

Majority (70%) of the prescriptions contained more than one anti-diabetic drugs, two drug therapy being most frequent (36.6%) (Table 4). Metformin and glimepiride were most commonly prescribed two drug combination whereas two patients received combination of 7 anti-diabetic drugs (Table 4). Whereas only 150 (30%) prescriptions contained single anti-diabetic drug and metformin (60%) was the most commonly prescribed drug. In four prescriptions, each pioglitazone and NPH insulin was prescribed as monotherapy.

DISCUSSION

Drug utilization studies facilitate the healthcare establishments to review existing drug use pattern which further help to identify bottle necks and develop solutions to delivery of appropriate pharmacotherapy.[11] Likewise, the appropriate use of anti-diabetic medicines may achieve euglycemia adequately to prevent T2DM related morbidity and mortality.

The mean age of the T2DM patients in this study was 52.69±10.25 years, which was lower than that reported in United States (60.1±14years) and Germany (67 years), suggesting that Indians manifest diabetes mellitus at an earlier age.[9,12,17, 13, 14]

In this study, the average number of anti-diabetic drugs per prescription was higher (2.5) as compared to other Indian studies where it varied between 1.4 to 2.2 per prescription.[13-15] The use of multiple anti-diabetic drugs per prescription could be due to high mean HbA1c levels of our study patients (8.39±2.42%). Though aforementioned studies did not document HbA1c levels, Yurgin et al, and Burgmann et al, reported the prevalence of monotherapy as patients had better glycemic control (6.9% and 7.66% respectively).[9,16]

In our study, 49% of anti-diabetic drugs were from within NLEM. In an earlier study, Agarwal et al reported higher (67%) proportion of anti-diabetic drugs from NLEM.[14] Though only 39% of the anti-diabetic drugs were generic versions, it was higher than that reported by other Indian studies (ranging from 0 to 4%).[13,14] Strict implementations of the NLEM and hospital drug formulary as well as increasing awareness among prescribers may further improve the generic prescribing and use of drugs from within the NLEM. The generic medicines are cheaper and therapeutically equivalent option hence their prescribing should be promoted.[17]

The most commonly prescribed anti-diabetic drug in our study was metformin, which has also been found to be most prescribed drug in many previous studies.[8,11,13,15,18] Metformin is included in most local hospital drug formularies as it has a favourable safety profile and efficacy as monotherapy and also in combination regimens.[19] Though liraglutide (a GLP-1 receptor agonist) use was only 0.48% of total anti-diabetic drugs prescribed, it was similar (0.5%) to another Indian study.[15] The lower use of GLP-1 receptor agonists in this study could be due to their higher cost[20] and need for parenteral administration. The average dose of all the anti-diabetic

drugs prescribed in our study was with in respective therapeutic range.

In this study, the use of DPP 4 inhibitors (viz. sitagliptin, linagliptin and vildagliptin) was higher (14%) than that reported by Khalam et al, (6.6%) and Alex et al, (9.5%) in India. Similar rising trend in their use was observed in a study from Southern Italy.[15,21,22]

The higher use of DPP 4 inhibitors may be justified as they effectively lower blood glucose levels in Asians despite being costly medicines and not listed in the NLEM, local hospital drug formulary and Indian Council of Medical Research (ICMR) guidelines to treat T2DM in Indian patients.[23,20] In addition, DPP 4 inhibitors improve cardiovascular risk factors and β-cell function.[20]

In this study, combinations of two and more anti-diabetic drugs were higher than monotherapy; this finding was consistent with the observation of other researchers.[11,13,15,22] In congruence with previous studies biguanides and sulphonylureas were most commonly used two drug combinations (Table 4).[11,13,24]

As the T2DM progresses, function of beta cells deteriorates which necessitates the need for combination therapy to achieve additive euglycemic control at lower doses of individual drugs. Various guidelines to treat T2DM viz, ICMR and International Diabetes Federation recommend the use of multiple anti-diabetic agents in case of inadequate glycemic control with metformin monotherapy.[25,26]

Among the fixed dose combinations of oral anti-hyperglycemic drugs, metformin+sitagliptin and metformin+linagliptin were most commonly prescribed in this study. In contrast, metformin+glimepiride and metformin+glibenclamide were commonly used FDCs in another Indian cross sectional study.[7]

This reflected reduction in the use of sulfonylureas as they are associated with risk of hypoglycemia and weight gain. NLEM does not mention FDCs of anti-diabetic drugs such as metformin+sitagliptin, metformin+linagliptin and metformin+glimepiride, though they improve treatment compliance and reduce pill burden.[10]

CONCLUSION

The prescribing trend of anti-diabetic drugs appears to be moving towards combination therapy and use of newer drugs is becoming prevalent. In light of availability of newer anti-diabetic drugs, there exists a need to review and modify NLEM and local T2DM treatment guidelines to achieve better glycaemic control.

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