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A study on prescribing pattern and potential drug-drug interactions in type 2 diabetes mellitus (inpatients) in a tertiary care teaching hospital

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ABSTRACT

The objective of this study was to evaluate prescribing pattern and potential drug-drug interaction in hospitalized patients with type 2 diabetes mellitus. A prospective, observational study was carried out at inpatient department of SRM medical college hospital and research centre kanchipuram district, Tamilnadu, India from July 2010 to February 2011. The demographic, disease and treatment data of patients with type 2 diabetes mellitus were collected in a specially designed proforma. Data of 142 patients were collected and analyzed, of which 69 (48.6 %) were males and 73 (51.4 %) were females. Mean ± SD of drugs per prescription was 6.1±2.3. 63.57% of the drugs were prescribed by their brand names. 45% of the drugs prescribed were from the WHO list of essential drugs. In type 2 diabetes mellitus metformin and human insulin were most frequently prescribed drugs. Monotherapy was used for 58.9% patients and 41.1% patients were prescribed with combination therapy. 65 potential drug-drug interaction were screened in 53 prescriptions, in which 3(4.6%) were major and 27(41.5%) were moderate level of severity identified. The potential drug-drug interactions found in type 2 diabetes mellitus prescriptions were often involved with medications used to treat co morbid illnesses. The potential drug-drug interactions are frequent in type 2 diabetes mellitus and hence deserve clinical attention. Implementation of an alert guidelines and a computer based screening would help to recognize and prevent potentially dangerous drug-drug interactions.

Keywords: Diabetes Mellitus, Potential drug-drug interaction, Prescribing pattern.

INTRODUCTION

Diabetes mellitus is an elevated blood glucose associated with absent or inadequate pancreatic insulin secretion, with or without concurrent impairment of insulin action [1]. According to the diabetes atlas published by the International Diabetes Federation (IDF), there is an estimated 40 million persons with diabetes in India in 2007 and this number is predicted to rise to almost 70 million people in 2025 [2]. The study of prescribing pattern is a component of medical audit that does monitoring and evaluation of the prescribing practice of the prescribers as well as recommends necessary modifications to achieve rational and cost-effective medical care and it

help to evaluate and suggest modifications in prescribing practices of medical practitioners so as to make medical care rational [3]. Reviewing prescribing patterns could provide feedback to prescribers and assures quality medical care. This study also attempts to analyze the current prescription patterns of drugs used in the treatment of type 2 diabetes mellitus patients. The findings of this study are expected to provide relevant and useful feedback to physicians.

The diabetes mellitus patients are generally treated with many pharmacological agents. In addition to the blood glucose control, treatment of concurrent illnesses and cardiovascular protective agents generally leads to polypharmacy and the chance to drug related problems in the prescriptions [4]. Drug-drug interaction is among the major drug related problems. A drug interaction is said to occur when the effect of one drug is changed by the presence of another drug, food, or by some environmental chemical agent [5]. A potential drug-drug interaction is an event that is likely to develop if pharmacists do not make any appropriate intervention. Drug-drug interactions pose significant challenge to health care providers and may affect morbidity, mortality and a patient's quality of life. In this present study we have sought to analyze the prescription trend and the potential drug-drug interactions in type 2 diabetes mellitus patients.

MATERIALS AND METHODS

Study design: A prospective observational study.

Study site: SRM medical college hospital and research centre, Kattankulathur, Kanchipuram district, Tamil Nadu.

Study period: The study was conducted during a period of 8 months from July 2010 to Feb 2011.

Inclusion criteria:

- Patients of both genders
- Patients diagnosed with type 2 diabetes mellitus
- Patients with or without concurrent illnesses
- Inpatients
- Patients of all ages.
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Exclusion criteria:

- Type 1 diabetes mellitus
- Outpatients

Level	Description
Severity	
1	Major: a severe adverse effect.
2	Moderate: an adverse effect can harm and treatment is required.
3	Small or no clinical effect, no treatment is required.
Scientific evidence	
1	Established: adverse effect confirmed by large clinical trials.
2	Probable: adverse effect with high likelihood of occurrence but without definitive randomized clinical trials.
3	Suspect: Adverse effect likely to occur, data derived from case reports.
4	Possible: Adverse effects may occur but data are scare.
5	Unlikely: Adverse effects may theoretically occur.

Patients' demographic, disease and prescription details were collected in a specially designed proforma. Drugs were classified into different groups according to the ATC classification of WHO's collaborating Centre for Drugs Statistics methodology for the prescription pattern analysis [6].

Potential drug-drug interactions were screened by using text books and journal references and the drug interaction facts software version 4.0. The statistical analysis is done by using SPSS version 17. The screened interaction is then classified based on severity and the level of scientific evidence [7]. Potential drug-drug interactions with scientific evidence level more than 3 are not considered in this study.

RESULTS

Table 1: prescription details in diabetes mellitus patients

DETAILS OF PRESCRIPTION	NUMBER (%)
Total number of prescription analyzed	142
Total number of drugs prescribed	925
Average number of drugs per prescription	6.51±2.3
Number of drugs from WHO essential drug list out of total number of drugs prescribed	446(48.21)
Number of drugs prescribed by generic name out of total number of drugs prescribed	135(14.59)
Number of fixed dose combinations out of total number of drugs prescribed.	111(12.0)
Number of injections out of total number of drugs prescribed	251(27.13)
Total number of antidiabetics out of total number of drugs prescribed	208(22.48)
Mean age of patients in years	54.93±5.48

Table 2: age wise sex distribution

AGE (IN YEARS)	MALE (N=69)	PERCENTAGE %	FEMALE (N=73)	PERCENTAGE %
0 – 20a	0	0	0	0
21 – 40	8	11.60	8	10.96
41 – 60	37	53.62	42	57.53
61 – 80	23	33.3	18	27.3
81 – 100	1	1.5	3	4.1

Table 3: distribution of concurrent illnesses

CONCURRENT DISEASE	NUMBER OF PATIENTS	PERCENTAGE (%)
Cardiovascular disorders	51	35.9
Renal disorders	14	19.9
Infectious diseases	17	24.1
Pulmonary diseases	20	28.4
Neurological disorders	9	12.8
Musculoskeletal and joint disorders	10	14.2
Gastrointestinal disorders	3	2.1
Diabetic foot ulcer	9	6.3

Data of 142 patients were collected and analyzed, of which 69(48.6 %) were males and 73 (51.4 %) were females. These patients were further categorized based on their age (Table 2). 16 patientas (11.26 %) belonged to the age group 21 - 40 years, 79 (55.63 %) to the age group 41 - 60 years, 41 (28.87%) to the age group 61 – 80 years and 4 (2.81%) to the age group 81 – 100 years. 69 (48.59%) patients out of 142 patients studied were found suffering from Concurrent illnesses. Distribution of concurrent illnesses is described (Table 3), 51 (35.9%) patients were

found to cardiovascular disorder, 20 (28.4%) were with pulmonary disease, 17 (24.1%) were with infectious disease and 14 (19.9%) with renal disorder.

Table 4: incidence of polypharmacy

NUMBER OF DRUGS	NUMBER OF PRESCRIPTION (N=142)	PERCENTAGE (%)
1	0	0
2	4	2.81
3	7	4.92
4	14	9.85
5	21	14.7
6	34	23.9
7	19	13.3
8	16	11.26
9	10	7.04
≥10	15	10.54

The number of drugs per prescription is shown in Table 4. The average number of drugs per prescription was 6.51±2.3. All prescriptions contained more than one drug, 17.6% of prescriptions contain 2 to 4 drugs, 71.13% of prescriptions contain 5 to 9 drugs, and 10.54 % of prescriptions contain 10 or more drugs. In research studies, it is stated that polypharmacy is defined as the concomitant use of five or more drugs [8].

Table 5: distribution of drugs in generic and brand name

PRESCRIPTION ITEM N = 925	NUMBER OF DRUGS (%)
Generic name	135 (14.59)
Brand name	787 (85.08)

Table 6: distribution of drug in essential drug list

PRESCRIPTION ITEM N = 925	NUMBER OF DRUGS (%)
Drugs from essential drug list	446 (48.21)
Drugs out of essential drug list	479 (51.78)

Table 7: distribution of single and fixed drug combinations

PRESCRIPTION ITEM n= 925	**NUMBER OF DRUGS (%)**
Single drug	814 (88.0)
Fixed drug combination	111 (12.0)

The prescription trend were analyzed, table 5 reveals, out of 925 drugs prescribed to the type 2 diabetes mellitus inpatients, 787 drugs (85.08%) were prescribed by their brand names, table 6 state that 48.21% (446) were prescribed from WHO essential drug list [10] and table 7 indicates the distribution of single drug and fixed drug combination were 814(88%) and 111 (12%).

Table 8 describes the distribution of drugs based on ATC classes [6]. Drugs from the alimentary tract and metabolism constitute 39.89% of the prescribed drug followed by cardiovascular drugs 20.0% and anti-infective for systemic use is 12.1%.

Table 8: distribution of drugs in different categories based on atc classification prescribed in type 2 diabetes mellitus

ANATOMICAL THERAPEUTIC CHEMICAL GROUPS	MEDICATIONS n=925 n (%)	PATIENTS n=142 n (%)
A Alimentary tract and metabolism		
Drugs used in diabetes	206 (22.27)	142(100)
Other drugs	163 (17.62)	82 (57.7)
B Blood and blood forming organs	64 (6.91)	42 (29.6)
C Cardiovascular system	185 (20.0)	94 (66.2)
D Dermatological	4 (0.43)	3 (2.1)
J Antiinfectives for systemic use	112 (12.1)	82 (57.7)
M Musculoskeletal system	13 (1.4)	11 (7.7)
N Nervous system		
Analgesics and antipyretics	43 (4.64)	43 (30.3)
Other nervous system drugs	37 (4.0)	36 (23.9)
R Respiratory system	78 (8.43)	34 (23.9)
V Various others	9 (0.97)	8 (5.6)

Table 9: drug utilization pattern of anti diabetic drugs

DRUG	TOTAL NUMBERS IN PRESCRIPTIONS(%)	
Monothorapy		
Biguanides (Metformin)		23 (14.1)
Sulfonylureas :glimepride	15	
glipizide	12	(26.99)
glibenclamide	9	
pioglitazone	8	
Alpha-glucosidase inhibitors (Voglibose)		1(0.61)
Insulin: Human insulin (short acting)	12	
Human insulin (long acting)	10	(17.18)
Human insulin (Mixtures)	5	
Analogue mixtures	1	
Combination therpy		
Metformin + Glibenclamide		9 (5.52)
Metformin +Glimepride		3 (1.84)
Human insulin (short acting + long acting)		23 (14.11)
Metformin + Human insulin		26 (15.95)
Glimepride + Human insulin		69 (3.68)

The pattern of antidiabetic drug utilization was studied (Table 9). A total of 208 antidiabetic medications were prescribed. 58.9% of patients were on monotherapy and 41.1% were on combination therapy for diabetic control. In monotherapy the most prescribed drug was sulfonylureas (26.99%) followed by insulin (17.18%) and metformin (14.1%). The most prescribed combination therapy was metformin+insulin (15.59%), followed by insulin combinations (14.11%) and metformin+glibenclamide(5.52%).

Table 10: distribution of potential drug-drug interaction

DRUG PAIR	LEVEL OF SEVERITY	LEVEL OF SCIENTIFIC EVIDENCE	MECHANISM	FREQUENCY
Atorvastatin-Clopidogrel	moderate	3	pharmacokinetic	8
ACE inhibitors-Aspirin	moderate	2	pharmacodynamic	6
Digoxin-Atorvastatin	moderate	3	unknown	1
Digoxin-Furosemide	moderate	1	pharmacokinetic	1
Phenitoin-Isoniazid	moderate	2	pharmacokinetic	1
Thiazide-Insulin	moderate	2	pharmacodynamic	2
Aspirin-Enoxaparin	moderate	3	pharmacodynamic	1
Calcium sup-Ferrous sup	moderate	2	pharmacokinetic	2
Aminoglycoside-Cephalosporin	moderate	3	unknown	2
Methotrixate-Salicylae	sever	2	pharmacokinetic	1
Methotrixate-Penicillins	sever	2	pharmacokinetic	1
Gentamycin-Torsemide	sever	1	pharmacodynamic	1
Ca channel blocker- Ca sup	moderate	3	pharmacokinetic	4
Insulin - Timolol	moderate	3	Unknown	1

Table 11: severity of potential drug interaction

SEVERITY OF POTENTIAL DRUG INTERACTION N = 65	NUMBER OF DRUGS (%)
Major	3 (4.6)
Moderate	27 (41.5)
Minor	35 (53.9)

Table 12: mechanism of potential drug interaction

MECHANISM N = 65	NUMBER OF DRUGS (%)
Pharmacokinetic	39 (60.0)
Pharmacodynamic	17 (26.1)
Unknown	9 (13.9)

Potential drug-drug interactions identified from the prescription were listed in table 10. The most frequently occurred were those with the atorvastatin and clopidogrel, ACE inhibitors and aspirin followed by Calcium channel blocker and Calcium supplement. 4.6% of the potential interactions were having a major and 41.5% having a moderate severity (Table 11). 60% of the potential interactions were the pharmacokinetic while 26.1% were pharmacodynamic mechanism (Table 12).

DISCUSSION

In this study we found the general prescription trend in diabetes mellitus patients; physicians prefer the well established compounds. The low percentage of generic drug reveals the hospital norm, is prescribing by brand name. The major co morbidity with diabetes mellitus was found to have systemic hypertension and the cardiovascular drug was the most prescribed class after antidiabetes medications. Average number of drugs per prescription (6.58) indicates the incidence of poly pharmacy, and in most cases it was unavoidable. Potential drug-drug interactions were found in type 2 diabetes prescriptions are often involved with medications to treat co morbid illness. This is of vital importance given that polypharmacy requires justification because of the increased risk of drug interactions and errors of prescribing [9].

CONCLUSION

The potential drug-drug interactions are frequent in type 2 diabetes mellitus and some of them deserve clinical attention. Implementation of an alert guidelines and a computer based screening would help to recognize and prevent potentially dangerous drug interactions

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