ORIGINAL ARTICLE

Pattern of Antidiabetic Drugs used in Outpatient and Hospitalized Patients in a Tertiary Health Institute of Central India

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Abstract

Introduction: *Diabetes mellitus (DM) is emerging as major health problem. There has been worldwide increase in prevalence of DM, especially in developing countries. With this increased prevalence of diabetes, drug utilization study of antidiabetic drugs is very useful from health care viewpoint.* ***Objective:*** *To study prescribing pattern of antidiabetic drugs used in outpatient and hospitalized patients and correlate association of diabetes with demographic details of patients.* ***Methodology:*** *After ethical approval, a cross sectional study was conducted. The prescriptions of patients of diabetic mellitus with or without co-morbidity were collected and analyzed.* ***Results:*** *Prescriptions of diabetic patients (n=300) including outdoor patients (n=150) and indoor patents (n=150) were noted. Metformin (69.33%) was the most prescribed drug followed by glimepiride (35.00 %). Prescriptions of Insulin alone were 26.70% and 30.66% in combination with oral antidiabetic drugs. Hypertension was found in association with DM in 52.33 % of cases. As per WHO prescribing indicator drug prescription by generic name were only 3.12% and mean number of drug per prescription was 4.57± 1.49.* ***Conclusion:*** *This cross sectional study of prescribing pattern of antidiabetic drugs showed metformin as the most commonly prescribed antidiabetic drug followed by glimepiride. All insulin preparations were human insulins. Hypertension was most common associated co-morbidity.*

Key words: *Anti diabetic drugs, diabetes mellitus, drug utilization study*

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Introduction

Presently drug utilization studies are evolving area. Scope of drug utilization studies is to evaluate the present state and future trends of drug usage. Drug utilization studies aim to evaluate factors related to the prescribing, dispensing, administering and taking of medication and its associated events.[1] According to the World Health Organization (WHO) drug utilization is defined as the marketing, distribution, prescription and use of drugs in a society, considering its consequences, either medical, social and economical.[2] The study of prescribing pattern is a component of medical audit that monitors and evaluates prescribing practices, and recommends necessary modifications to achieve rational drug use.[3]

Diabetes mellitus (DM) is a chronic disorder emerging as major health problem; this increases the rate of morbidity and mortality. [4] Diabetes is also a major risk factor for cardiovascular disease, stroke, and kidney failure. [5] There has been worldwide increase in prevalence of DM, especially in developing countries. The prevalence of diabetes for all age groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. [6,7] As per WHO, around 31.7 million individuals in India were affected by diabetes during the year 2000 which may further rise to 79.4 million by the year 2030.[8] In India onset of diabetes is about a decade earlier than their western counterparts. [9] Drug utilization studies can provide useful insight into the prescribing patterns and patient

medication taking behavior. [10] Hence present project was designed to study pattern of antidiabetic drug use in out patients and hospitalized patients of tertiary health institute of central India.

Objectives

The objective of the work was to study prescribing pattern of antidiabetic drugs used in outpatient and hospitalized patients of tertiary health institute of central India and to correlate association of diabetes with demographic details of patients.

Materials and Methods

Before the study was initiated, approval of the study was obtained from Institutional Ethics Committee. From January 2013 to December 2013, a cross sectional study was conducted to see prescribing pattern of antidiabetic drugs used in outpatient and hospitalized patients of NKP Salve Institute of Medical Sciences and Research Center, Nagpur. In this study prescriptions of patients who were diagnosed with DM with or without co-morbidity were included.

For hospitalized patients, data was obtained from the case record forms of medical record section. Data of OPD prescriptions was collected from the OPD of department of medicine. Drugs prescribed mainly for DM and other co-morbidities were noted. Details of drugs like name of drug, its dose, route of administration, frequency, and duration of administration were noted. Age and gender of the patients were also noted. Mean ±SD and percentage of variable were calculated using MS Excel.

Results

Prescriptions of diabetic patients (n=300) including outdoor patients (n=150) and indoor patents (n=150) were noted. Out of which 135(45%) were female and 165 (55%) were male. Most commonly affected age group was in between 60 to 69 years 142 (47.33%) followed by 50 to 59 years age group 92 (30.66%) table-1. Among all DM patients (n=300), 10 (3.33%) patients were of type 1 (juvenile DM) and remaining 290 (96.66%) were of type 2 (maturity onset) diabetes.

Table -1: Age wise distribution of Diabetes Mellitus

Age	OPD	%	IPD	%	Total	%
<39	0	0	23	15.3	23	7.7
40-49	8	5.3	28	18.7	36	12
50-59	57	38	35	23.3	92	30.7
60-69	79	52.7	63	42	142	47.3
>70	6	4.0	1	0.7	7	2.3
	150		150		300	

Out of total 300 patients, 243 patients had associated co-morbidities like hypertension, coronary artery disease, cerebrovascular events, hypothyroidism, surgical cases etc. Remaining were plain diabetic patients with or without associated diabetic complications (uncontrolled diabetes, diabetic ketoacidosis). Hypertension was common co-morbidity associated with DM (52.33%) table- 2.

Table- 2: Prevalence of co-morbidities in DM (n=300)

Co-morbidity	OPD	%	IPD	%	Total %
Hypertension	89	59.3	68	45.3	52.3
Surgeries/ Infections/ Chronic Obstructive Pulmonary Diseases	0	0	56	37.3	18.7
Hyperlipidemia	30	20.0	18	12.0	16.0
Ketoacidosis/Uncontrolled Diabetes Mellitus	0	0	37	24.7	12.3
Ischemic Heart Disease	17	11.3	19	12.7	12.0
Upper Respiratory Tract Infections/ Fever	13	8.7	0	0	4.3
Hypothyroidism	8	5.3	6	4.0	4.7
Cerebrovascular Episodes	0	0	7	4.7	2.3

Antidiabetic agents prescribed were injectable agents (different types of insulin) and oral antidiabetic drugs of different groups; sulfonylureas, biguanides, thiozolidionediones, α- glucosidase inhibitor and GLP (glucogan like peptide-1) analogues (di peptidyl peptidase-4 inhibitors). All prescribed insulin preparations were human insulin. Most commonly prescribed antidiabetic drug was metformin 69.33% (121=80.66% OPD cases and 87=58% IPD cases) followed by Glimepiride which was prescribed to 35% (45=30% OPD cases and 60=40% IPD cases) table-3.

Table -3: Anti-diabetic drugs prescribed in OPD and IPD (n=300)

Drugs	OPD	%	IPD	%	Total %
Metformin	121	80.66	87	58.00	69.33
Glimepiride	45	30.00	60	40.00	35.00
Glipizide	9	6.00	12	8.00	7.00
Gliclazide	0	0	4	2.66	1.33
Metformin+ Glimepiride	34	22.66	15	10.00	16.33
Voglibose	31	20.66	0	0	10.33
Pioglitazone	11	7.33	5	3.33	5.33
Sitagliptin	5	3.33	0	0	1.66
Short acting (Inj Actrapid, HAI)	21	14.00	83	55.33	34.66
Intermediate acting (Inj Isulatard)	11	7.33	26	17.33	12.33
Premix-(Inj Lupisulin)	13	8.66	19	12.66	10.66
Insulin+ Oral Hypoglycemic Agents	31	20.66	61	40.66	30.66

WHO prescribing indicator [11]

- Percentage of drug prescription by generic name: only 3.12% prescriptions were found with generic name while in remaining 96.78% prescriptions drugs were prescribed by brand name.
- Average number of drugs per prescription: mean number of drugs per prescription (MND) was 4.57± 1.49 **(**OPD: 3.15± 1.30 and IPD: 6±1.67)
- Drugs from essential drug list: insulins (regular, intermediate), metformin, gliclazide, enalapril ,atorvastatin.

Discussion

To tackle epidemic of diabetes mellitus globally there has been development of a wide range of armamentarium of treatment options for diabetes, which provides additional tools for clinicians. The primary objective of management in diabetic patient is to achieve glycemic control and prevent complications associated with uncontrolled blood glucose level. However treatment decisions are influenced by age, life expectancy, co-morbid conditions and severity of vascular complications. [12]

In present study metformin, which belongs to biguanides group was most frequently (69.33%) prescribed drug, either as monotherapy (41.38%) or in combination with other antidiabetic drugs (34%), followed by glimepiride (35%) that belongs to sulfonylurea group. This prescribing pattern is according to guidelines of American Diabetes Association. They recommend that metformin should be started along with lifestyle changes at the time of diagnosis. [4]

In late 1990 sulfonylurea was the most frequently prescribed drug.[13] However prescribing trends have been changing as most of recent studies conducted in different parts of world showed metformin as most prescribed drug in diabetic patients.[14,15, 16, 17] Results of present study are in agreement with it. Metformin is well established safe drug over the period of use. Metformin has a many advantages like beneficial effect on cardiovascular risk factor and it does not promote weight gain.

Metformin improves lipid profile. Metformin can delay progression of diabetes and prevents microvascular as well as macrovascular complications. It reduces insulin resistance, is unlikely to induce hypoglycaemia and may have a positive influence on pancreatic β cell. It can be combined with any other oral or injectable antidiabetic, if required. [18, 19]

Being more potent and clinically superior than first generation, only second generation sulphonylureas are used now.[19] Glibenclamide and glimepiride are the second generation sulphonylureas most widely used in the united sates.[20] In present study it was noticed that second generation sulphonylureas glimepiride (35%) and glipizide (7%) were most commonly prescribed. Advantage of lower incidence of hypoglycemia might be reason for recommendation of glimepiride and glipizide among second generation sulphonylureas. [21]

Several studies showed that a combination of sulfonylurea with metformin has been most widely used. [22] In the present study prescriptions of combination of sulfonylurea and metformin as fixed drug or separately were detected in 16.33% cases. Co-prescription of a biguanides and sulfonylurea is a common practice. [23]

Adding a second agent is usually better than increasing the dosage of an agent that has already been given in a nearly maximum dosage. In some patients three drug combinations may be useful. [12] It was observed that addition of pioglitazone (5.33%) was associated with two or three oral antidiabetic drugs. Glitazones tends to reverse insulin resistance. In addition it lowers serum triglyceride level and raises HDL. Pioglitazone is primarily used to supplement sulphonylureas/ metformin and in cases of insulin resistance. [18]

In the present study among glitazones only pioglitazone was prescribed in few OPD and indoor patients. Fewer prescriptions of glitazones indicate awareness among clinician about recent news of bladder cancer associated with pioglitazone. [24]

Prescription of voglibose (α-glucosidase inhibitor) was noted in 10.39% of patients. Voglibose is a mild antihyperglycaemic and not hypoglycemic. It is helpful in reduction of post prandial glycaemia without significant increase in insulin level. In diabetics it reduces cardiovascular events. [19]

Addition of di peptidyl peptidase-4 (DPP-4) inhibitor sitagliptin (1.66%) in prescription indicates that it has emerged as important adjuvant drug in type 2 DM. It is competitive and selective DPP-4 inhibitor which potentiates the action of GLP-1(glucagon like peptide-1) and GIP (glucose dependent insulinotropic peptide), increases post prandial insulin release, decreases glucagon secretion and lowers blood glucose in type 2 DM. It carries very low risk of hypoglycaemia at individual level and has no effect on body weight, appetite, gastric emptying. [25]

In most patients, the failure of three oral agents used together calls for the use of insulin alone (26.70%) or in addition to oral agents (30.66 %). Results of various studies have shown that a combination of insulin and sulphonylurea is more effective than insulin alone in treatment of patients with type 2 DM after secondary failure to oral drugs, leading to better glucose profile and decreased insulin need. [26,27]

Sulphonylureas are known to promote insulin secretion in response to glucose while insulin therapy supplements endogenous insulin, thus the combination of the two agents provides an additive effect thus increasing insulin levels.

Increase in utilization of insulin was recorded in majority of the patients due to presence of co-morbid conditions or resistance to oral hypoglycemic drugs. [23] This justifies higher use of short acting insulin (55.33%) in hospitalized patients in present study. Even use of insulin in maturity onset diabetic patients is justified because they have depleted insulin reserve. Oral antidiabetic agents in such cases may not suffice and insulin therapy need to be instituted for replacement. The rationale for using insulin in combination with metformin is that combing insulin with an agent that is known to sensitize the liver to the action of insulin is at least additive or may be synergistic action in controlling blood sugar level. [27]

In the present study hypertension was most common co morbidity associated with DM (52.33%). Among hypertensive patients maximum prescription of ACEI/ARB (Angiotensin Converting Enzyme Inhibitor/ Angiotensin Receptor Blocker) was found (62 %) followed by calcium channel blocker (35%).

Rationale behind preference of ACEI in prescription is its role in suppressing the development and progression of diabetic nephropathy and macro and microvascular complications. [18, 19, 25] Thus choice of ACEI as antihypertensive in diabetic patients is justified.

Prescriptions of gabapentin or pregabalin in 29.8% of indoor and 4% of OPD patients were found in this study. Diabetes is one of the common causes of neuropathy. Diabetic neuropathy causes refractory diabetic ulcers and wounds in the patients. Diabetic neuropathy is common in patients who have poorly controlled blood glucose, have hypertension and are obese. Gabapentin is known to improve pain and paresthesia associated with diabetic neuropathy. [28]

Diabetes is now commonly recognized equivalent to the coronary heart disease. This is mainly attributed to the high rates of dyslipidemia among diabetic patients, which is accounting for high percentage of deaths among diabetics due to cardiovascular diseases. [29] In this study use of atorvastatin was found in 30% of OPD prescription. Guidelines recommend that statin therapy be added to lifestyle therapy, irrespective of baseline lipid levels for diabetic patients. [30] Regardless of clinicians' awareness about guidelines, reason for not having statin in every prescription might be either patient's lipid levels were normal or to avoid side effects and drug interactions of multiple drug therapy as well as considering cost of additional drug.

In the present study, out of total 300 patients, 135 were female and 165 were male. Male domination in the study population is in agreement with the results of another study in India. [23] Mean age ±SD of patients in present study was 57.47 ± 9.65 years within a range between 13 years to 72 years. Study conducted in Malaysia showed 52.60% diabetic patients were in between 30 and 50 years of age. [31] In present study highest number of patients were between ages 60-69 (47.33%) followed by 30.66% in 50-59 range. This data has similarity with the study conducted in Nepal. [17] Range of age correlates with the data given by WHO that in developing country maximum diabetes patients are found between 35-74 years of age. It indicates that the majority of the patients develop diabetes in the most productive years of their life. Hence it may frequently affect the quality of lives of patients as well as family members.[32] An implication of having disease at this period of life is often associated with loss of productivity causing socio- economic and psychological setback.[17]

The average or mean number of drugs per prescription is an important index for review. Polypharmacy is defined as prescription of five or more medications to one patient at one time. [33] Keeping in mind possibility and increased risk of drug interactions and errors of prescribing, higher number of drugs always needs to be justified. Higher number of drugs indicates irrational prescribing practice. Mean number of drugs per prescription (MND) of diabetes patients in this study was 4.57 ± 1.49 (OPD: 3.15± 1.30 and IPD: 6± 1.67). Another study conducted in Nepal showed similar results. [34] The reason for higher MND in hospitalized patients might be to achieve adequate glycemic goal, as well as associated with co morbidities, for that use of two or three antidiabetic agents is justified.

According to WHO, essential drugs are defined as 'those that satisfy the priority healthcare needs of majority of population, available at all times and in adequate amounts, in appropriate dosage forms, with assured quality and at affordable cost to individual and community'. Essential drugs are selected on the basis of public health relevance, evidence on efficacy and safety and cost. Adoption of essential medicine list has resulted in improved availability of medicine, with economic range and more rational use of drugs. [35] In present study drug from essential list were insulins (regular, intermediate), metformin, gliclazide, enalapril, atorvastatin. It is not necessary that drugs which are not included in essential drugs list are non essential drugs.

Generic names were mentioned in very few indoor prescriptions (3.12%). False notion among prescribers that generic medicines are of inferior quality might be reason for prescribing by brand name. Advantage of prescribing drugs by their generic names is that it will definitely help in reducing cost of drugs. Also it will be helpful in minimizing promotional influence of pharmaceutical companies.

Limitations & Suggestions

Being a cross sectional study, data was collected at given time. So no record of subsequent treatment was noted. For optimizing drug therapy in diabetic patients it has to be correlated with HbA1c level. In present study record of HbA1c level was not found in prescription/ case sheet. To achieve therapeutic goal, compliance of patients about pharmacological and non pharmacological treatment is necessary. Diabetes mellitus is a chronic condition and demands active participation by the patients in adherence to treatment. To study compliance of patient about treatment, questionnaire based interview regarding awareness, adherence can be planned in second phase of this study.

Conclusion

This cross sectional study of prescribing pattern of antidiabetic drugs shows metformin was the most commonly prescribed antidiabetic drug followed by glimepiride. All insulin preparations were human insulins. Hypertension was most common associated co morbidity in diabetic patients. Incidence of diabetes has been found higher in male as compared to female and majority of the patients develop diabetes in the most productive years of their life. Such type of prescription pattern study may provide base for continuous prescription audit in a hospital setting and may be helpful for formation of institutional prescribing policy.

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