PRESCRIPTION PATTERN STUDY IN TYPE 2 DIABETES MELLITUS IN DIABETIC OUT PATIENTS AT PRIVATE CLINIC

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ABSTRACT

Aim: To evaluate drug utilization pattern of antidiabetic drug in type-2 diabetic patients attending at private diabetes clinic. So that, this information can be used in assessment of quality of care provided as well as to facilitate the rational use of drugs in populations

Objective: To evaluate the current trends of prescribing patterns of antidiabetic drug in type

2 diabetic patients

Material and Methods: An observational prospective study undertaken at diabetes clinic from January 2015 to April 2016 after approval from institutional ethic committee. Total 600 patients of type 2 diabetes mellitus were enrolled. Data related to demographic details of the patient (age, gender and BMI, occupation, social status), past history, family history, personal history, all investigations, drug treatment and adverse drug reaction were recorded in suitable case record form. Follow up was carried out for all patients every 3rd, 6th, 9th and 12th month visit for glycaemic control. Data were entered into Microsoft excel 2010 and analysed by descriptive statistics (percentage, mean, standard deviation) and chi square test.

Results: Out of 600 patients, 58.67% were males and 41.33% were females. The mean age of the patients was 51.85 ± 4.24 years. Hypertension (31%) was most common co-morbid illness.Most common complaint was weakness (18.33%). Majority prescriptions had fixed dose combination (FDC) of two antidiabetic drugs (93.2%). Most commonly prescribed FDC was of sulfonylureas (Gliclazide) and Biguanide group (Metformin)in 552(92%). Average number of drugs per encounter was 3.02, 0.3 % drug was prescribed by generic name, 4.17% drug was antibiotic, 7.7% drug was injectable medicine, 14.27% drugs was

prescribed from national list of essential medicine and 11.35% drugs were prescribed from WHO essential list of medicine. Fixed dose combinations were prescribed in 57.27% of patients. Glycaemic controlled was observed in 32.84 % patients.

Conclusion: Sulfonylurea and Biguanide combination most commonly used to treat type 2 DM and among them Gliclazide and Metformin combinations was most commonly prescribed.

Key Words: Type 2 Diabetes, Anti-diabetic drugs, Drug Utilization.

INTRODUCTION

Type-2 diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia arising from a combination of insufficient insulin secretion together with resistance to insulin.[1] The epidemic of type 2 diabetes mellitus(DM) is increasing worldwide (85 % of overall incidence of diabetic worldwide) resulting in increased health burden and reductions in life expectancy.[2]As per World Health Organization , 31.7 million individuals were affected by diabetes in India during the year 2000which may further rise to 79.4 million by the year 2030.[3]

Good glycemic control delays micro and macro vascular diabetic complications and thereby reducing morbidity and mortality.[2] Type 2 diabetic patients are treated with oral hypoglycemic agents andmost of the orally administered anti-diabetes medications have been approved by FDA Since 1995.[4]Management of type 2Diabetes mellitus using pharmacological treatments has become increasingly complex with the variety of agents and treatment guidelines available.[5]Drug utilization studies are important for the optimization of drug therapy and have received a great attention in recent years. The study of drug utilization or prescribing patterns is a component of medical audit, which seeks monitoring, evaluation and necessary modifications in the prescribing practices to achieve rational and cost-effective pharmacotherapy. Studies on antidiabetic drug utilization are important for the optimization of drug therapy and disease control. Therefore, the present study aimed to evaluate the drug utilization pattern of standardantidiabetic drugs in a private diabetes clinic.

MATERIALS AND METHODS

This was an observational prospective study undertaken at diabetes clinic from January 2015 to April 2016 after approval from institutional ethic committee. All patients aged more than 18 year and above, of either gender attending the diabetic clinic, who had been diagnosed as type -2 diabetes mellitus (diagnostic criterias: Symptom of DM, plus RBS $\geq$ 200mg/dl, or FBS $\geq$ 126mg/dl, or $PP_2BS \geq$ 200mg/dl, HBA1C>6.5gm %) were included in the study after verbal informed consent. Type -1 diabetic patients, gestational diabetic patients and those whowere not willing to participate were excluded. Data related to demographic details of the patient (Age, gender and body-mass index, occupation, social status, past history, family history, personal history), investigations, drug treatment were recorded. Follow up was carried out for all patients every 3rd, 6th, 9th and 12th month visit for glycemic control. Data were entered into Microsoft excel 2010 and analyzed by descriptive statistics (percentage, mean, standard deviation) and chi square test.

RESULTS

Based on the study criteria, total 600 patients were enrolled in the study and among them352 (58.67%) were males and remaining were females 248 (41.33%). Diabetics (36.67%) patients were more in the age group 51-60 years (51.85 ± 4.24). More than half of (58.83%) patients were newly diagnosed cases of type - 2 diabetes mellitus. Majority diabetics (67.34%) were Overweight while remaining (30.83 %) were normal weight. Family history of DM was present in 19.17% patients. History of Smoking was found in 11 % patients and Alcohol consumption in 0.6% patients. Among Comorbidities, most common was hypertension (31%) followed by dyslipidemia (4.5%) and ischemic heart disease (4%).

Most common presenting symptoms at the time of enrollment was weakness (18.33%) followed by Neurological symptoms {headache (13.67%) tingling and numbness (9.5%) and burning sensation in the sole of the foot (1.5%)}. Polyuria and Polyphagia were reported in 3.33% and 0.83% respectively. Diabetic retinopathy (3.17%), Diabetic neuropathy (2.17%) and Cataract (1.83%) were present in known case of diabetics.

Table: 1 Prescribing Pattern of antidiabetic drugs: (N=600)

Drug class	Combination drugs	Number of patients(%)
Sulfonylureas+ Biguanides	Gliclazide+ Metformin	467(77.83)
	Glimepiride +Metformin	74(12.33)
	Glipizide +Metformin	11(1.83)
Thiazolidinedione+ Biguanides	Pioglitazone +Metformin	73(12.17)
Thiazolidinedione+ Sulfonylureas	Pioglitazone+ Glimepiride	2(0.33)
DPP VI inhibitor +Biguanides	Vildagliptin +Metformin	20(3.33)
Sulfonylurea+Biguanides+Thiazolidinedione	Glimepiride+Metformin +Pioglitazone	52(8.67)
Adjuvant drugs:		
Alpha glucosidase inhibitor	Voglibose	49(8.17)
Sodium glucose co-transport inhibitor	Dapagliflozin	2(0.33)

*We excluded case of Patient who were on insulin therapy.

Majority prescriptions had fixed dose combination (FDC) of two antidiabetic drugs (93.2%) (Table:1).Biguanide(Metformin) was commonest component of majority of FDC. Most commonly prescribed FDC was of sulfonylureas (Gliclazide) and Biguanide group(Metformin)in 552 (92%). In our study, per prescription average two antidiabetic drugs were prescribed by Physician.

Concomitantly prescribed medications were Angiotensin receptor blocker (28.83%), HMG CoA reductase inhibitor (24.5%), Antiplatelet drugs (12%), Proton pump inhibitor (16.16%) andAntiemetic (14%).

Table 2: WHO Core Drug PrescribingIndicators.

Prescribing Indicator	Value
Average number of drugs per prescription	3.02
Percentage of drugs prescribed by generic name	0.3 %
Percentage of patients prescribed antibiotics	4.17%
Percentage of patients prescribed injectable medicines	7.7 %
Percentage of drugs prescribed from National list of essential medicine (2011)	14.27%
Percentage of drugs prescribed from WHO essential list of medicine (2015)	11.35%

The average number of drugs per encounter was 3.02.   14.27 % of drugs were prescribed from National list of Essential Medicine and 11.35% drugs were prescribed from WHO essential list of medicine. Only 0.3 % drugswere prescribed by generic name while rest all were prescribed by brand name. Fixed dose combinations were prescribed in 57.27 % of patients.Antibiotic usage was 4.17% and injectable medicine was 7.7%. (Table-2). Glycemic control was achieved in 32.84% in this study.

Two adverse reactions of vomiting with Diarrhoea and single case of vitamin B12 deficiency were reported. It was found with the use of gliclazide+metformin fixed dose combination. As per causality assessment by WHO-UMC scale vomiting and diarrhea was "possible" and Vit B_{12} deficiency was "probable" category. These ADR were moderate (Level- 4B) in severity according to Hart wing severity scale and "not preventable" according to modified schumock and Thronton preventability scale and not predictable.

DISCUSSION

Therapeutic practice is primarily based on evidence provided by pre–marketing clinical trials, but complementary data from the post–marketing period are also paramount for improving drug therapy.[6] Drug utilization studies are conducted to know current prescribing trends and to evaluate nature, extent and determinants of use. This will help to determine and employ rational use of drugs among population.[7]

Diabetes mellitus is a major public-health problem worldwide. Its prevalence is rising inmany parts of the developing world and also India is no exception to this. India will become diabetes capital of the world in near future.[3] Diabetes being chronic debilitating disease requires lifelong management. The sedentary stressful life style, lack of exercise, irregular food habits all these factors along with the predominant genetic inheritance increase the risk of type 2 diabetes mellitus.[8]

In our study, highest number of diabetes patients were in the age group of 51-60 years (36.67%) which was similar in study done by Patel B et al. in Ahmedabad.[3]The mean age of thepatients was 51.85 ± 4.24 years which was similar in the study done by M. S. Alam et al., in New Delhi in which mean age of patients was found to be 50.4 ± 11.7 years.[9] Comparatively higher (56.8± 10.5) mean age was found in study done by Kannan et al.[10]

Majority of thepatients were Overweight (67.34%) which was comparatively higher than (19.3%) study of Patel B et al.[3]this finding suggesting that obesity is the major risk factor for the occurrence of type 2diabetes mellitus in our study.The association between family history of diabetes and risk for the disease has been welldocumented. Family history of diabetes mellitus was present in (19.17%) patients in our study, which was lesser than previous study done by Brahmbhatt et al., [8] where 30% patients had apositive family history, suggesting the role of coexisting factors. 11% patient had history of bidi and cigarrate smoking which was lower (24%) than the study of Brahmbhatt et al. [8]

Regarding symptoms in our study, most common complaint reported was weakness (18.33%) which was comparatively lower than (77.2 %) found in the study done by Patel B.et. al[3]other symptoms like tingling and numbness in (9.5%), Polyuria in (3.33%) and Polyphagia in (0.83%) were also found in present study, these symptoms were also comparatively lower than study done by Patel B.et al.(59.6%, 47.4% and 17.5% respectively).[3]

Regarding comorbidities, most common co-morbid condition was hypertension (31%)followed by Dyslipidemia (4.5%) which was comparatively lower than the study done by Alex et al., in which hypertension was found in 68.5% and Dyslipidemia in 39.6% patients.[11] Differentstudies from India and other countries have reported a similar observation with regard to the comorbidity in patients with diabetes. However, the prevalence of hypertension has ranged from 31 to 70%. [12]Complications of diabetes mellitus were diabetic Retinopathy in 19 (3.17%), diabeticNeuropathy in 13 (2.17%) and foot infection in 6 (1%) patients were reported in our study which was also lower than study done in Kerala, India. (17.2%, 9.6% and 7.6% respectively).[11] thisfinding suggested that, if glycemic control was not properly done, the chances of occurrence of complications like retinopathy, neuropathy and nephropathy were high. 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. [13]

Regarding concomitant drug prescribed, among hypertensive patients, maximumprescription of Angiotensin Receptor blocker was found (28.83%) followed by hypolipidemic agents (statins – 24.5%) and Antiplatelet (12%) which was in contrast with the study of Patel B etal. in which Antiplatelet drugs (61.4%) formed the most commonly prescribed drug group forcardiovascular co-morbidities, followed by statins (56%).[3]Similar results were found in the studyof Dashputra et al., in which maximum prescription of ACEI/ARB (Angiotensin ConvertingEnzyme Inhibitor/ Angiotensin Receptor Blocker) was found (62 %) followed by calcium channel blocker (35%).[14] In our study Telmisartan was most commonly prescribed drug amongAngiotensin receptor blocker and from statin Rosuvastatin and Atorvastatin was frequentlyprescribed drugs.

In our study most of the drugs were prescribed by their brand name. Majority prescriptions had fixed dose combination (FDC) of two antidiabetic drugs (93.2%). Biguanide (Metformin) was commonest component of majority of FDC. Most commonly prescribed FDC was of sulfonylureas (Gliclazide) and Biguanide group (Metformin)in 552(92%). Fixed dose combination (FDC) ofGliclazide + Metformin (77.83 %) was most commonly prescribed followed by Glimepiride +Metformin (12.33 %) and

Pioglitazone+Metformin (12.17%).In the study of Datta S.et al, Most commonly prescribed FDC wasMetformin + Glimepride (74.40%) followed by Metformin + Gliclazide (9.76%), Metformin +Glimepride + Pioglitazone (9.76%), Metfomin + Glibenclamide + Pioglitazone (3.66%) and Metformin + Pioglitazone (2.44%).[15] In the study of Kannan et al, Glimepiride and Metformincombinations were commonly (46.81%) prescribed which was higher (12.33%) than present study.[10]

Average number of drugs per prescription was 3.2 in our study, similar finding (3.98) was observed in study done by Dutta S.et al.[15]Comparatively higher (5.15) drugs per prescription was found in the study of Ramachandran G.et al.[16] Possible reason for polypharmacy could bebecause of comorbid conditions in diabetic patients. Doctors should refrain from prescribingunnecessary medicines like multivitamins, minerals and enzymes unless absolutely required bythe patient. The study of prescribing pattern and evaluation of the prescribing practice mayrecommend necessary modifications to achieve rational and cost-effective medical care bypractitioners for making medical care rational. Patients with diabetes mellitus are generally treatedwith many pharmacological agents which may leads to polypharmacy and drug related problems in the prescriptions.[17]

The percentage of drugs prescribed by generic name in the present study shows 0.1%. Which was comparable with study done by Alam MS et al., in which 0.7% were prescribed by generic name.[9] the prescribers of hospital need to improve in prescribing pattern by using moreof generic name. Our study also showed much lower percentage of prescriptions with genericname. The reason for which could be many; namely lucrative advertisements by the pharmaceutical companies, limited awareness about the prescribing guidelines of WHO by theprescribers, insufficient availability of generic drugs in private clinic. Prescribing generic drugscould be a viable alternative as it decreases the economic burden on the patients. Further,educational intervention methods and strict compliance to WHO drug policies could play a role in generic prescribing.

Percentage of encounters in which antibiotics were prescribed was 4.7%, comparatively higher (22.66%) result was observed in other study.[16] the optimum percentage of prescriptions withantibiotics shows that the doctors are judiciously using antibiotics.

Percentage of injectable drug (7.7 %) was higher than (1.8%) in study done in Uttarakhand, India.[15] and similar result was found in study of Chakrabarty et al. in which 6.93% injections were prescribed.[18] comparatively higher (20.5 %.) injections were prescribed in the study of Ramachandran G et al.42 In our study 14.27 % drugs was prescribed from National list of essential medicine(NLEM) [19] and 11.35% drugs were prescribed from WHO essential list of medicine (WHO EML),[20] both were lower than study of Sharma et al., in which drug on NLEM were 50.90% and WHO EML were 49.09%.[21] Among different drugs prescribed by physician on out patient's basis 57.27% drugs were fixed dose combinations. Similar results were found in the study of Alam MS et al., in which 58.1% fixed dose combinations were prescribed.[9]

In our study glycemic controlled was observed in 32.84 % patients. Comparatively higher (68.7%) glycemic control was achieved in the study of Das P et al. [22]

Regarding adverse drug reaction, only three adverse drug reactions (1 case of vomiting, 1case of vomiting with diarrhoea and 1 case of vitamin B12 deficiency were reported by use ofGliclazide + Metformin fixed dose combination) were reported during our

study period. In thestudy of Alex et al., 17 case of adverse drug reactions were reported, in which hypoglycemia was the most common ADR observed in eight patients and 2 patients had diarrhea.[13] Reason for lessADR in our study was, this study was done in Private diabetic clinic and physician also prescribedanti-emetic or Antacids with anti-diabetic drugs, so chances of occurrence of vomiting and GIdisturbance was less. At the study center Dietitians was also available so proper education aboutdiet, exercise and if hypoglycemia occurs how to manage was explain by physician.

CONCLUSIONS

Sulfonylurea and Biguanide combinations are most commonly used to treat type II DMand among these Gliclazide and Metformin combination was most commonlyprescribed.

LIMITATIONS OF THE STUDY

- Measurement of HbA1c level, which is considered as the gold standard and gives better judgment about 3 months glycemic control, was done in 31.5 % patients, due to its highcost.
- Cost of drug Therapy was not analyzed
- Due to the lack of awareness about side effect of the drugs, less adverse drug reaction wasreported
- Short duration of the study

REFERENCES

1. Drucker DJ, Sherman SI, Gorelick FS, Bergenstal RM, Sherwin RS, Buse JB.Incretin-based therapies for the treatment of type 2 diabetes: evaluation of the risksand benefits. Diabetes Care. 2010; 33(7):428-33.
2. Kokic S, Radman M, Capkun V, Dovzak, Kokic D, Tesanovic S. Comparativeassessment of the treatment of type 2 diabetes mellitus. Annals of Saudi Medicine.2002; 22(3):163-6.
3. Patel B, Oza B, Patel KP, Malhotra SD, Patel VJ. Pattern of antidiabetic drugs use intype-2 diabetic patients in a medicine outpatient clinic of a tertiary care teachinghospital. International Journal of Basic & Clinical Pharmacology. 2013; 2(4):485- 91.
4. Libman I, Arslanian S. Type 2 diabetes in childhood. The American perspective.Horm Res. 2003; 59(1):69-76.
5. Itamar Raz. Treatment of Type2 Diabetes: From "Guidelines" to "Position statements" and back. Diabetic care 2016;39(supp.2):S146-S153
6. Thakkar KB, Jain MM, Billa G, Joshi A, Khobragade AA. - A drug utilization studyof psychotropic drugs prescribed in the psychiatry outpatient department of a tertiary care hospital. Journal of Clinical and Diagnostic Research. 2013; 7(12):2759–64.
7. World Health Organization, WHO International Working Group for Drug StatisticsMethodology, WHO Collaborating Centre for Drug Statistics Methodology, WHOCollaborating Centre for Drug Utilization Research and Clinical

PharmacologicalServices. Introduction to Drug Utilization Research. Geneva: WorldHealthOrganization. 2003; What is drug utilization research and why is it needed?:8-12.

8. Brahmbhatt SV, et al. A prospective study on drug utilization pattern & rationality intreatment of type II diabetes mellitus: a population-based analysis. InternationalJournal of Research in Medical Sciences. 2014; 2(3):983-87

9. Alam MS, Aqil M, Qadry SA, Kapur P, Pillai KK. Utilization pattern of oralhypoglycemic agents for diabetes mellitus type 2 patients attending out-patientdepartment at a university hospital in New Delhi. Pharmacology & Pharmacy. 2014;5(7): 636-645.

10. Kannan, Arshad, Kumar S. A study on drug utilization of oral hypoglycemic agents intype 2 diabetic patients. Asian Journal of Pharmaceutical and Clinical Research.2011; 4:60-4.

11. Alex SM, et al. Drug Utilization pattern of anti-diabetic drugs among diabeticPatients in a tertiary care hospital. Asian Journal of Pharmaceutical and ClinicalResearch. 2015; 8(2):144-6.

12. John LJ, Arifulla M, Sreedharan J, Muttappallymyalil J, Das R, John J, et al. Age andgender-based utilization pattern of antidiabetic drugs in Ajman, United ArabEmirates. Malay J Pharm Sci. 2012; 10:79-85.

13. Rajeshwari S, Adhikari PM, Pai MR. Drug utilization study in geriatric type 2diabetic patients. Journal of Clinical and Diagnostic Research. 2007; 1(5):440-3.

14. Dashputra AV, Badwaik RT, Borkar AS, Date AP, Kalnawat NR. Pattern ofantidiabetic drugs used in outpatient and hospitalized patients in a tertiary healthinstitute of central India, J Cont Med A Dent. 2014; 2(3):48-54.

15. Dutta S., Beg MF, Anjoom M, Varma A, Bawa. Study of prescribing pattern indiabetes mellitus patients in a tertiary care teaching hospital at Dehradun,Uttarakhand.International Journal of Medical Science and Public Health. 2014; 3(11):1351-4.

16. Ramachandran G, Rohith V, Isabella T. Evaluation of prescribing pattern of antidiabetic drugs using WHO prescribing indicators in a tertiary care hospital inPuducherry: A cross-sectional study. The Pharma Innovation Journal. 2015; 4(5):76-80.

17. Kumar MA, Nizar A, Shailaja K, Jayasutha J, Ramasamy C. A study on prescribingpattern and potentials drug-drug interactions in type-2 diabetes mellitus (inpatients) ina tertiary care teaching hospitals. Der Pharmacia Lettre. 2011; 3(4):13-9.

18. MaitiT, Chakrabarty S, Mandal S, Panda A, Gangopadhyay T, Dan S. A study ondrug utilization pattern in patients of type 2 diabetes mellitus attending referraldiabetic clinic at a tertiary care teaching hospital in rural Bengal- European Journal ofPharmaceutical and Medical Research. 2016; 3(9):641-7.

19. National List of Essential Medicines of India 2011. Available from URL:www.cdsco.nic.in/.../National%20List%20of%20Essential%20Medicine-.(Lastaccessed on 8/10/2016)

20. 19th WHO Model List of Essential Medicines (April 2015). Available from URL:www.who.int/medicines/.../essentialmedicines/EML2015_8-May-15.pdf (Lastaccessed on 8/10/2016)

21. Sharma P, Sharma N, Parakh R, Sharman, Gautam B, Motiwale S. Screening ofprescriptions in patients of type-2 diabetes mellitus in a tertiary care teachinghospital.International Journal of Pharmaceutical Research and Bio-Science. 2014;3(1):401-9.

22. Das P, Das BP, Raunar GP, Roy RK, Sharma SK. Drug utilization pattern andeffectiveness analysis in diabetes mellitus at a tertiary care centre in eastern Nepal.Indian J. Pharmacol. 2011; 55(3):272-80.