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PATTERN OF UTILIZATION OF ORAL HYPOGLYCEMIC AGENTS FOR TYPE 2 DIABETES MELLITUS PATIENTS ATTENDING OPD IN NEW DELHI

Medicine

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ABSTRACT

Background: India carries a huge diabetic population which is swelling further, medicine utilization studies might be one of the strategies to rationalize the medicine use in diabetics and to manage disease better in the community.

Objectives: Our study mainly aimed at describing patterns of prescription of medicines to diabetics attending the OPD and also to assess patient's compliance.

Material and Methods: It was a prospective, observational and non-comparative study conducted at Medicine OPD in western part of New Delhi/NCR, India. The study was carried out in a minimum of 200 established type 2 diabetes patients, who visited the clinic for treatment during the time period of June 2016 to December 2016. The purpose and other details of the study was discussed with the patients. An oral consent was also taken from all the participating patients, prior inclusion in the study.

Results: A total of 200 diabetes mellitus patients were enrolled in the study, out of which 54% were males and 46% were females. The study revealed that Metformin was the most commonly prescribed single OHA in 25 (12.5%) patients. Among the drug combinations, 30 (15%) patients received glimepiride and metformin whereas metformin and sitagliptin combination was used in 35 (17.5%) patients. It was observed that only 160 (91.4%) of the patients showed good compliance (≥80% intake of recommended dosage regimen) with the metformin mono therapy. More compliance was observed in case of female (n = 86, 55.5%) as compared to male patients (n = 69, 44.5%).

Conclusion: The study have shown that majority of the patients with type 2 diabetes in LYF Hospital/ Dr Gupta's OPD were managed with Metformin mono therapy while the current OHA prescribing strategy did achieved satisfactory glycemic control on majority of the patient. Hence, combination therapies of Metformin with different OHAs were prescribed for proper glycemic control.

KEYWORDS

Diabetes, Compliance, OHA, Mono therapy, Combination therapy

Introduction:

Diabetes mellitus (DM) is one of the oldest diseases known to man, which was the first reported in Egyptian literature about 3000 years ago.[1] The name diabetes was first given by the Greek Physician Aretaeus (30 - 90CE). Avicenna, is the famous Arabian physician who first described the complications and progression of the disease.[2] People living with type 2 DM are more vulnerable to various forms of both short and long-term complications, which often lead to their premature death.

Diabetes mellitus type 2 is a chronic disease characterized by coexisting insulin deficiency and insulin resistance, with the resultant hyperglycemia leading to micro and macro vascular complications.[3-6] Complications include altered metabolism of lipids, carbohydrates, protein and an increased risk of vascular disease complication.[7,8] Type 2 diabetes is much more common and accounts for around 90% of all diabetes cases worldwide. It occurs most frequently in adults but is being observed increasingly in adolescents as well.[8-11] WHO has estimated that, in 2000, 31.7 million individuals were affected by diabetes in India and these figures are expected to rise to 79.4 million by the year 2030.[12] A recent survey depicts that 4% of the adults in India suffered from diabetes in the year 2000 and it is expected to increase to 6% by the year 2025.[13] Indeed, India today leads the world with largest number of diabetic subjects in any given country.[14,15] Type 2 diabetes affects over 7% of the general US population at an annual cost of $132 billion.[16]

Considering the fact that, India carries a huge diabetic population which is swelling further, medicine utilization studies might be one of the strategies to rationalize the medicine use in diabetics and to manage disease better in the community.

Aim and Objectives:

There were two aims of the study:
- To describe patterns of prescription of medicines to diabetics attending the OPD in New Delhi/NCR.
- To assess patient compliance, which will serve as a good reference in analyzing prescribing trends and to formulate guidelines for rational prescribing of diabetic medicines in the management of Diabetes in OPD setting.

Materials and Methods:

(i) **Study Design:** It was a prospective, observational and non-comparative study conducted at Medicine OPD in western part of New Delhi/NCR, India.

(ii) **Sample size:** The estimated sample size was calculated by the formula $Z1-a/2^2 \ p \ (1-p) / d^2$ So, $Z1-a/2^2$ = standard normal variant (at 5% type1 error (p<0.05) it is 19.6) P = expected proportion in population based on previous studies (13%) d = absolute error or precision (at absolute error of 5% and at type 1 error of 5%. Sample size = $1.962^2 \times 0.13 \ (1-0.13)/5^2$ So the sample size is calculated as 180

(iii) **Methodology:** The study was carried out in a minimum of 200 established type 2 diabetes patients, who visited the clinic for treatment during the time period of June 2016 to December 2016. The purpose and other details of the study was discussed with the patients. An oral consent was also taken from all the participating patients, prior inclusion in the study.

(iv) **Inclusion criteria:** Type 2 diabetes mellitus patients, irrespective of age and sex, who were prescribed at least one OHA will be included in the present study.

(v) **Exclusion criteria:** Diagnosed diabetic patients who do not receive pharmacological therapy, unable to reply verbal questions as well as mentally retarded and unconscious patients will be excluded from the study.

(vi) **Procedure:** Once the consultation by the physician will be over, the prescriptions were reviewed and the patients were interviewed using structured questionnaire (open question method). On every visit, information regarding the use of medicines was given to the patients. All the participating patients will be asked to bring the remaining medicines as well as empty strips with them on next visit. Data was collected by a registered pharmacist that included registered patients only. The information included patients demographic details like age, sex, body weight, height, major disorders, co-morbid conditions, family history, number of medicines prescribed, classes of medicines prescribed, medicine brand, secondary failure and compliance with the therapy. Residual tablet counting method is more feasible as it is less time consuming, does not require any biological testing, hence in our setting, patients' compliance will be determined by residual tablet counting method. Compliance data will be documented as either

<80% or >80% intake of recommended dosage regimen with the therapy at each visit.

(vii)Statistical Analysis: The differences in proportions was compared by unpaired t-test where appropriate. Statistical significance was set for $p < 0.05$. All statistical analysis will be performed using SPSS version 17.0.

Results and Observations:

A total of 200 diabetes mellitus patients were enrolled in the study, out of which 54% were males and 46% were females (Table 1). Most patients belong to the age group of 45-60 years (35%) followed by > 60 years (30%). 20% had positive family history of Diabetes whereas majority ie. 50% had a BMI = 25-29.9 Kg/m².

Table 1: Distribution of patients

| Study Population	No.	%
Gender		
Male	108	54
Female	92	46
Age in years		
<15	10	05
15-29	20	10
30-44	40	20
45-60	70	35
>60	60	30
BMI (Kg/m²)		
>18.5	10	05
18.5-24.9	20	10
25-29.9	100	50
30-34.9	60	30
>35	10	05
Family History		
Positive	40	20%
Negative	160	80%

Out of 200 patients, 105 (52.5%) patients were found suffering from Concurrent illnesses. Distribution of concurrent illnesses is described (Table No. 2) where Hypertension was the most common co-morbidity present in 35 patients (33.3 %) followed by hypertension with Ischemic heart disease (15.2%).

Table 2: Distribution of Concurrent illness

Co morbidity	No. of patients (n=105)	%
Hypertension (HTN)	35	33.3
HTN+ Ischemic heart disease (IHD)	16	15.2
HTN+ Congestive heart failure (CHF)	4	3.8
Chronic Renal Failure (CRF)	7	6.6
Hypothyroidism	3	2.8
Coronary Artery Disease (CAD)	5	4.7
Chronic Obstructive Pulmonary Disease (COPD)	2	1.9
Others	33	31.4

Table 3/Fig 1: Pattern of Oral Hypoglycemic agent prescription

Anti Diabetes Drug prescribing pattern	No.
Mono therapy	50
Combination therapy	125
Fixed Dose	25
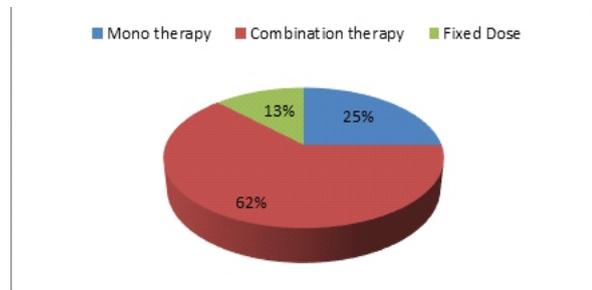
The percentages of patients on anti diabetic mono therapy, combination therapy and fixed dose therapy were 50 (25%), 125(62%) and 25 (13%) respectively (Fig. 1).

Table 4: Pattern of utilization of Oral hypoglycemic agents

Drugs	Total no of prescriptions	%
Mono therapy		
Biguanides		
Metformin	25	12.5
Sulfonylureas		
Glimepride	10	5.0
Glicalzide	02	1.0
Glibenclamide	03	1.5
Glipizide	00	0.0
Alpha glucosidase inhibitors		
Voglibose	01	0.5
Acarbose	00	0.0
DPP 4 inhibitors		
Sitagliptin	05	2.5
Vildagliptin	00	0.0
Linagliptin	00	0.0
SGLT2 inhibitors		
Canagliflozin	03	1.5
Dapagliflozin	02	1.0
Emplagiflozin	00	0.0
Combination therapy		
Metformin + Glipizide	05	2.5
Metformin + Glimepride	30	15.0
Metformin + Gliclazide	03	1.5
Metformin + Sitagliptin	35	17.5
Metformin + Vildagliptin	02	1.0
Metformin + Linagliptin	00	0.0
Metformin + Voglibose	00	0.0
Metformin + Glimepride + Pioglitazone	25	12.5
Metformin + Gliclazide + Voglibose	05	2.5
(Metformin + Glimepride + Pioglitazone) + Sitagliptin	15	7.5
Metformin + Glimepride + Pioglitazone) + Depagliflozin	05	2.5
Fixed dose combination		
Metformin + Glimepride	25	12.5

The study revealed that Metformin was the most commonly prescribed single OHA in 25 (12.5%) patients. Among the drug combinations, 30 (15%) patients received glimepiride and metformin whereas metformin and sitagliptin combination was used in 35 (17.5%) patients. Triple drug combination was used in 25 (12.5%) were pioglitazone with (glimepiride and metformin) was given. 25 (12.5%) patients were on a fixed dose combination of oral hypoglycemic agent (metformin + glimepride) (Table no. 4).

Table 5: Patient's compliance with Oral Hypoglycemic Agents

Class of OHA prescribed	Name of OHA prescribed	Total no. of OHA	No. of OHA compliance	% compliance
Biguanides	Metformin	175	160	91.4
Sulphonylurea	Glimepride	65	50	76.9
	Glicalzide	05	03	60.0
	Glibenclamide	03	03	100
	Glipizide	05	04	80.0
	Total	78	60	76.9
Thiazolidinedions	Pioglitazone	15	11	73.3
Alpha glucosidase inhibitors	Voglibose	06	03	50.0
	Acarbose	00	00	0.0
	Total	06	03	50.0
DPP 4 inhibitors	Sitagliptin	55	50	90.9
	Vildagliptin	02	02	100
	Linagliptin	00	00	0.0
	Total	57	52	91.2
SGLT2 inhibitors	Canagliflozin	03	03	100
	Dapagliflozin	07	05	71.4
	Emplagiflozin	00	00	0.0
	Total	10	08	80.0
Meglitinides	Ripaglinide	00	00	0.0

It was observed that only 160 (91.4%) of the patients showed good compliance (≥80% intake of recommended dosage regimen) with the metformin mono therapy. More compliance was observed in case of female (n = 86, 55.5%) as compared to male patients (n = 69, 44.5%). Patients were found to be more compliant with biguanides, (91.4%), followed by DPP4 inhibitors (91.2%), SGLT2 inhibitors (80%), sulphonylureas (76.9%), thiazolidinediones (73.3%) and alpha-glucosidase inhibitors (50%). Maximum compliance was observed with glibenclamide (100%), followed by Vildagliptin (100%) and Sitagliptin (90.9%) (Table 5).

Discussion:

Diabetes mellitus is one of the major non communicable diseases which are growing very fast in this modern era. The prevalence of Diabetes Mellitus in our study set up was 13.94%. These results are found to be much similar with the study conducted in Bangalore where the prevalence rate was found to be 4-11.6% in urban dwellers.[12] In our study the prevalence of type2 diabetes was high in males 57.14 %. Males predominated in the study population which is in agreement with the results of various other studies in India[13] and United States.[14]

There was higher prevalence of diabetes mellitus in middle age group, highest being 35 % in age group 41-60 years and 30 % in above 60 years age group. This higher prevalence in younger age group may be due to the lifestyle of the younger population and also the stress factor which unmasks diabetes causing blood sugar to rise.[15] A total 105 (52.5%) patients suffered from co-morbid condition. Hypertension accounted for 33.3 % of the total complications which was lower than in the study reported in Nepal (Hypertension accounted for 70.62% of the total complication).[15] Our study findings are also similar to the study conducted by Arauz-Pacheco et al. in Texas medical center that hypertension is more common complication affecting 20-60% of people with diabetes.[16]

The average number of drugs per prescription is 12.2; this was high when compared to previous records of 2.60, 3.03 and 4.07 from various specialty clinics in India and 2.9 from Hong Kong.[17] The high average number of drugs prescribed to patients with diabetes is not surprising. It is recognized that patients with diabetes mellitus are generally prescribed more drugs than other patients. Prescriptions for Injections and antibiotics were 34.42% and 4.61% respectively. 99.22% of drugs were prescribed by their brand names which is higher and 0.78% were prescribed by their generic names which is lower than study conducted by M Ashok Kumar et al. in tertiary teaching care hospital, Tamilnadu.[19] The average number of drugs per prescription, percentage of drugs from WHO essential drug list and injections were found to be 12.2, 73.77% and 34.43%, respectively which were quite higher whereas the percentage of anti diabetics prescribed was found to be lower than the study conducted by Adibe M.O et al[17], L. sutharson et al.[18] and M.Ashok et al.[19]

The pattern of anti diabetic drug utilization was studied. 25% of patients were on monotherapy and 62% were on combination therapy for diabetic control which is similar to the study conducted by M Ashok Kumar et al. in tertiary teaching care hospital, Tamilnadu[19] while another study conducted by Kannan et al. in Tamilnadu also revealed that monotherapy (2.47%) is lower and combination therapy (56.93%) is higher than our study.[20]

A Drug utilization study is considered to be one of the most effective methods to assess and evaluate the prescribing attitude of physician and help to promote rational use of drugs. In patients with type-2 diabetes treatment may be initiated with monotherapy followed by early intervention with a combination of oral agents, including a sulfonylurea/biguanides as a foundation insulin secretagogue in addition to a supplemental insulin sensitizer. In our study metformin as a monotherapy secured highest utilization percentage (12.5%) amongst all anti diabetic drugs. Several studies showed that a combination of sulfonylurea with metformin has been most widely used.[21] The present study also showed that a combination of sulfonylurea and metformin was most frequently prescribed 15%.

Metformin does not promote weight gain and has beneficial effects on several cardio vascular risk factors. Accordingly, metformin is widely regarded as the first drug of choice for most patients with type-2 diabetes mellitus .Our study also supports the same 62 % received metformin combination with other oral antidiabetic drugs.

In this study among the second generation sulfonylureas, glimepiride was most commonly prescribed. 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. In this study, 29.52 % patients received two drugs which is higher, 15% patients received three drug and 10% patients received four drug combination of anti diabetics which are[20] lower as compared to the study conducted by Kannan et al. Drugs from the alimentary tract and metabolism constituted 82.86%, cardiovascular drugs 66.67% of the prescribed drug which is similar to, 55.24% and 39.05% of drugs from blood forming organs and NSAIDS (Analgesics) respectively which was slightly higher than the study conducted by M Ashok Kumar et al. in tertiary teaching care hospital, Tamilnadu.[19] In our study, we found 42 Potential drug-drug interactions which is lower than the study carried out by M Ashok Kumar et al.[19]

Conclusion:

The study have shown that majority of the patients with type 2 diabetes in LYF Hospital/ Dr Gupta's OPD were managed with Metformin mono therapy while the current OHA prescribing strategy did achieved satisfactory glycemic control on majority of the patient. Hence, combination therapies of Metformin with different OHAs were prescribed for proper glycemic control. The potential drug-drug interactions (DDI) are frequent in type 2 diabetes mellitus and some of them deserve clinical attention. The actual and potential DDIs increase as per number of drugs in prescription. The management of clinically relevant DDIs can be improved by clinical pharmacist interventions. Advice on withdrawal or substituting the precipitant drug would be beneficial.

Limitations of Study:

As it is a single centre study with a relatively small study population, results cannot be generalized to the entire population.

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