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Prescribing pattern and efficacy of Oral hypoglycaemic agents in maintaining optimal glycemic levels in diabetic patients

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Abstract
Background: Regardless of the availability of various effective anti-diabetic drugs to reduce the blood glucose by various mechanisms, still major diabetic population on anti-diabetic drug therapy have recorded poor glycemic control and high diabetic vascular complications.
Aims and Objectives: The aim of this research is to study the prescribing pattern and efficacy of anti-diabetic drugs in maintaining ideal glycemic levels in diabetic patients.
Materials and Methods: A prospective, cross sectional, observational study has been conducted on a sample size of 150 patients of diabetes mellitus and attending diabetes outpatient departments at Department of Medicine and Department of Pharmacology, L N Medical College and research Center Bhopal, Madhya Pradesh for 6 months from Jan 2018 to July 2018. Blood glucose level was measured with the help of glucometer, to determine the glycemic control.
Results: Average number of anti-diabetic drugs prescribed per prescription was 1.4. Drug class Sulfonylureas the most common on the prescriptions. However among the hypoglycemic agents (OHA), metformin (biguanide) was the most common prescribed individual drug. In combination drugs fixed dose of biguanide and sulfonylurea was majorly prescribed. Monotherapy has been used more than the polytherapy and the percentage use of insulin in Type 2 diabetics was very high. Out of 150, only 63(42%) patients on anti-diabetic therapy had recorded optimal glycemic control. The recorded association between the anti-diabetic therapy with lifestyle changes and glycemic control was statistically significant ($P = 0.0011$).
Conclusions: OHAs was still dominating the drugs prescribed, however in cases of Type 2 diabetes mellitus a clear shifting trend toward the insulin preparations was noticed. In our study we found that in optimal glycemic control, anti-diabetic drugs has efficacy of 42% only and therefore increase of current drug treatment along with planning of multiple drug interventions with lifestyle modification is essential.

Keywords: prescribing pattern, glucometer, sulfonylurea, biguanide

Introduction

Diabetes mellitus is a pandemic disease that has struck each and every corner of the world. According to the Indian Council of Medical Research Indian Diabetes study (ICMR), a national diabetes study, India currently has 62.4 million people with diabetes [1]. This is set to increase to over 100 million by 2030 [2]. The prevalence of diabetes among adults has reached approximately 20% in urban and approximately 10% in rural populations in India [3].

Various classes of anti-diabetic drugs including insulin and oral hypoglycemic agents (OHA) are currently used in the treatment of diabetes, which acts by different mechanisms to reduce the load of glucose levels to maintain optimal glycemic control [4, 5].

The United Kingdom Prospective Diabetes Study (UKPDS) showed intensive blood glucose control by either sulfonylureas or insulin substantially decreased the risk of microvascular complications [6, 7].

The currently used anti-diabetic drugs are very effective, however because of lack of patient compliance, clinical inertia, insulin resistance, lack of exercise and lack of dietary control leads to unsatisfactory control of hyperglycaemia [8-15].

In India, limited studies have focused on diabetes care and provide an insight into the current profile of patients' andtheir management. More than 50% of people with diabetes have poor glycemic control, uncontrolled hypertension and dyslipidaemia, and a large percentage have diabetic vascular complications [16, 17].

Therefore, this study was carried out to find the current prescribing pattern of anti‑diabetic drugs and efficacy of these drugs in maintaining adequate glycemic control in diabetic patients attending a tertiary care teaching hospital in Navi Mumbai.

Materials and methods

It was a cross sectional, prospective, observational study conducted at Department of Medicine and Department of Pharmacology, L N Medical College and research Center Bhopal, Madhya Pradesh.

A formal approval of the ethics committee was secured before

commencement of the study. A sample 150 patients was used for this study, as per the World Health Organization (WHO) manual to evaluate the drug usage at individual facilities. [18]

A total 150 diabetes patients of age 18 years or above and who were receiving anti-diabetic therapy for more than1 year, patients fulfilling the inclusion/exclusion criteria were randomly selected for participation.

After receiving the informed and formal consent, data recorded for socio-demography, details of anti-diabetic drug therapy, duration of treatment and life style modifications (food habits, physical activities). Additional data for fasting and postprandial blood glucose was measured using the AccuChek Active glucometer.

Patients who were newly diagnosed or on anti-diabetic therapy for <1 year or diabetic coma patients or repeat attendance or patients not willing for consent and blood glucose investigation, excluded from this study.

The following patient details were recorded and analysed:

Average number of anti-diabetic drugs prescribed per prescription, percentage of different class of anti-diabetic drugs prescribed, most common class and type of anti‑diabetic drugs prescribed, percentage of anti‑diabetic drugs prescribed from the list of essential drugs (Indian National Essential Drug List or WHO). [19, 20] Patients were grouped as per the optimal controlled glycaemic level based on the blood glucose level (fasting <100 mg/dL and/or postprandial <180 mg/dL) measured by glucometer.

Data collected for this study was analyzed on the Statistical Package for the Social Sciences version 20 (Chicago: SPSS Inc), with value $P < 0.05$ was considered to be statistically significant. Chi square test was used for categorical data to test for the association. Analysed data was expressed in terms of the actual number, mean of it, and percentages.

Results

Data collected from one hundred fifty (n = 150) patients of Type 2 diabetes was analysed. Details of 140 anti-diabetic products which were prescribed to patients were analysed.

Out of 150 subjects: 56% (n = 84) were male, 44% (n = 66) were female and mean age of the sample was 58.12 (±10.5) years.

During the study period, number of anti-diabetic drugs prescribed per prescription varied from one to four and the averagedrugs per prescription was 1.4.

Out of 140 prescribed anti-diabetic drugs, OHA were 79 (56.4%) and 61 (43.6%) were insulin.

In this study OHA's was the more common class of anti-diabetic drugs prescribed. Out of prescribed OHAs, sulfonylureas were (34.14%) were the most common class followed by the biguanides (31.65%) and prescribed combination of these 2 OHAs as fixed dose combination (FDC) was 20.25%.

Metformin as the individual OHA was the most commonly prescribed and accounted for 31.65%, others prescribed drugs were glimepiride (sulfonylurea) 20.25%followed by FDC of glimepiride plus metformin 11.40% [Table 1].

Table 1: Frequency of commonly drugs prescribed

OHA (s)	Number (n=79)	Percentage
Metformin	25	31.65
Glimepiride	16	20.25
Gliclazide	7	8.86
Glipizide	2	2.54
Glibenclamide	2	2.54
Acarbose	2	2.54
Voglibose	1	1.26
Pioglitazone	5	6.33
Sitagliptin	1	1.26
Saxagliptin	1	1.26
Glimepiride + metformin	9	11.4
Gliclazide + metformin	5	6.33
Glyburide + metformin	1	1.26
glipizid e + metformin	1	1.26
Voglibose + metformin	1	1.26

Other prescribed classes of OHA were thiazolidinedione's 6.33%, alpha glucosidase inhibitor 3.8%, and dipeptide peptidase4 inhibitors (DPP 4 inhibitors) was 2.5%, respectively. Insulin preparations accounted for 43.6% of the total anti‑diabetic drugs and the most common preparation was short acting insulin preparation.

All the drugs prescribed in this study were branded names (100%). Percentage of drugs prescribed from WHO essential drug list was 74.2% (104) and National Essential Drug List of India was 67.1% (94).

Out of 150, Type 2 diabetic patients on anti-diabetic drugs, 63 (42%) had controlled glycemic levels, while 87 (58%) had inefficiently controlled glycemic levels [Table 2]. Association of optimal glycemic levels was statistically significant in diabetic patients on anti-diabetic therapy with modification in lifestyle ($P = 0.0011$); however, this association with type and duration of treatment was not significant statistically ($P > 0.05$).

Table 2: Comparing patients' characteristics as per the HbA1c levels

Characteristics	Glycemic level		n=150	P value
	Controlled	Uncontrolled		
Age (years)				
<40	6	3	9	0.66
40-60	30	48	78	
>60	26	37	63	
Sex				
Males	34	50	84	0.64
Females	30	36	66	
BMI (mg/kg2)				
Normal (18.5-24.9)	28	38	66	0.34

Overweight (25-30)	25	27	52	
Obese (above 30)	10	22	32	
Type of anti-diabetic therapy				
Monotherapy	38	51	89	0.73
Combination therapy	24	37	61	
Duration of treatment				
<5	27	40	67	0.96
between 5 to 10	24	34	58	
>10	11	14	25	
Anti-diabetic therapy				
With life style modifications	52	49	101	0.0011
Without life style modifications	9	40	49	

Discussion

This study was carried out to understand the current prescribing pattern and trend of anti-diabetic drug therapy, it also attempted to understand efficacy of these drugs in maintaining an optimal glycemic level in diabetic patients.

Average number of anti-diabetic drugs prescribed per prescription in this study was 1.4. In the previous hospital based studies average was reported as 2-5 drugs per prescription in India and Abroad. [21-26]. Findings of this study reflects the restraint on polypharmacy.

In current study commonly prescribed drugs were OHAs and accounting for 56.40% of all prescribed drugs. Sulfonylureas (34.14%) were the commonest prescribed class, same as previous studies, [22, 24, 27] this is followed by biguanides (31.65%) and FDC of this drugs is accounted for20.25%. Collected data shows that the sulfonylureas and biguanides arstill prevalent choice of physicians in the Type 2diabetes cases.

Despite the sulfonylurea being the most common class, study shows that metformin (biguanide) was the most common individual OHA being prescribed 31.65%, same has been found out in several previous studies [21, 23, 27- 29], it is followed by glimepiride (sulfonylurea) 20.25%.

High prevalence of metformin may be due to the fact that it was the only drug of its class to be prescribed. Whereas in case of sulfonylureas, many second generation sulfonylureas are available and were prescribed making their individual frequency low, however as a group/class their prescribing was higher than iguanid class. This study reported low prescribing rate of newer OHAs (thiazolidinedione and DPP 4 inhibitors). Newer OHAs were used in combination of other OHAs to achieve better glycemic control, same observation is also recorded in to previous studies [22, 28].

A per the collected data insulin preparations makes 43.6% of the total prescribed anti-diabetic drugs and the commonest preparation was short acting insulin preparation. In this study we observed higher percentage of insulin prescription and insulin based therapy compared to the Indian studies conducted in past. [23, 24] Insulin preparations provides intensive, near physiologic delivery of insulin and help in achieving better glycemic control. [30].

Observation of this reflects a change in prescribing trend and shifts towards the insulin based therapy from the dominated OHA based therapy in Type 2 diabetes treatment.

In this study, all drugs recorded were prescribed by brand name shows the popularity and influence of pharmaceutical companies on the physicians. A branded products are costly therefore prescribing generic for cost effectiveness is advisable. Percentage of drugs prescribed from national essential drug list was 67.1% which highlights the awareness and selection from essential drug list for rational use of drugs.

In this study 42% patients on anti-diabetic drugs had controlled optimal glycemic levels, while 58% had inadequate/uncontrolled glycemic levels. Several studies [15, 31-34]. Have documented it from 50% to 86%, which were higher than current study.

The most prevalent anti-diabetic therapy was monotherapy either with OHA or insulin, while combination therapy with OHA's and insulin was to a lesser extent. Study by Willey *et al*. [32]. has documented good glycemic control on monotherapy. By in this study, association of glycemic control with monotherapy and combination therapy was not statistically significant ($P > 0.05$), however, observations shows it statistically significant association between glycemic control and anti-diabetic drug therapy with lifestyle modifications. Therefore lifestyle modification combined with anti-diabetic drug is more likely to improve glycemic control compared to optimized anti-diabetic drug treatment. [6, 7, 35]

This study supports the domination of OHA, it also highlights the shifting trend towards insulin intreatmentof Type 2 diabetes. It stress on the need for periodic blood-glucose monitoring in patients receiving anti-diabetic drug treatment to identify inadequately controlled glycaemic levels, so that drug required can be intensified or multiple drug interventions can be planned in order to achieve an optimal glycaemic level. This study positively highlights theneed and impact of lifestyle modification measures along with anti-diabetic drug treatment for achieving optimal glycaemic control in patients of Type 2 diabetes.

Measurement of HbA1c level, which is considered as the gold standard and gives better judgment for about 3 months glycaemic control, was not conducted because of budget constraints. Measurement of blood glucose was done with the help of AccuChek Active glucometer instead of laboratory peroxidase test, this glucometer was easy to use and its results are correlated well with the laboratory test results [36].

Conclusion

Findings of this study concluded that the oral hypoglycemic agents (OHAs) were prescribed more commonly, but at the same time there was a shifting trend towards the insulin preparations for the management of Type 2 diabetes mellitus. In achieving optimal glycemic control, the efficacy of the anti-diabetic drugs was only 41%; therefore intensification of

current drug treatment as well as planning multiple drug interventions with lifestyle modification is essential toprevent diabetic complications.

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