

ANTIDIABETICS/ANTIHYPERTENSIVES PRESCRIPTION PROFILE IN OSUTH, SAGAMU AND ENVIRONMENT

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ABSTRACT

Purpose of the Study: The aims of this paper are to investigate drug utilization in the management of diabetes mellitus and hypertension in Sagamu, Ogun state and its environment and to evaluate their agreement with established guidelines.

Methodology: Prescriptions on both diabetes and hypertension were collected over a period of two weeks at the Ogun state University Teaching Hospital and from a general (state) hospital in its environment. Statistical analysis was by using a chi-square test for proportions and students t-test for parametric data. A p-value of less than 0.05 was considered significant.

Results: The study involved 1360 consecutive prescriptions from the medical unit of the general hospital and 1440 consecutive prescriptions from the teaching hospital (712 from the diabetic clinic and 728 from the hypertensive clinic). A total of 210 patients (15.4%), 1040 patients (76.5%) and 110 patients (8.1%) in the general hospital were prescribed one or more antidiabetic agents, antihypertensives and combination of both respectively. In the teaching hospital a total of 330 patients (22.9%), 633 patients (43.9%) and 477 patients (33.1%) were considered respectively to be diabetic alone, hypertensive alone and combined diabetic and hypertensive. In both settings, most diabetics were of the type 2 type, been treated with sulfonylureas more commonly than biguanides. In both populations, over 50% of the diabetics were treated with glibenclamide, About 90(27.3%) of the patients in the general hospital were on two sulfonylureas. Insulin was prescribed to 3(0.9%) and 16(2.2%) of the general hospital and teaching hospital patients respectively. The combination therapy of insulin with an oral agent was prescribed rarely in both hospitals; even when prescribed, it is in combination with a sulfonylurea.

The use of antihypertensive drugs was more prevalent among patients without diabetes than those with diabetes in both populations [general hospital 202(19.4%) Vs 28(2.7%) and in the teaching hospital 129(20.4%) vs 27(4.3)%, $p < 0.0001$]. Among the patients without diabetes treated with a single antihypertensive drug. Diuretics 61(37.2%), methyldopa 59(29.2%) and propranolol 32(15.9%) were prescribed most frequently in the general hospital, whereas diuretics 46 (35.6%), nifedipine 39(30.2%) and aldomet 25(19.3%) were frequent choices in the teaching hospital. In the group with diabetes, propranolol 9(32.1%) and centrally acting drugs 9(32.1%) were used slightly more commonly than diuretics 5(17.8%), and calcium channel blockers 5(17.8%) in the general hospital. The choice of diuretics was limited in the two hospital settings.

Conclusions: The prescription pattern of antidiabetics and more importantly antihypertensives is still at variance with established guidelines in these hospitals.

KEYWORDS: Prescription Profile, Antidiabetics, Antihypertensives.

INTRODUCTION

Diabetic Mellitus is the commonest metabolic disease encountered in Nigeria¹ as in many parts of the world^{2,3}. The national prevalence in Nigeria is 2.2% with the highest prevalence rates found in Lagos Mainland (7.2%) and Lagos Island (4.7%) while the lowest prevalence rates were seen in Mangi, Plateau State (0.6%) and Ibadan, Oyo State (1.5%). It affects 3% of the population in the western countries⁴. Currently, the leading cause of end state renal disease in the United States, Japan and in most industrialized Europe is type 2 diabetes mellitus accounting for nearly 90% of all cases of diabetes⁵. However, hypertensive renal damage is the main cause of end state renal disease in black populations both in the western countries⁶ and in West Africa^{7,8}. Diabetes mellitus although on its own a major public health problem, it often co-

exists with a cluster of other potent cardiovascular risk factors including hypertension, dyslipidaemia and increased tendency for thrombosis, and increases the risk of early death from cardiovascular causes by about three fold⁹. Hypertension is the most common cardiovascular disease among Africans¹⁰. The national survey gave crude national prevalence ratio of 11.1% for men and 11.2% for women and age-adjusted rates of 9.2% and 9.3% respectively⁴. While the prevalence of hypertension in adults in the western countries has decreased during the past decade¹¹, that in black Africans has been reported to be on the increase¹⁰. There are close association between type 2 diabetes mellitus, hypertension and early mortality in these patients.¹²

In view of the potential adverse effects of diuretics and beta-blockers on carbohydrate and lipid metabolism^{13,14} angiotensin converting enzyme inhibitors and calcium-channel blocking agents are recommended as first-line treatment of hypertension in patients with diabetes^{15,16}

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Combination therapy of insulin with an oral hypoglycemic agent has been shown recently by a meta-analysis study¹⁷ to improve glycemic control in type 2 diabetics. Generally oral hypoglycemic agents are recommended apart from dietary therapy and weight control in treating type 2 diabetes¹⁸. Biguanides however have been recommended as the first-line treatment in obese patients with type 2 diabetes mellitus while the combined use of a sulfonylurea with biguanide is often synergistic because of the insulinogenic effects of the former and the beneficial effects of the later on insulin resistance¹⁸. Despite these recommendations, there have been only a few pharmacoepidemiologic studies examining the patterns of prescribing among patients with diabetes mellitus within the general population^{19, 20, 21}. Such data are important for identifying any discordance between published recommendations and clinical practice regarding the use of antidiabetic and antihypertensive drugs. The World Health Organization, as a measure of performance in pharmaceutical prescribing patterns²², endorses pharmacoepidemiologic studies. Data relating to the use of therapeutic agents other than those for diabetes allow the estimation of co-morbidities, for example cardiovascular diseases, in patients with diabetes¹⁹. These can be used to increase awareness among prescribers to identify priorities, or to quantify the impact of interventions²².

The aims and objectives of this paper are to investigate drug utilization in the management of diabetes mellitus and hypertension in Sagamu, Ogun state and its environment and to evaluate their agreement with established guidelines.

METHODOLOGY

Medical prescriptions on both diabetes and hypertension were collected over a period of two weeks at the Ogun state University Teaching Hospital and from a general (state) hospital in its environment. In both hospitals, drugs are usually dispensed directly from pharmacies located on the same site as the hospital so that prescription survey in these largely reflect the treatments for patients attending these healthcare institutions. Although patients with higher incomes use private hospitals predominantly, because medical insurance is not yet functional in Nigeria, the medical practitioners in the public sector treat many patients with hypertension and diabetes. The general hospital studied has about thirty medical beds with medical staff strength of three, mainly non-specialists. A visiting Consultant staff consults once every fortnight. The specialist hospital has about forty-five medical beds with two Consultant staff and two medical residents in training at any point in time. A patient is defined as having diabetes mellitus if the individual was prescribed one or more antidiabetic drugs, and as having hypertension if prescribed one or more cardiovascular drugs in a hypotensive dosage. The drugs used in the treatment of cardiovascular diseases were categorized according to the British National formulary²³, which are used by many medical practitioners as a quick reference. Seven classes of drugs were considered to have potential antihypertensive actions including diuretics, beta-blocking agents, calcium channel blocking agents, angiotensin converting enzyme inhibitors, vasodilators, alpha-adrenoreceptor antagonists and centrally acting drugs.

The medical staffs of the two hospitals were not informed of the survey to avoid possible bias because of a potential change in the physicians prescribing habits.

Statistical analysis was by using a chi-square test for proportions and students t-test for parametric data. A p-value of less than 0.05 was considered significant.

RESULTS

The study involved 1360 consecutive prescriptions from the medical unit of the general hospital and 1440 consecutive prescriptions from the teaching hospital (712 from the diabetic clinic and 728 from the hypertensive clinic). In the general hospital, the medical patients were not separated into different clinics. Table 1 shows the age and sex distribution, the duration for which the treatment was prescribed and the number of drugs on each prescription at the two study locations.

A total of 210 patients (15.4%), 1040 patients (76.5%) and 110 patients (8.1%) in the general hospital were prescribed one or more antidiabetic agents, antihypertensives and a combination of both respectively. They were considered respectively to be diabetic alone, hypertensive alone and combined diabetic and hypertensive. Similarly in the teaching hospital a total of 330 patients (22.9%), 633 patients (43.9%) and 477 patients (33.1%) were considered respectively to be diabetic alone, hypertensive alone and combined diabetic and hypertensive. The pattern of use of antidiabetic drugs in the two populations is summarized in Table 2. Majority for the diabetic patients in both populations were treated with oral agents [327(99.1%) in the general hospital population and 696(95%) in the teaching hospital population] in the form of sulfonylurea mainly (monotherapy or combined with biguanides - particularly in the teaching hospital population). Glibenclamide was the most common choice of sulfonylurea in both locations. Metformin was used alone and also usually in combination with a sulfonylurea. Ninety diabetics (28.3%) in the general hospital were treated with two sulfonylureas compared to 10(1.4%) in the teaching hospital population. There was a significant difference in the use of the long-acting sulfonylurea (chlorpropamide) between patients below and above age 65 years at the teaching hospital (68.8% vs 21.2%) as against the situation in the general hospital (55.1% vs 54.5%), $p < 0.001$. Insulin therapy was prescribed more commonly in the teaching hospital than in the general hospital; combination therapy of oral hypoglycemic agents with insulin was prescribed to only 10 (1.4%) patients attending the specialist hospital and none in the general hospital population.

There were 1040 (76.5%) patients in the general hospital and 633(43.9%) patients in the specialist hospital been treated with antihypertensive drugs. Among these patients, the use of antihypertensive drugs was more prevalent among patients without diabetes than those with diabetes in both populations [general hospital 202(19.4%) Vs 28(2.7%) and in the teaching hospital 129(20.4%) vs 27(4.3)% $p < 0.0001$]. Table 3 shows the pattern of use of antihypertensive drugs as monotherapy in both populations. Among the patients without diabetes treated with a single antihypertensive drug, diuretics 61(37.2%), methyl dopa 59(29.2%) and propranolol 32(15.9%) were prescribed most frequently in the general hospital, whereas diuretics 46(35.6%), nifedipine 39(30.2%) and aldomet

25(19.3%) were frequent choices in the teaching hospital. In the group with diabetes, propranolol 9(32.1%) and centrally acting drugs 9(32.1) were used slightly more commonly than diuretics 5(17.8%), and calcium channel blockers 5(17.8%) in the general hospital whereas calcium channel blockers 15(55.5%) were preferred in the teaching hospital. The choice of diuretics was limited in the two hospital settings. Indapamide, a metabolically neutral thiazide diuretic was not used at all in both hospitals.

DISCUSSION

Limitation of Study: The study excludes diabetics in the study population whose diabetes is controlled by diet alone. Nevertheless, the ease of a prescription-based approach enabled the survey of a fairly large number of patients.

Use of Antidiabetic Drugs: During the period under study, patients attending both hospital were of about the same average age but those attending the specialist hospital received fewer drugs than the other group suggesting that polypharmacy might be a common practice in the latter setting. It has been observed that 10% of general practitioners engage in polypharmacy²⁴. In both settings, most diabetics were of the type 2 type, been treated with oral agents - sulfonylureas been prescribed more commonly than biguanides. This is in accordance with the preponderance of type 2 diabetes mellitus in the local populations²⁵. In both populations, over 50% of the diabetics were treated with glibenclamide, resulting from its long history of clinical use and the lower cost of its generic formulations. The use of long-acting sulfonylureas such as chlorpropamide is associated with an increased risk of hypoglycemia, especially in the elderly and those with impaired renal function²⁸. In these patients, shorter acting sulfonylureas such as glicazide and glipizide are preferred. About 90(27.3%) of the patients in the general hospital were on two sulfonylureas - a combination that does not offer additional therapeutic advantage but increase the possibility of adverse effects and complicates the patients' drug regime. The preference for metformin in obese type 2 diabetics¹⁸ appears to be abided within the specialist hospital population, although the weights of these patients were not documented. In contrast to the common use of combination therapy of metformin and sulfonylureas, metformin monotherapy is more commonly prescribed especially in the teaching hospital setting.

Insulin was prescribed to 3(0.9%) and 16(2.2%) of the general hospital and teaching hospital patients respectively. This may be due to higher prevalence of type 2 diabetes mellitus. However, more than 50% of patients with type 2 diabetes mellitus will require insulin treatment as a result of progressive pancreatic beta-cell failure²⁸. The addition of an oral agent, mainly sulfonylureas to therapy of patients with insulin improved glycemic control²⁷. Furthermore, supplementing insulin, often given at bedtime to suppress nocturnal hepatic glucose production while oral agents are continued, is associated with a lower insulin requirement and less weight gain than in insulin monotherapy²⁷. Despite these

potential advantages, this survey showed that the combination therapy of insulin with an oral agent was prescribed rarely, even in the specialist hospital setting. Even when prescribed, it is in combination with a sulfonylurea. Considering the beneficial effect of metformin on insulin resistance, it is recommended that metformin-insulin treatment should be encouraged compared with sulfonylurea - insulin treatment.

Use of Antihypertensive Drugs: The choice of antihypertensive when prescribed as monotherapy was different in the two settings and varied with the co-existence of diabetes. In the group without diabetes, diuretics, centrally acting drugs (mainly methyldopa) and betablockers were the most popular choices in the general hospital whereas diuretics and calcium channel blocks often were used as monotherapy in the specialist hospital. In view of the beneficial effects of diuretics and beta-blocker on long-term mortality mainly because of a reduction in incidence of stroke^{28, 29}. These two classes of drugs are widely recommended in the treatment of hypertension. However, beta-blockers are not very effective amongst blacks because of the low renin status³⁰. The popularity of methyldopa and the lack of use of angiotensin converting enzyme(ACE) - inhibitors and calcium channel blockers in the general hospital may reflect the costs of these preparations, which is an important factor in the choice of treatment in this environment. The use of diuretics and beta-blockers has been shown to precipitate diabetes in predisposed individuals or worsen glycemic control in patients with diabetes^{6, 7}. Apart from their effect of reducing counter-regulatory responses leading to hypoglycemic unawareness, beta-blockers may worsen glucose tolerance because of inhibition of beta-mediated insulin release from the pancreatic islets³¹. Therefore, calcium - channel blocking agents and ACE inhibitors are now recommended as first-line antihypertensive treatment in patients with diabetes^{8, 16}. The non-availability of in dapamide expose the patients to the deleterious effects of the other non-metabolically neutral diuretics available.

In conclusion, the vast majority of patients with diabetes mellitus in this environment are treated with oral agents; glibenclamide is the most commonly prescribed sulfonylurea. This is the case irrespective of age in the general hospital. The use of combination therapy (insulin and oral agent) is not a common practice. In patients without diabetes, diuretics, methyldopa and propranolol were used extensively as antihypertensive monotherapy in the general hospital whereas diuretics, calcium channel blockers and methyldopa were prescribed frequently in the specialist hospital. The prescription pattern of antidiabetics and more importantly antihypertensives is still at variance with established guidelines in these hospitals.

Despite some limitations, prescription based surveys are a simple method of documenting both the magnitude of common diseases in a health care - sector and the pattern of drug usage. In view of the common use of these drugs, studies are required to correlate these findings with clinical outcomes and cost effectiveness.

Table 1: Age Gender And Prescription Pattern (duration And Number Of Drugs) In The Populations Studied

	GENERAL HOSPITAL			SPECIALIST HOSPITAL		
	M	F	TOTAL	M	F	TOTAL
NUMBER	309	970	1360	520	920	1440
*AGE (years)	62.9±28.7	57.7±27.3	59.9±26.5	61.7±29.3	59.7±16.3	60.9±18.2
*DURATION OF PRESCRIPTION (Weeks)	6.8±1.8	6.3±1.2	6.5±1.5	4.2±0.9	4.8±0.8	4.5±0.8
*NUMBER OF DRUGS ON EACH PRESCRIPTION	5.2±1.1	6.1±1.5	5.6±1.3	4.4±1.8	4.3±1.6	4.3±1.7

*Mean±SD

Table 2: Use Of Antidiabetic Agents

DRUG THERAPY	GENERAL HOSPITAL (N=330)			SPECIALIST HOSPITAL (N=712)		
	N	%	Daily Dose (mg)*	N	%	Daily Dose*
Glibenclamide	220	66.7	10 (2.5-15)	380	53.4	15 (2.5-20)
Chlorpropamide	80	24.2	500 (250-500)	100	14.0	375 (250-500)
Metformin	90	27.3	1000 (500-1500)	320	44.9	1000 (250-500)
Insulin	3	0.9		6	0.8	
Glibenclamide + Chlorpropamide	90	27.3		10	1.4	
Glibenclamide + Metformin	80	24.3		300	42.1	
Chlorpropamide + Metformin	10	3.0		6	0.8	
Insulin + Biguanide	0	0		0	0	
Insulin + Sulfonylurea	0	0		10	1.4	
Others	0	0		0	0	

* median (range)

Table 3: The Pattern Of Use Of Antihypertensives As Monotherapy In Both Populations (with And Without Diabetes)

DRUG CLASS	GENERAL HOSPITAL				SPECIALIST HOSPITAL			
	DIABETES + HYPERTENSION		HYPERTENSION ONLY		DIABETES + HYPERTENSION		HYPERTENSION ONLY	
	N	%	N	%	N	%	N	%
INDAPAMIIDE	0	0	0	0	0	0	0	0
LASIX	0	0	1	0.5	1	3.7	6	4.6
MODURETIC	5	17.9	61	37.2	2	7.5	46	35.6
ALDOMET	4	14.3	59	29.2	4	14.8	25	19.3
BRINEROIN	5	17.9	20	9.9	1	3.7	3	2.3
PROPANOLOL	9	32.1	32	15.9	0	0	1	0.7
ATENOLOL	0	0	0	0	0	0	1	0.7
NORVASC	0	0	0	0	3	11.1	0	0
NIFEDIPINE	5	17.9	20	9.9	12	44.4	39	30.2
ZESTRIL	0	0	4	1.9	3	11.1	6	4.6
ENALAPRIL	0	0	2	1	0	0	0	0
CAPTOPRIL	0	0	2	1	1	3.7	2	1.5
HYDRALLAZINE	0	0	1	0.5	0	0	0	0
	28	100	202	100	27	100	129	100

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