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A TRANSITION IN ANTIHYPERTENSIVE MEDICINES PRESCRIBED FOR OUTPATIENTS AT TEACHING HOSPITALS

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ABSTRACT

ACEIs are often prescribed at the lowest rates in previous studies about the use of antihypertensive medications. As long as ACEIs are used appropriately in the black population, they can provide additional cardio- and renal protection benefits. This research is to understand the recent trend of usage of antihypertensive medicines, particularly ACEIs, so as to identify potential changes. The current use of antihypertensive medicine was assessed in 150 randomly selected patients in a 450-bed premier teaching hospital. Among the 150 random cohorts, 119 females (78%) had an average age of 55.7 years. Hypertension was diagnosed in 53.33 percent of cases. From 7.59% and 22%, respectively, to 26.39% and 35.86% (p 0.001), the usage of ACEIs and long-effective CCBs (amlodipine) increased. During the first two months of the study, thiazide diuretics were used 38.04 % and 22.03% less than during the previous year ($p<0.0001$). ACEIs cause 2 % of adverse drug reactions, while the urea, creatinine and the serum potassium level are only monitored in 35% of cohorts. A total of 26% of cohorts showed potentially harmful interactions between drugs, the most common being ACEIs with NSAIDs (52.03%) and ACEIs with amiloride / hydrochlorothiazide (21.69%). A lot of antihypertensive medicines are now being used in combination with dihydropyridine CCBs and ACEIs. Methyldopa and thiazides are no longer widely used. There appeared to be a greater awareness of long-term benefits of ACEIs in a high-risk group such as black hypertensives.

Keywords: ACE-Inhibitors, Calcium-channel blockers, Anti-hypertensive agents, Heart disease.

INTRODUCTION

Strokes and cardiac disorder are more likely to occur in humans with untreated or badly treated hypertension [1-3]. Hypertensive patients can control their blood pressure with antihypertensive medications that are safe, effective, and convenient [4-6]. Although malignant hypertension is prevalent by 10% in both rural and urban areas, fewer patients are aware of it. In hospitalized patients, end organ damage often results in chronic complications that are detected late [7,8].

We conducted a study and published it about 10 years ago showing a consistent trend in the prescribing of antihypertensive medications [9]. Thiazide diuretics are often prescribed as the most common antihypertensive medications, followed by dihydropyridine calcium channel blockers and methyldopa as a centrally acting agent.

There was a time when angiotensin-converting enzyme inhibitors and angiotensin receptor blockers were rarely used to treat hypertension during that period [10-14]. The most commonly prescribed antihypertensive medications, about ten years ago, were ACEIs and beta blockers [9]. It has been reported that ACEIs reduce blood pressure relatively less than other ACEIs, especially when used as monotherapy, among Black patients. [15]. ACEI responses that are race-blind are controversial, however, because they are affected by factors such as age and body mass index. Since patients who delay seeking treatment, have comorbid illnesses such as diabetes, and lack equitable access to functional health care, they are more likely to develop high entry/baseline blood pressure levels and severe hypertension. Besides lowering blood pressure, Cardiovascular health can be improved when ACEIs and thiazide diuretics are taken together in appropriate doses. As a result, ACEIs appear to provide benefits beyond just reducing blood pressure. Furthermore, black hypertensive patients are more likely to develop malignant hypertension, chronic kidney disease, left ventricular hypertrophy, congestive heart failure, and ischaemic heart disease as a result of adverse cardiovascular and cerebrovascular events. However, ACEIs are still rarely prescribed for black hypertensive patients despite their therapeutic benefits. The study examined whether ACEIs were being used more frequently in the current antihypertensive landscape by examining their usage frequency.

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METHODS

The Medical Outpatient Clinic Hospital conducted a cross-sectional study to assess how antihypertensive medicines were utilized by 150 randomly selected hypertensive patients. 450 beds are available in this premier teaching hospital with medical residents.

Research and ethics committees at a university approved and cleared the study protocol. The study sample frame included all hypertensive patients at the study site who attended Medical Outpatient Clinics during the study period. The weekly Hypertension clinic saw an average of 45 patients per week. Following the collection of clinic appointment cards and seating of patients in the waiting area, patients were selected for clinic appointments. From the collected pool of clinic appointment cards, 38 were randomly selected each week. Data extraction was conducted after consulting with physicians regarding 38 case notes. Analyzing 150 case notes of randomly selected patients was conducted using pretested data collection instruments. To test completeness and relevance of data collection, ten case notes from study participants were used to pre-test the instrument's first draft. Pre-testing results were incorporated into the final draft of the instrument, but the results of the pre-testing were not included. Case notes were used to collect data:

1. Hospital number, age, and gender of patients
2. Readings of the diastolic and systolic blood pressure during your first visit to the clinic.
3. The last clinic attendance's diastolic and systolic blood pressures
4. Diagnosis and management of coexisting diseases related to hypertension.
5. Prescription of ACEIs and ARBs for hypertension.
6. ARBs and ACEIs adverse drug reactions identification and documentation
7. HbA1c, urea, and creatinine testing at baseline and follow-up
8. The cost of antihypertensive drugs and ACE inhibitors and ARBs on a monthly basis.
9. Interactions and contraindications between drugs

At the last clinic visit, the systolic and diastolic blood pressure readings should be less than 130/85 mmHg to determine whether blood pressure has been adequately controlled. [23]. By using the British National Formulary, we assessed the appropriateness of antihypertensive drug doses, intervals of administration, and possible interactions between drugs [24]. An analysis of the data was performed using descriptive and chi-square statistics using Statistical Program for the Social Sciences (SPSS) version 15.0 with a significance level of p0.05 considered significant.

RESULTS

A random cohort of 150 participants had the following clinic-demographic characteristics, as shown in Table 1. In the study cohort, 119 females had a mean age of 55.7 years (78%) and the majority were females (68%). Of the hypertensive patients, 54% had stage 2 hypertension and 27.33% had stage 1 hypertension while 18.66% had isolated systolic hypertension. There were 20.83 percent of patients with diabetes mellitus and 31.94 percent of patients with osteoarthritis coexisting. Blood pressure control appears to be adequate based on the results of the cohort study. A calcium channel blocker and an ACEI were the most commonly prescribed antihypertensive medicines. Diuretics, centrally acting agents, and angiotensin II receptor blockers (ARBs) were the types of medications prescribed to the cohort. ACEIs and calcium channel blockers were the most commonly prescribed medications, amlodipine and ramipril. Amiloride/hydrochlorothiazide combination represented 85.45% of thiazide diuretics, whereas losartan accounted for 93.56% of ARBs. As far as aldosterone antagonists and beta blockers were concerned, methyldopa, atenolol, and spironolactone were the only drugs prescribed.

Non-antihypertensive medicines that were most frequently prescribed on non-hypertensive patients were aspirin, clopidogrel, and non-steroidal anti-inflammatory drugs (NSAIDs). Each patient paid for his or her medicines out of pocket. There were no contraindications reported among the cohort studied concerning the doses and dosing intervals of antihypertensive and nonantihypertensive medicines. In cohort, only dry cough was documented as an adverse drug reaction (ADR) caused by ACE1s. ARBs were not documented to have an adverse reaction. Cohorts of participants were monitored for potassium, urea, and creatinine levels. The parameters were tested at both baseline and follow-up for these studies. Cohorts' study identified potential drug-drug interactions that could be harmful. ARBs + amiloride/hydrochlorothiazide and ARBs + spironolactone were listed in table 2 as the most common dangerous interactions between ACEIs and NSAIDs, ACEIs + amiloride/hydrochlorothiazide, and ACEIs + spironolactone.

Table 1: Clinic and demographic profile of hypertensive patients

Age (years) (n = 150) Mean age male Mean age female		 65.69 55.7
	n	%
Gender (n = 150) Female Male	 119 31	 78 22
Hypertension diagnoses		

Stage 2 hypertension	81	54
Stage 1 Hypertension	41	27.33
Isolated Systolic Hypertension	28	18.66
Co-morbidity (n = 72)		
Osteoarthritis	23	31.94
Malaria	17	23.61
Diabetes mellitus	15	20.83
Peptic ulcer disease	4	5.55
Congestive heart failure	4	5.55
Asthma	3	4.16
Psychosis	1	1.38
Impaired vision	1	1.38
Renal dysfunction	1	1.38
Stroke	1	0.69
Left ventricular hypertrophy	1	0.69
Benign prostatic hyperplasia	1	0.69
Laboratory monitoring tests (n = 150) (electrolytes, urea and creatinine levels)	95	63.33
None baseline only	52	34.66
Baseline & follow up	3	2.0
Cost of anti-hypertensive medicines		N 1,782.71
Mean monthly cost of anti-hypertensive medicines mean monthly cost of ace inhibitors		N 1,121.53

Table 2: Pattern of use of antihypertensive and non- antihypertensive drugs

Antihypertensive drugs (n = 304)	**Number**	**%**
Calcium channel blockers (n=112)		36.84
Amlodipine	88	78.57
Nifedipine	24	21.42
Ace inhibitors (n=91)		29.93
Ramipril	50	54.94
Lisinopril	29	31.86
Enalapril	12	13.81
Thiazide diuretics (n=49)		16.11
Amiloride + hydrochlorothiazide	43	87.75
Hydrochlorothiazide	6	12.44
Centrally acting agents (n=30)		9.86
Methyldopa	30	100
Arb (n=10)		3.28
Losartan	9	90
Valsartan	1	10
Beta blockers (n=6)		1.97
Atenolol	6	100
Aldosterone antagonist (n=6)		1.97
Spirinolactone	6	100
Non-antihypertensive medicines (n=180)		
Aspirin	48	26.66
Clopidogrel	32	17.77
Diclofenac	18	10.0
Artemeter + lumefantrine	18	10.0
Metformin	14	7.77
Glucosamine + chondroitin	7	3.88
Glimepiride	7	3.88
Anxiolytics	7	3.88
Calcium lactate	5	2.77
Neurobion	5	2.77

Meloxicam	4	2.22
Mist.magnesium trisilicate	3	1.66
Glibenclamide	3	1.66
Orphenadrine	2	1.39
Pioglitazone	2	1.11
Antipsychotics	2	1.11
Omeprazole	1	0.55
Digoxin	2	1.11

DISCUSSION

We found that the frequency of dihyropyridine CCBs and ACEIs prescribed for antihypertensive treatment has increased in our study. Meanwhile, thiazide diuretics were used less frequently 37.24%, a significant downward trend. These findings contrast sharply with those we reported about 10 years ago about the use of anti-hypertensive medicines at this study site. According to the present study, ACEIs were among the least commonly prescribed antihypertensive medications 10 years ago, accounting for 7.9% of prescriptions; however, In terms of frequency of use, the number has increased to 27.8% ($p<0.0001$). These medications are prescribed more frequently to black hypertensives as a result of clinicians' awareness of the long-term cardiovascular and renal benefits associated with ACEIs. Despite this, we believe it is necessary to carry out more research to identify the factors behind this increase in the use of ACEIs. When individuals have co-morbid conditions such as diabetes, thiazide diuretics are inappropriate as first-line antihypertensive drugs. According to the landmark trial Anti-hypertensive and Lipid lowering Treatment to Prevent Heart Attack (ALLHAT), which recommended thiazides as a first-line treatment for hypertension, thiazides caused a greater incidence of hypokalemia, hyperglycemia, and diabetes mellitus than ACEIs, ARBs, and CCBs. Thiazides have also recently been linked to an increased risk of new-onset diabetes mellitus, while ACEIs and ARBs have a lower rate. Hypokalemia associated with thiazide is also associated with insulin resistance and poor glucose utilization. Even though this biochemical derangement is well documented, the long-term macro- and microvascular consequences may not be readily apparent due to the duration of follow-up. Anti-hypertensive medicines are now prescribed differently from in the past and they appear to be scientifically proven to be effective short- and long-term. When hypertension patients are treated in this way, they are more likely to achieve optimal therapeutic outcomes. As a result, the use of methyldopa declined dramatically as affordable generic versions of anti-hypertensive medicines became more widely available with relatively better safety profiles. Furthermore, the negative impact of low patient adherence on cardiovascular outcomes may also contribute in a high risk group such as Nigerian hypertensives who take medicines with poor adverse reactions profiles.

In our report ten years ago, we noted that Nigeria does not have an effective system to monitor, prevent, detect, and document adverse drug reactions. There is therefore an association between ACEIs and ARBs and adverse drug reactions. There is no reliable system for detecting and documenting ADRs, despite the fact that they are not often reported. ACEIs and ARBs were administered to most of the patients in clinical trials without adequate laboratory monitoring of pertinent laboratory parameters like potassium, urea, and creatinine. This supports our position. Through laboratory parameters relevant to drug-drug interactions, many patients were identified as potentially impacted by drug-drug interactions. In about half of the cohorts, NSAIDs and ACEIs were co-prescribed without close monitoring necessary to prevent potential harm to patients. As well as being well documented, ACEIs and thiazide diuretics have a reduced antihypertensive effect when prescribed with NSAIDs on a chronic basis. In spite of this, it is not readily apparent to what extent these drug-drug interactions contribute to low blood pressure control among the cohorts studied. A high frequency of ACEIs being prescribed in conjunction with potassium-sparing diuretics, such as amiloride with hydrochlorothiazide, or aldosterone antagonists, such as spironolactone, may result in negative cardiovascular events associated with hyperkalemia, especially if serum potassium and creatinine levels were not monitored adequately at baseline and at follow-up.

Since the study was conducted at a tertiary hospital, the result of this study is limited. Although the choice was based on quality and reputation, it is also a major referral center for other healthcare facilities. Additionally, a major part of its mission is to train physicians during their undergraduate and postgraduate years, respectively. Therefore, physicians in other parts, or settings, were also considered as determining factors of clinical practices and prescription habits. In chronic medical conditions such as hypertension, monitoring patients' progress and long-term outcomes was almost impossible without an integrated functional monitoring and documentation system. Moreover, female patients tended to be selected more often. In epidemiological studies, a mid-year random sample strategy may mitigate probable selection bias, since it is a valid procedure. Furthermore, the pattern of distribution observed may suggest that female hypertensive patients are likely to regularly attend clinics for hypertension management or seek medical treatment in relatively greater proportions at the study site based on the distribution pattern observed. Future research should address this issue.

CONCLUSIONS

It appears that physicians are prescribing ACEIs more frequently, dihydropyridine CCBs longer acting, and thiazide diuretics and methyldopa less frequently as antihypertensive medicines. ADRs are not thoroughly detected and documented as a result of baseline and follow-up monitoring of relevant laboratory parameters.

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