

# CHOICE OF ANTIHYPERTENSIVE MEDICATIONS AMONG PHYSICIANS AND ITS IMPACT ON BLOOD PRESSURE CONTROL AMONG NIGERIANS LIVING WITH HYPERTENSION

<sup>1</sup>Mijinyawa Muhammad Sani, <sup>1</sup>Yusuf Mohammed Shehu, <sup>1</sup>Mohammed Hamza,  
<sup>2</sup>Saidu Hadiza, <sup>3</sup>Sulaiman Balarabe Aminu, <sup>1</sup>Uloko Andrew E.

<sup>1</sup>Department of Medicine, Bayero University, Kano, Nigeria & Department of Medicine, Aminu Kano Teaching Hospital, Kano Nigeria.

<sup>2</sup>Department of Medicine, Bayero University, Kano, Nigeria & Department of Medicine, Murtala Mohammed Specialist Hospital, Kano, Nigeria.

<sup>3</sup>Department of Medicine, Aminu Kano Teaching Hospital, Kano, Nigeria.

## ABSTRACT

### BACKGROUND

Hypertension, if untreated or uncontrolled, leads to damage of vital organs such as the brain, heart and the kidneys among others. These complications have been shown to be severer in black Africans. Benefit of treatment has been repeatedly demonstrated by many studies. Therefore, many guidelines have been produced by relevant bodies in different countries in order to assist physicians in making the right choices for blood pressure (BP) control. Most of these bodies produce the guidelines based on the peculiarities of hypertension in their respective population. Several reports have shown how different hypertension is, in black Africans, still there is no published unified guideline for its treatment in this population.

### METHODS

This was a survey of known hypertensives who were on follow up visit. Their prescriptions were assessed for drug name, class and number. Their blood pressures at that visit were also recorded. Prevalence of single therapy and combination therapy were determined. Compliance with the AHA recommended 2 – drug combination was determined. The percentage of BP control as well as the prescribed drugs in each group were also obtained.

### RESULTS

Those on single agents were 13% out of which 52% were controlled. 87% were on various combination of 2 or more drugs of whom 41.9% of those on 2 drugs and 21.1% of those on more than 2 drugs had controlled BP. BP control in those on 2 drugs was better than in those with > 2 drugs, ( $p=0.0027$ ). ACEI were the commonest used drug either as single agent (55.9%) or as 2 – drug combination as seen in 54.8% of the subjects on 2 – drug combination. 13 different 2 – drug combinations were identified with the best control in ARB + Diuretic, ACEI + Diuretic and CCB + Diuretic. The least control was observed in the ACEI + CCB group. Compliance with AHA recommendation was good but still 7.7% were under unacceptable group while another 7.7% were unclassified.

### CONCLUSION

ACE-Is are becoming the drugs of choice both as monotherapy and as combination therapy. Despite good compliance to AHA recommendation on drug combination, overall control is still a problem which calls for a revisit of these recommendations in Africans.

**KEY WORDS:** Antihypertensives; Physicians; Impact; Blood Pressure; Nigerians.

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## INTRODUCTION

**H**ypertension if untreated or uncontrolled, leads to damage of vital organs such as the brain, heart and kidneys among others.<sup>1</sup> With about one billion people affected, hypertension (HTN) is the most prevalent Cardio-Vascular Disease (CVD)

that contributes to cardiovascular morbidity and mortality world-wide.<sup>2</sup> Complications of HTN have been shown to be severer in black Africans.<sup>3</sup> Benefit of treatment has been repeatedly demonstrated by many studies.<sup>4,5</sup> However, treatment of HTN in several regions of the world remains suboptimal due to various barriers pertaining to the patient, to the health care professionals or to the health system. Many guidelines have been produced by relevant bodies in different countries in order to assist physicians in making the right choices for blood pressure (BP) control.

**Correspondence:** Dr. Andrew E. Uloko,

Associate Professor of Medicine and Consultant Physician, Department of Medicine, Bayero University, Kano, Nigeria & Aminu Kano Teaching Hospital, Kano Nigeria.

**Email:** andyuloko@yahoo.com **Mobile Phone:** +2348037037749

Most of these bodies produce the guidelines based on the peculiarities of hypertension in their respective population. Several reports have shown how different hypertension is, in black Africans<sup>6,7</sup>, but still there is no published guideline for effective treatment of hypertension in this population. This study therefore seeks to find the pattern of prescription for hypertension and its impact on BP control in Nigerians with hypertension.

## METHODS

This was a cross sectional study in which consecutive patients who attended the cardiac clinic of Aminu Kano Teaching Hospital, for follow up visit were recruited for the survey. Information on their personal data like age, sex and duration of hypertension were obtained. Their prescriptions were assessed to check the number of drugs, name of the drug(s), and class of the drug(s). Their blood pressures at that visit were also obtained and recorded. Prevalence of single therapy and combination therapy were determined. The percentage of BP control in each group was also determined. The commonest prescribed antihypertensive as well as the commonest 2 - drug combination were found. BP control in these groups was also assessed. Compliance with the American Society of Hypertension (ASH) recommended 2 - drug combination<sup>8</sup> was also determined.

The statistical analysis was carried out using Statistical Package of Social sciences (SPSS) version 16.0 software. Frequencies, ranges, and means with standard deviations were used to describe patients' characteristics where appropriate. Chi-squared, Fisher's exact, and Student's t tests were used to compare categorical and continuous variables as appropriate. A statistical significance was set at the conventional  $p < 0.05$ .

## RESULTS

A total of 331 subjects completed the study comprising of 128 males and 203 females (sex ratio 1:1.6). The mean duration of hypertension in the study subjects was  $8.49 \pm 7.17$  years. Their ages ranged from 18-85 (with mean of  $55.97 \pm 11$ ) years.

Those on single agents were only 43 (13.0%) out of the total subject number of 331. In this group, various Angiotensin Converting Enzyme Inhibitors (ACEIs) were the commonest prescribed anti-hypertensives as it was used in 24 of the 43 subjects (55.9%). This was followed by diuretics that was used in 16.3%, Calcium Channel Blockers (CCB) in 9.3%, Beta Blocker ( $\beta$ . Blocker) in 7.0%, centrally acting agent 7% and lastly Angiotensin Receptor Blocker (ARB) that was prescribed for 4.7%. Central alpha-2 receptor agonists, renin inhibitors and direct vasodilators are not among

the prescribed drugs as single agents in this study population.

The vast majority of the subjects, 288 (87.0%), were on various combination of 2 or more drugs, out of which 155 were on 2 drugs, 112 were on 3 drugs and 21 on various 4 drug combinations. A total of 13 different two drug combinations were observed. As with the drug of choice in those on single drugs, ACEIs were the most frequently used agent in two drug combination. It was observed to be used in 85 of the 155 subjects (54.8%). Table 1 shows the frequency of the various combination therapies.

Of the various 2 drug combinations that were observed in this study, 53.6% fell under the "preferred" 2-drug recommendation of the American Society of Hypertension (ASH) recommendation, 31% fell under "acceptable" recommendation, 7.7% were under "less effective" group while another 7.7% were combinations that were not classified in the ASH recommendations.

Table 1: The Various Combination Therapies in the study population

S/No	Combination Therapy	Number	Percentage (%)
1	ACEI & Diuretics	53	18.4
2	ARB & Diuretics	6	2.1
3	ACEI & CCB	22	7.6
4	ARB & CCB	2	0.7
5	$\beta$ . Blocker & Diuretic	7	2.4
6	CCB & Diuretic	42	14.6
7	ACEI & $\beta$ . Blocker	7	2.4
8	ARB & $\beta$ . Blocker	1	0.3
9	CCB & $\beta$ . Blocker	4	1.4
10	Diuretics & Centrally Acting	5	1.8
11	ACEI & Centrally Acting	3	1.0
12	ARB & Centrally Acting	1	0.3
13	CCB & Centrally Acting	2	0.7
14	3 Drug Combination	112	38.9
15	4 Drug Combination	21	7.3
<b>16</b>	<b>Total</b>	<b>288</b>	<b>100</b>

Abbreviations: ARB = Angiotensin receptor blocker; ACEI = Angiotensin Enzyme Inhibitor; CCB = Calcium Channel Blockers;  $\beta$  = beta as illustrated in table 2, the subjects that were on single drugs had better BP control while the participants on 2 drugs have a statistically significant higher chance of BP control than those on more than 2 drugs, ( $p = 0.0027$ ).

Table 2: Frequencies, and control status by number of drugs.

Number of drugs	Frequency	No. with controlled BP		No. without controlled BP	
		n	(%)	n	(%)
Single agent	43	22	(52.0)	21	(48.0)
2-drug combination	155	65	(41.9)	90	(58.1)
>2 drug combination	133	28	(21.1)	105	(78.9)

In those on 2 drug combination, the best control was seen in ARB & Diuretic group (Table 3), in which 3 of the 6 patients on this combination had their BPs under control (50%), this was followed by the ACEIs & Diuretic group in which control was seen in 24 of 52 (46.2%). In those on CCB & Diuretics, control was seen in 18 of the 42 (42.9%) subjects. A much lesser control rate of 9.1% was observed in the CCB combined with ACE-Is group.

Table 3: Types of 2 – drug combination therapies by BP control

S/No	Type of combination	Controlled BP		BP not Controlled		Total n (%)
		n (%)	n (%)	n (%)	n (%)	
1	ACEI/Diuretics	25 (47.2)	28 (52.8)	53 (100)		
2	ARB/Diuretics	3 (50.0)	3 (50.0)	6 (100)		
3	ACEI/CCB	2 (9.1)	20 (90.9)	22 (100)		
4	ARB/CCB	1 (50.0)	1 (50.0)	2 (100)		
5	β. Blocker/Diuretic	3 (42.9)	4 (57.1)	7 (100)		
6	CCB/Diuretic	18 (42.9)	24 (57.1)	42 (100)		
7	ACEI/β. Blocker	6 (85.7)	1 (14.3)	7 (100)		
8	ARB/β. Blocker	0 (0.0)	1 (100)	1 (100)		
9	CCB/β. Blocker	1 (25.0)	3 (75.0)	4 (100)		
10	Diuretic/Central Acting	1 (20.0)	4 (80.0)	5 (100)		
11	ACEI/Central Acting	2 (66.7)	1 (33.3)	3 (100)		
12	ARB/Central Acting	1 (100)	0 (0.0)	1 (100)		
13	CCB/Central Acting	0 (0.0)	2 (100)	2 (100)		
14	3-Drug Combination	23 (20.5)	89 (79.5)	112 (100)		
15	4-Drug Combination	5 (23.8)	16 (76.2)	21 (100)		
Total		94 (32.6)	194 (67.4)	288 (100)		

## DISCUSSION

There were 43 (13.1%) patients on single antihypertensive agent, while the majority, 86.9% were on combination of 2 or more anti-hypertensives. This seemingly high proportion of combination therapy is consistent the findings in other parts of Nigeria where the proportions were 80% in Sokoto,<sup>9</sup> and 73% in Ibadan.<sup>10</sup> This high proportion of patients on combination therapy suggests that most of our hypertensives have either moderate or severe hypertension, just in keeping with the knowledge that hypertension is severer in blacks. It may also be the result of compliance to current trends where combination therapy is advocated.<sup>11</sup> Angiotensin Converting Enzyme-Inhibitors were the most commonly used antihypertensives as a single agent as it was prescribed to 55.8% of those on single drug. This was followed by diuretics that was prescribed to 16.3%, then CCB had 7.0%, centrally acting agents had 7.0% and ARB 4.6%. This observation is different from those of earlier Nigerian reports in which diuretics were the most commonly prescribed single agents.<sup>9,10</sup> It is also different from other studies where CCB were found to be the most frequently prescribed single agents.<sup>12,13</sup> This shift of choice of single agent may be due to current knowledge of the advantages of ACE-Is in treating hypertensives with chronic kidney disease. Furthermore, more recent findings suggest that BP response to ACE-Is does not vary with patient's race but with individual factors such as age, body mass index, baseline BP readings and presence of Diabetes Mellitus.<sup>14,15</sup> Generally speaking, the choice of ACE-Is in our environment is commendable because hypertensives usually present late when cardiac and renal complications would have set in. It is not surprising that  $\beta$ -Blockers were the least prescribed as observed in this study because studies from other parts of Nigeria<sup>12,13</sup> made the same observations.

ACE-Is was also the most used agent in two drug combinations which was used in 85 of the 155 subjects on two drug combination (54.8%). Lisinopril was the ACE-I used in nearly all cases of single and combination therapies, because it is cheap and readily available. Combinations of ACE-Is and diuretics was the most prescribed combination. The choice of diuretics as an add-on can be due to the belief that hypertension in blacks responds more to this class of drugs than it does for other agents. Furthermore, it is believed that combination of ACE-Is with thiazide diuretics in black hypertensives results in improved BP control and target organ protection.<sup>16</sup> The above combination is among the preferred combinations recommended by the American Society of Hypertension (ASH),<sup>17</sup> 1996 Nigerian Society of Hypertension guideline<sup>18</sup> and 2014 South African Hypertension guidelines.<sup>19</sup> It is quite commendable to

find, from this study, that only a few patients (7.7%) were on the less effective 2 drug combinations based on ASH guidelines<sup>17</sup> and another 7.7% were on combinations that were not recognized by the ASH. This clearly indicates familiarity, acceptability and high level of adherence to the guidelines on combination of antihypertensives.

Our study has shown that patients on two drug combinations achieved higher BP control (41.9%) than patients on 3 or more drugs (21.1%), but the best control was observed in those on single agents (52%). This is probably due to the fact that patients on more than 2 drugs are the ones with high CVD risk with very difficult to treat BP, additionally, polypharmacy discourages patient compliance. This, therefore, points towards encouragement of developing fixed combination drugs which will potentially enhance patient compliance and perhaps better BP control. Putting all the patients of this study together, the proportion of those with controlled BP was 34.7%. This is not different from other reports from Nigeria<sup>9,20</sup> and other parts of the world<sup>21</sup> in which control rates were also low.

Among the patients on 2 drug combinations, the best control was seen in those on either ACE-Is or ARBs combined with diuretics, where control was achieved in 47.5%. This relatively high control rate when compared with reported control rates,<sup>9,20</sup> could be due to the fully additive BP reduction of the 2 classes of drugs used.<sup>22,23</sup> Diuretics cause intravascular volume depletion following which renin-angiotensin-aldosterone system (RAAS) becomes activated which then produces vasoconstriction. Addition of either ACE-Is or ARB therefore abolishes this counter-regulatory mechanism. A near similar control rate (42.9%) was observed in those on combination of CCB with diuretic. Though the control rate is not good enough, it is also higher than the overall control rate of 34.7% observed in the patients of this study and higher than that of other reports. The control rate in this group can partly be due to the overlap in the pharmacological properties of the 2 classes of drug which produces a partial additive BP reduction.<sup>24,25</sup> Diuretics cause increased renal sodium excretion so also CCB but to a lesser extent. It is also known that prolonged use of both classes of drugs lead to vasodilatation. The relatively low control rate that was seen in the CCB with ACE-Is group is quite surprising because this combination is supposed to also produce a fully additive BP reduction.<sup>26,27</sup> This unexpected finding may be due to the small number of the patients in this group (22). Additionally compliance to the drugs cannot be ascertained just like in all other groups with the various combination therapy.



## CONCLUSION

The results suggest that ACE-Is are the most prescribed agents both as monotherapy and as combination treatment. While BP control was better in those on single agent, it was observed to be more among those on either ACE-Is or ARB with diuretic in the patients on 2-drug combination. However, the control rates are still low despite compliance to AHA recommendation on drug combination. Overall, control is still a problem which calls for a revisit of these recommendations in Africans.

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