

ASSESSMENT OF ANTIHYPERTENSIVES UTILIZATION IN A PRIVATE TEACHING HOSPITAL IN NIGERIA

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ABSTRACT

Objectives: The study objectives were to assess comparability of mode of utilization of antihypertensives in the private teaching hospital with recommendations of JNC- 7 and to examine the patterns of prescription of antihypertensives.

Methods: Two hundred and fifty case notes of patients on antihypertensive drugs or hypertensive patients diagnosed after 2003 were randomly selected for evaluation. They were assessed for comparability with JNC-7 guidelines on hypertension management as well as prescription patterns of the antihypertensive drugs.

Data analysis was carried out using Microsoft excel and Statistical Package for Social Sciences (SPSS) 16.0 for windows. Presentation of data was by using descriptive statistics. Means of Systolic Blood Pressures (SBPs) and Diastolic Blood Pressures (DBPs) were compared using Student t-test. Categorical variables such as number of drugs prescribed (at diagnosis and last clinic visit) and number of patients in the various BP categories were reported as simple percentages. A P-value of 0.05 at two-tail test was considered significant.

Results: Two hundred and eight patients met the study criteria out of which 125 (60.1%) were males, while 83 (39.9%) were females. The mean diagnostic SBP and DBP were; 157.9±19.2 and 98.6±13.6, while last clinic visit values were; 132.2±18.6 and 84.9±12.1 respectively (P < 0.0001). The overall BP control was adequate in only 16.2% of the cohort. Most cases of hypertension were seen in patients with weights greater than 80kg (40.4%). The commonest co-morbid conditions were cardiovascular diseases (21.2%), followed by diabetes mellitus (13.9%). In majority of patients, average of three drug combinations was used for the initiation (41.8%) and maintenance (41.3%) of therapy.

Diuretics were the most prescribed drugs for therapy initiation and maintenance (49.8%, 46.9 % respectively) followed by calcium channel blockers (21.0%, 21.8%). Thiazides constituted the most prescribed of the diuretics (48.4%, 50.9%), while among the fixed dose combination groups, amiloride/hydrochlorothiazide was the most frequently prescribed both for initiation (94.4%) and maintenance (88.0%) of therapy.

Conclusion: JNC-7 guidelines were somewhat adhered to at the private teaching hospital and diuretics and calcium channel blockers were the most frequently utilized.

Keywords: Antihypertensives, Drug Utilization, JNC-7, Teaching hospital, Nigeria.

INTRODUCTION

Preventing and managing hypertension are collectively a major challenge in the art of patient care ¹ given that as at, year 2000, the total global estimate of adults living with the ailment was put at 972 million (333million in economically developed countries and 639 million in economically developing countries, Nigeria inclusive). The number of adults with high blood pressure in 2025 has been predicted to increase by 60% to a total of 1.56 billion. ²

However, limited data exist in Nigeria to give a clear picture of patterns of antihypertensives utilization and BP control. ³ This being the situation has greatly impeded progress in hypertension management in terms of making available requisite medications ⁴ by the necessary authorities using appropriate indicators. In spite of increase in public awareness about the importance of timely diagnosis of hypertension, improvement in cardiovascular disease rates have not followed in parallel. Though, many guidelines emphasize the importance of achieving optimal blood pressure particularly in high-risk patients such as those with diabetes, only a few of hypertensive patients have blood pressure controlled to the recommended target values. ^{1,4-6}

Nigeria is one of the (economically developing) countries where hypertension control has been slow despite the availability of a wide range of antihypertensive drugs to choose from. ^{2,7,8} This can be partly attributed to patient factors, non-affordability or non-availability of drugs, and inefficiencies in the health systems such as non-availability of national hypertension guidelines. ⁴ Bearing these shortcomings in mind, it is important to assess the patterns of antihypertensives' utilization in reputable health institutions in Nigeria such as the chosen private (teaching) hospital.

METHODS

It is a retrospective study conducted between 1st August to 30th November, 2011 in a private teaching hospital following approval by the hospital authority. The study centre is located in Ikeja, the capital of Lagos State, South West Nigeria. Two hundred and fifty case notes ⁹ of patients on antihypertensives or diagnosed with hypertension and attending the Medical Outpatient Clinic of the hospital were randomly selected using the patients' attendance register.

Only 208 of the selected case notes met the inclusion criteria which required that patients must be on at least an antihypertensive, and if hypertensive must be first diagnosed after 2003. This is because the JNC 7 and a number of other hypertension management guidelines came into focus in 2003. ¹⁰

The requisite patients' information was extracted and recorded using previously validated data collection form. These included: hospital number, age, gender, body weight, occupation, systolic and diastolic BP readings (at diagnosis and last clinic attendance), prescribed drugs and dosages (at diagnosis and last clinic attendance), co-morbid conditions, and number of drug change during study period.

The classification of hypertension in the study was based on JNC 7 guidelines. ¹ The pattern of antihypertensives prescribed in the studied population was observed and attention paid to whether patients were on mono-therapy or multi-therapy (multi-therapy, defined as two or more drug combinations).

Data analysis

Data analysis was carried out using Microsoft excel and Statistical Package for Social Sciences (SPSS) 16.0 for windows. Presentation of

data was by using descriptive statistics. Means of systolic blood pressures (SBPs) and diastolic blood pressures (DBPs) which are continuous variables were compared using Student t-test with the aid of GraphPad InStat version 3.10 for Windows, GraphPad Software, San Diego California USA, www.graphpad.com. Categorical variables such as number of drugs prescribed (at diagnosis and last clinic visit) and number of patients in the various BP categories were reported as simple percentages. A p-value of 0.05 at two-tail test was considered significant.

RESULTS

Table 1: Hypertensive cases in patients based on weight

Weight (kg)	N (%)
31-50	4 (1.9)
51-60	17 (8.2)
61-70	55 (26.4)
71-80	48 (23.1)
>80	84 (40.4)

N, number of subjects

At diagnosis, SBP of more patients were in either stage 1 (47.1%) or stage 2 (47.6%) hypertension categories, while for the DBP, proportions of stage 1 and stage 2 were 25.0% and 62.5% respectively.

There was a statistically significant reduction in SBPs and DBPs in all patients ($P < 0.0001$) with an overall success rate in combined BP reduction of 16.2% following commencement of antihypertensive

therapy (Table 2). After four months of the antihypertensive therapy review, only 16.4% of patients had their SBP well controlled. Fifty percent of patients had their SBP in pre-hypertension stage while 19.7% and 13.9% of patients were still in either stage 1 or stage 2 respectively. For the DBP, 27.9% and 17.8% of patients were still in stage 1 and stage 2 respectively, while 37.5% had their DBP in pre-hypertension stage and 16.8% in normal range (Table 2).

Table 2: Patients' Blood Pressure categorization

Classification of BP	Systolic Blood Pressure N (%)		Diastolic Blood Pressure N (%)	
	At diagnosis	At last clinic	At diagnosis	At last clinic
Normal	-	34(16.4)	8(3.8)	35(16.8)
Pre-hypertension	11(5.3)	104 (50.0)	18(8.7)	78(37.5)
Stage 1 hypertension	98(47.1)	41(19.7)	52(25.0)	58(27.9)
Stage 2 hypertension	99(47.6)	29(13.9)	130(62.5)	37(17.8)
Average BP*	157.9±19.2	132.2±18.6	98.6±13.6	84.9±12.1

*Average Blood Pressure, (Mean±SD), $p < 0.0001$, 16.2%.

Cardiovascular diseases such as angina pectoris, myocardial infarction, and heart failure (21.2%) were the commonest co-morbid conditions followed by diabetes mellitus (13.9%), asthma (0.5%) among others (Table 3).

Table 3: Co-morbid distribution in the studied population

Co-morbid state	N (%)
Nil	95 (45.7)
Cardiovascular diseases	44 (21.2)
Diabetes mellitus	29 (13.9)
Hyperlipidaemia	11 (5.3)
Arthritis	7 (3.4)
Peptic Ulcer Disease	5 (2.4)
Chronic Kidney disease	3 (1.4)
Asthma	1 (0.5)
Others	12 (5.8)

The antihypertensive drugs encountered in the study included Diuretics-D (Loop, Thiazide, and Potassium sparing diuretics), Beta-blockers-BB, Calcium channel blockers-CCB, Angiotensin converting enzyme inhibitors-ACEI, Angiotensin receptor blockers-ARB, Vasodilators-V, Alpha receptor blockers, Centrally acting agents-CAA and brinerdin® (containing reserpine, dihydroergocristine and clonamide).

An average of three-drug combination was used for the initiation (41.8%) and maintenance (41.3%) of therapy. Drug change was recorded at least once (38.5%) during the study period in most of the patients. A wide variety of drugs from different antihypertensive classes were prescribed for the patients both as single drug and as

fixed dose combinations. For the initiation of therapies, diuretics were the most prescribed antihypertensives at a rate of 49.8%, either as mono-therapy or in combination with other agents followed by CCBs (21.0%), ACEIs (10.3%), centrally acting agents (9.1%), BBs (8.4%), ARBs (0.8%), and alpha receptor blockers (0.4%), while vasodilators were rarely prescribed. The prescription pattern was not too different as at last clinic attendance with diuretics still remaining the most widely prescribed (46.9%) followed by CCBs (21.8%), and ACEIs (11.7%) (Table 4).

Among the fixed dose combinations, amiloride/hydrochlorothiazide was the most frequently prescribed both for initiation (94.4%) and maintenance of therapy (88.0%). (Table 4).

Further analysis of the diuretic class revealed the thiazides to be the most frequently prescribed at a rate of 48.4% for initiation and

50.9% for therapy maintenance, followed by the potassium sparing types (45.7%, 45.7%) and loop diuretics the least (5.9%, 3.4%).

Table 4: Pattern of utilization of different antihypertensive classes and some fixed dose combinations

Drugs	Therapy initiation N (%)	Last clinic visit N (%)
Diuretics	256(49.8)	269(46.9)
Beta blockers	43(8.4)	50(8.7)
Calcium channel blockers	108(21.0)	125(21.8)
ACEIs	53(10.3)	67(11.7)
ARBs	4(0.8)	25(4.4)
Vasodilators	0(0.0)	1(0.2)
Alpha receptor blockers	2(0.4)	4(0.7)
Centrally acting agents	47(9.1)	32(5.6)
Others (Brinerdin®)	1(0.2)	-
Fixed dose combinations		
Amiloride/hydrochlorothiazide	102(94.4)	103(88.0)
Atenolol/chlorthalidone	2(1.9)	3(2.6)
Lisinopril/hydrochlorothiazide	2(1.9)	2(1.7)
Candesartan/hydrochlorothiazide	1(0.9)	3(2.6)
Valsartan/hydrochlorothiazide	1(0.9)	6(5.1)
Grand total	108	117

ACEIs (Angiotensin converting enzyme inhibitors), ARBs (Angiotensin receptor blockers).

Brinerdin® contains reserpine, dihydroergocristine and clopamide

DISCUSSION

The study revealed a considerable rate of reduction in average BP of all the patients. However, the overall BP control was adequate in only 16.2% of the cohort. This low success rate is consistent with earlier reports^{4-7, 11} though in contrast to a finding reported elsewhere.¹² The unsatisfactory observation may be attributed to lateness in presentation for treatment by most of the patients and possibly non adherence to recommended drug and non drug therapies. Also, inefficiencies in the health system⁴ are factors to consider. To redress this situation, the health care providers, the care givers as well as the patients need to be encouraged to play their respective roles in ensuring that BPs are reasonably controlled to target values.

That more males were seen in this study contradicts previous reports^{10, 13, 14} and may imply a changing health seeking behavior between both sexes. Also, more cases of elevated blood pressures in patients with higher weights confirmed earlier observations.^{15, 16}

Cardiovascular diseases were the commonest co-morbid conditions encountered in this study in line with some studies^{17, 18} conducted outside Nigeria. This is however in contrast to observations made in Ibadan⁵ and Benin City¹⁰ in which diabetes mellitus was commonly seen. Whatever the case, these findings necessitate the need for proper patient evaluation for the presence or not of other disease conditions, and that hypertension should not be treated in isolation.

The frequent prescription of diuretics particularly thiazides as drug of first choice either as monotherapy or in combination therapy is similar to previous studies^{5, 19} and in conformation with the recommendation of the JNC-7.¹ Recommendation of JNC-7 posited that: "a thiazide-type diuretic must be part of the antihypertensive treatment, either alone or in combination." The pattern of antihypertensives utilization in this study reflects the use of low dose of a diuretic as the first choice, and addition of a second and (or) third drug depending on the level of BP control and the presence or not of compelling indications. This can be linked to the documented efficacy of diuretics in blacks and the frequencies of compelling indications, such as coronary heart diseases (CHDs) and diabetes mellitus observed in this study as previously reported.²⁰

Also, efficacy as well as intrinsic activities of the ACEIs, BBs and ARBs were exploited based on target BP requirements and observed co-morbid conditions. Their prescription patterns and frequencies were suspected to be due to their positive effects on renal function in hypertensive patients with diabetes (i.e. ACEIs and ARBs) and

cardiovascular and cerebrovascular functions^{20, 21} (i.e. ACEIs, ARBs and BBs).

It was noted that alpha-methyldopa was well prescribed in this study often in therapy initiations for the purpose of crashing very high BPs. The level of usage is however lower comparing to previous report in a public teaching hospital.⁵ The seemingly low rate of use of alpha methyldopa may be due to its side effects such as rebound hypertension, salt and water retention, weight gain, sexual dysfunction in men as well as severe depression in some patients.²²⁻²⁴ In addition, probable adherence to JNC-7 recommendations¹ by prescribers may also be a factor. The same is true for Brinerdin®-reserpine-based combination,⁵ vasodilator (hydralazine) and an alpha receptor blocker (prazosin) which was rarely used in this study.

The limitations of study include the fact that population of patients sampled may not be the true representation of hypertensive population in Nigeria since only one study centre was used; hence, caution needs to be exercised in generalizing the results. In addition private hospitals are profit oriented unlike public health institutions.

CONCLUSION

In conclusion, this study revealed that the JNC-7 guidelines were somewhat adhered to at the private teaching hospital with diuretics and calcium channel blockers being the most widely utilized agents, however overall BP control rate of 16.2% is very low and requires a lot of improvement in drug and non drug therapy management.

REFERENCES

1. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The 7th report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *JAMA* 2003; 289: 2560-71.
2. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet* 2005; 365: 217-23.
3. Salako BL. Blood pressure control in sub-Saharan Africans: a physician's perspectives. *Postgrad Doc Afr* 2003; 25: 4-7.
4. World Health Organization -International Society of Hypertension Writing Group. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) Statement on Management of Hypertension. *J Hypertens* 2003. 21:1983-1992.

5. Yussuf KB, Balogun OB. Pattern of drug utilization among hypertensives in a Nigerian teaching hospital. *Pharmacoepidemiol Drug Saf* 2005;14(1):69-74.
6. Szuba A, Martynowicz H, Zatorska K, et al. Prevalence of hypertension in a sample of Polish population – baseline assessment from the prospective cohort 'PONS' study. *Ann Agr and Envir Med* 2011; 18(2): 260-264.
7. Akinkugbe OO. Non-communicable diseases, the next epidemic: Nigerians' preparedness. *Nig J Clin Pract* 2000; 3(2): 17-42.
8. Sever PS, Messerli FH. Hypertension management 2011: optimal combination therapy. *Eur Heart J* 2011; 22: 1-10.
9. The research advisor. Sample Size Table. 2006. Available from <http://research-advisors.com> (Accessed 22 July, 2011).
10. Odili VU, Oghagbon EK, Ugwa NA, Ochei UM, Aghomo OE. Adherence to International Guidelines in the Management of Hypertension in a Tertiary Hospital in Nigeria. *Trop J Pharm Res* 2008; 7(2): 945-952.
11. Grassi G, Cifkova R, Laurent S, et al. Blood pressure control and cardiovascular risk profile in hypertensive patients from central and eastern European countries: results of BP CARE study. *Eur Heart J* 2011; 32: 218-225.
12. Yoon S, Ostchega Y, Louis T. Recent trends in the prevalence of high blood pressure and its treatment and control, 1999–2008. NCHS data brief, no 48. Hyattsville, MD: National Center for Health Statistics 2010.
13. Adebisi SA, Oghagbon EK, Jimoh AK. Glycated haemoglobin and associated variables in diabetics: Ilorin experience. *West Afr J Med* 2003; 22:318-320.
14. Pitsavos C, Miliatis GA, Demosthenes DB, Xenaki D, Panagopoulos G, Stefanadi C. Prevalence of self-reported hypertension and its relation to dietary habits, in adults; a nutrition & health survey in Greece. *BMC Public Health* 2006; 6:206.
15. Oghagbon EK, Okesina AB. Pattern of some risk factors for cardiovascular disease in untreated Nigerian hypertensive patients. *West Afr J Med* 2006; 25(3): 190-194.
16. Boris AKG, Huguette YMC, Laure NJ, Oben E. The effect of weight on the incidence and prevalence of hypertension in Yaounde. *J Diabetes Endocrinol* 2010; 1(1): 6-12.
17. Lewington S, Clark R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002; 360: 1903-1913.
18. Levy P, Ye H, Compton S, Zalenski R, Byrnes T, Flack JM, Welch R. Subclinical Hypertensive Heart Disease in Black Patients With Elevated Blood Pressure in an Inner-City Emergency Department. *Ann Emerg Med* 2012. Available from <http://www.sciencedaily.com/releases/2012/06/120608160128.htm>. (Accessed 5 July, 2012).
19. Adigun AQ, Ishola DA, Akintomide AO, Ajayi AA. Shifting trends in the pharmacological treatment of hypertension in a Nigerian tertiary hospital: a real world evaluation of the efficacy, safety rationality and pharmacoeconomics of old and new antihypertensive drugs. *J Hum Hypertens* 2003; 17(4): 277-285.
20. Schoen M, Tanzi MG. Role of calcium channel blockers in treatment of hypertension. *Pharmacy Today* 2008; 14(4): 50-65.
21. Panahpour H, Nouri M. Post-Ischemic treatment with candesartan protects from cerebral ischemic/reperfusion injury in normotensive rat. *Int J Pharm Pharm Sci* 2012; 4(4): 286-289.
22. Methyl dopa. Available from <http://www.inchem.org/documents/pims/pharm/methyl.do.htm> (Accessed 10 July, 2012).
23. Bello SI. Adherence and generic substitution among hypertensive patients in a specialist hospital. *Glo Adv Res J Med Med Sci* 2012; 1(1): 008-016.
24. Joshi UH, Ganatra TH, Desai TR, Tirgar PR. Evaluation of antihypertensive activity of *Evolvulus alsinoides* in adrenaline induced hypertensive rats. *Int J Pharm Pharm Sci* 2012; 4(4): 194-198.