

# Study of Pharmaceutical Formulations Used in the Management of Hypertension in Nsukka, Nigeria

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## Abstract:

### Background.

There is increasing death and complication arising from the chronic illness- hypertension in Nsukka area even with the increased addition of antihypertensive drugs into the Doctors Armamentaria. There is also expected to be improved knowledge on part of doctors and pharmacists on the prevailing trend in the management of hypertension which would have impact on the quality of life of the hypertensive patients but there seems to be no correlation yet.

### Objective

The study aims at ascertaining the availability, frequency of use and correctness of usage of the antihypertensive drugs by the medical team in the Hospitals. Two secondary Hospitals that act as the major referral and most patronized in Nsukka.

### Method:

The prescription paper and folders of hypertensive patients were directly collected and antihypertensive drugs prescribed sorted out and recorded. Using the signature on the prescriptions, the number of doctors that prescribed antihypertensive drugs within the period was determined. The data for prescribed antihypertensive drugs were analysed using percentage frequency method. The prescription pattern and frequency of the doctors were also determined using percentage frequency.

### Result:

A total of 543 cases were encountered. Hospital a had 379 case (68.8%), Hospital B had 164 cases (31.2%). A total of 19 formulations were also encountered out of which 2 formulations were presented in both parenteral as well as in tablet forms, and 17 others were in different tablet forms. Parenteral formulations were given in only 24 cases (4.42%), and 23 prescription papers (4.2%) were not signed at all by the doctors. The frequencies of prescribed formulation are Aspirin (47.5%), Amiloride/ HCT (42.5%), □- methyl dopa (22.6%), lisinopril (21.6%) amlodipine besylate (21.60%) Nifedipine (14.73%) Nifedipine SRO (14.37%) furosemide (28.7%).

Hospital A had Amiloride /HCT (52.1%), Aspirin (48.7%), Amlodipine besylate (30.0%), Lisinopril (28.7%), □-methyl dopa (18.2%). While Hospital B had Aspirin (44.5%), Nifedipine (32.9%), □-methyl dopa (32.9%), furosemide (28.7%), Amiloride/ HCT (19.5%) etc. A total of 16 doctors and 11 pharmacists were encountered. Hospital A had 10 pharmacists and B 1 pharmacist. Hospital A had 9 doctors with the following prescription/treatment frequencies: A<sub>B</sub> (45.9%), A<sub>C</sub> (14.5%), A<sub>D</sub> (11.9%), A<sub>A</sub> (9.2%), A<sub>E</sub> (6.9%), A<sub>F</sub> (0.8%), A<sub>G</sub> (6.3%), A<sub>H</sub> (2.4%) and A<sub>I</sub> (2.1%).

Hospital B: B<sub>A</sub> (22.6%) B<sub>B</sub> (5.5%) B<sub>C</sub> (9.2%) B<sub>D</sub> (7.9%) B<sub>E</sub> (23.8%) B<sub>F</sub> (29.9%) and B<sub>G</sub> (1.2%). Inclusion of Digoxin, phenytion, I V fluid and 3 diuretic combinations were some suspected medication errors noted.

### Key Word:

Hypertension, Prescription frequency, medication error, Pharmaceutical formulation, Blood pressure.

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## IMPACT OF FINDING ON PRACTICE

- There will be increased effort by Government and research pharmacist to increase the availability and affordability of antihypertensive drugs
- The pharmacist and Doctors will understand the need to abreast themselves with present management options eg available pharmaceutical care that will improve the quality of life of Hypertensive patients.
- The Hospital will be obliged to employ the services of only expert in management of Hypertension
- The Hospital management will be able to support the establishment of drug information centres and wholesome acceptance of pharmacists as indispensable part of the health care Team.

## INTRODUCTION

Hypertension, an asymptomatic cardiovascular disorder is still a major health problem in Nigeria representing a major public health issue which affect over one billion people worldwide <sup>(1)</sup>. The prevalence rate increases with age and it is higher in blacks (30%) than white (25%)[2]. Prevalence in Nigeria is estimated to be 10.3%.[3] in sub Saharan Africa 14-33% [4] of adult population.

Hypertension is a chronic disease that has no well defined aetiology or cure, as such; management is the only treatment option except in about 10-15% cases which are as a result of other underlying treatable illnesses [5]. Due to its chronic cause, hypertension has been implicated as most common risk factor stroke [1,6,7] heart failure, Ischemic heart failure, atherosclerosis, chronic kidney disease, coronary artery disease and dementia [1,8-10] and death. Since Hypertension is characterised by abnormal

persistent elevation of blood pressure above  $\frac{115-139}{75-89}$  mmHg [11,12] for normal adult, and it has been shown that 10mmHg reduction of blood pressure is associated with 37% and 56% reduction in coronary heart disease and stroke respectively.

Hypertension in various patients vary in intensity and presentation which led to clinical grouping of hypertension into borderline, sustained, accelerated, malignant, emergency and urgency. In emergency situation potent intravenous drugs [2] are used to bring about reduction in blood pressure within minutes to an hour, while in urgency conventional dosage forms and supportive measures are employed to control BP within hours to days. A variety of systems are involved in elevation of blood pressure [13-15] which makes the use of mono-therapy not to be advocated except in mild hypertension<sup>16</sup> that is unresponsive to salt restriction [1,11, 17]. It is also worth noting that in management of hypertension, other co-morbid illness should also be considered and a choice of drug that affect both should be considered for example, the choice of Lisinopril (ACEIs) in Hypertensive patients with renal complication and diabetes [18] and enalapril in Hypertensive patients with left ventricular Ejection failure and congestive failure<sup>18,19</sup>, and also the avoidance of thiazide diuretic in diabetic hypertensive patients. It is also advisable that through family history [20] and other social history should also be investigated and medication review be taken to ascertain drugs that cause increase in blood pressure, which may interfere with antihypertensive effect of planed drug therapy [21, 22]

#### METHOD.

The basic tools used in this study were the patient folders and prescription papers, from which the prescribed formulation and patient information were extracted. Ethical clearance was sought from the relevant authorities in each of the Hospitals used before data collection commenced.

The study population was drawn from both in-patient and out patient folders and prescription papers. Only adult patient records were selected and no distinction was made between males and females. Records of patient with co-morbid condition were also used where the antihypertensive drugs prescribed were extracted. The hospitals used include University medical centre, University of Nigeria, Nsukka campus

and Bishop Shanahan Hospital Nsukka, both in south Eastern Nigeria. The Hospitals were chosen because, they are the major referral and most patronized Hospitals in Nsukka. The last 7 months duration of this survey lasted (from Jan-July 2007) was chosen to ascertain the most recent practice in the area. In the result the names of the Hospital were blinded in other to maintain confidentiality.

The medication errors were just recorded and little comment made about them. The prescription pattern of Doctors was analysed using an arbitrary scale developed for easy reference.

The signatures on the prescription paper were also used to group prescriptions according to doctors. The determination of number pharmacists was by visual observation and oral interview. Some of the factors that might have influenced prescription habit were arrived at by oral interview and market survey to find out the price of the Antihypertensive drugs (data not shown).

#### RESULT

The total number of cases encountered was 543, made up of Hospital A 379 (68.8%).Hospital B 164 (31.2%). 23 (4.2%) of the prescriptions were not signed by the prescriber. The cases are for adults and no distinction was made between male and female.

The number of pharmaceutical formulations surveyed was 19 which 2 among them were presented in both parenteral and tablet dosage form while others were in tablet forms. Table 1 represents the percentage frequency of the 19 formulation in both hospitals. The five most prescribed were Aspirin (adjunct antihypertensive) 47.5%, Amiloride/HCT (42.5%), □- methyl dopa (22.65%), Lisinopril (21.6%), Amlodipine (21.0%), all in brand names. On the other hand the five least prescribed were ramipril (0.2%), Amlodipine (unbranded) (0.2%), metoprolol unbranded (0.2%), Ramipril/felodipine (0.4%) and propranolol (2.01%). Table 2 represents the prescription pattern of Doctors in both Hospitals while Table 3 represents the arbitrary chart used in the interpretation of the prescription pattern of Doctors.

Table 4 represents the prescription frequencies of doctors in the two hospitals. The frequency of dosage forms for 3 formulations that were not presented in the conventional oral tablet forms are shown in Table 5.

**Table 1: showing prescription frequencies of the 19 formulations**

S/N	Formulation	Hospital A	Hospital B	Total of frequency
1	Aspirin (branded)	48.7	44.5	47.5
2	Amiloride/ HCT (branded )	52.1	19.5	42.5
3	□-methyldopa (branded )	18.2	32.9	22.65
4	Lisinopril (branded )	28.2	6.1	21.60
5	Amlodipine (branded )	30.0	-	21.00
6	Nifedipine (unbranded )	6.9	32.9	14.73
7	Nifedipine SRO (unbranded )	14.5	14.0	14.37
8	Furosemide (branded )	7.6	28.7	14.00
9	Isosorbide dinctrate branded	11.8	-	8.3
10	Atenolol (unbranded )	9.0	2.4	7.0
11	Reserpire/clopamide dehydroergocristine (branded )	1.6	15.2	4.79
12	Spironolactone (branded )	1.6	9.8	4.79
13	Potassium chloride (branded )	-	12.8	3.87
14	Hydrochlorthiazide (branded )	4.7	0.6	3.5
15	Lisinopril (unbranded )	0.5	9.2	3.13
16	Hydralazine (unbranded )	-	9.2	2.76
17	Propranolol (branded )	1.3	3.7	2.01
18	Ramipril/ felodipine (branded )	0.5	-	0.4
19	Metoprolol (unbranded )	-	0.6	0.20
20	Amlodipine (unbranded )	-	0.6	0.20
21	Ramipril (unbranded )	-	0.6	0.20

**Table 2 Showing Prescription Pattern of Doctors in Percentage Frequency**

S/N	Formulation	A <sub>A</sub>	A <sub>B</sub>	A <sub>C</sub>	A <sub>D</sub>	A <sub>E</sub>	A <sub>F</sub>	A <sub>G</sub>	A <sub>H</sub>	A <sub>I</sub>	B <sub>A</sub>	B <sub>B</sub>	B <sub>C</sub>	B <sub>D</sub>	B <sub>E</sub>	B <sub>F</sub>	B <sub>G</sub>
1	Aspirin	40(D)	63.2(C)	4.82(G)	22.2	23.08	-	16.67	100.0(A)	50.0	37.8	55.6	33.0	84.6(A)	48.7	34.7	100.0(A)
2	Amiloride HCT	60.(C)	51.7(D)	67.27(C)	46.67	53.85	33.3	37.5	22.2	37.5	8.1	33.3	6.5	-	5.2	44.9	50.0
3	□-methyldopa	48.57(D)	11.5(G)	16.36(F)	35.56	7.69	33.3	8.3	22.2	-	16.2	33.3	46.7	30.8	20.5	51.0	50.00
4	Lisinopril	5.7(G)	38.5(E)	29.09(F)	28.89	50.0	-	12.5	-	37.5	2.7	11.1	-	53.8	-	2.0	-
5	Ramipril	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6	Amlodipine	20.0(F)	31.04(E)	16.36(F)	20.0	73.08	33.3	33.3	22.2	62.5	-	-	-	-	-	-	-
7	Nifedipine unbranded	8.6(G)	-	25.46(F)	8.89	-	-	-	55.56	-	18.0	33.3	26.7	15.4	15.4	63.3	50.0
8	Nifedipine SRO	2.86(G)	29.29(F)	7.27(G)	6.67	7.69	-	4.17	-	12.5	27.0	44.4	20.0	7.7	10.3	2.0	-
9	Furosemide	11.40(G)	5.75(G)	5.46(G)	4.4	30.77	-	8.3	-	12.5	24.3	33.3	20.0	38.5	28.2	30.6	50.0
10	Isosorbide dinitrate	-	18.97(F)	3.64(G)	8.89	7.69	-	8.3	11.1	12.5	-	-	-	-	-	-	-
11	Atenolol	14.29(G)	7.41(G)	1.82(G)	26.67	-	-	8.3	-	12.5	8.1	-	-	-	2.6	-	-
12	Reserpine clopamide dehvsoergocristine	--	--	--	--	--	-33.3	--	--	--	-8.1	--	-20.0	--	-46.1	-2.0	--
13	Spironolactone	-	-	-	-	-	-	-	-	-	5.4	-	6.5	23.1	10.3(2.6)	12.2	-
14	Potassium chloride	-	-	-	-	-	-	-	-	-	16.2	11.1	13.3	15.4	20.5	4.1	-
15	HCT	-	-	3.64(G)	-	-	33.3	-	-	37.5	2.7	-	-	-	-	-	-
16	Lisinopril unbranded	-	1.15(G)	-	-	-	-	-	-	-	16.2	-	-	7.7	2.6	16.3	-
17	Hydralazine unbranded	-	-	-	-	-	-	-	-	-	16.2	-	13.3	7.7	2.6	8.2	50.0
18	Propranolol	-	2.87(G)	-	-	-	-	-	-	-	2.7	-	13.3	-	7.7	-	-
19	Ramipril felodipine	-	-	-	-	7.69	-	-	-	-	-	-	-	-	-	-	-
20	Metoprolol unbranded	-	-	-	-	-	-	-	-	-	2.7	-	-	-	-	-	-
21	Amlodipine unbranded	-	-	-	-	-	-	-	-	-	2.7	-	-	-	2.6	-	-

**Table 3: Chart for Interpretation of Prescription Patter of Doctors**

%Frequency	Grade	Interpretation
80-100	A	Virtually in all patients
70-79	B	3 in every 4 patients
60-69	C	2 in every 3 patients
40-59	D	1 in every 2 patients
30-49	E	1 in every 3patients
15-29	F	1 in every 5 patients
<15	G	1 in every 10 patients

**Table 4: Percentage Prescription for Doctors in Both Hospitals**

<i>Hospital A(379 cases)</i>		<i>Hospital B (164 cases)</i>	
Doctors	% cases	Doctor	% cases
A	9.20	A	22.6
B	45.9	B	5.5
C	14.5	C	9.2
D	11.9	D	7.9
E	6.9	E	23.8
F	0.8	F	29.9
G	6.3	G	1.2
H	2.4		
I	2.1		

**Table 5: Showing Frequency of Dosage form for 3 Formulation**

S/N	Formulation	Presentation	Ratio	Total occurrence
1	Nifedipine	Sublingual: conventional tablet	14.66	80
2	Lasix (furosemide)	Parenteral: tablet	20.56	76
3	Hydralazine	Parenteral: tablet	4.11	15

### DISCUSSION

From the study the adjunct antihypertensive Aspirin (47.5%) was the most frequently prescribed. This is in line with generally accepted practice that patient with previous cardiovascular disease require treatment with antiplatelet [2,3,17], Aspirin is also associated with about 25% reduction in vascular event in patient with unstable angina without myocardial infarction [26,27] and low risk of gastrointestinal haemorrhage at low doses [28,29]

The second most prescribe was diuretic Amiloride/ HCT which also supports the efficacy of diuretics in the blacks and elderly [30-33]. The third class of drug that was prescribed was calcium of antagonist. The high use of this class of drug, are also supported by literature<sup>(30-33)</sup>.

The high use of ACEIs (lisinopril, Ramipril, Ramipril/felodipine) is not unconnected with the fact that diabetes is the most co-morbid condition in hypertensive patients. ACEIs have been favoured as the right choice in this situation because it offers protection against some diabetic complications.[34]

Beta blocker was among the least prescribed class of drugs. Although earlier studies showed that Beta blockers have some advantages in blacks [2], however recent studies are at variance with these findings. These current studies suggest less effectiveness and higher incidence of stroke when Beta blockers are used as first line drug [12,35-39] that notwithstanding, they should not be discontinued if the clinical condition is stable and controlled [40]. The incidence of combination therapy was high in this study. This is in consonance with most reports that

combination therapy and polypills given to people at high absolute risk of cardiovascular disease are more effective[41-46]

The prescription pattern of the doctors revealed much use of mere brand as against generic names, which is against best practices and pharmaco-economic principles [42-46]

Lastly, the medication errors detected (i.e. the inclusion of Digoxin, Phenytoin, IV infusion and triple diuretic combination at their full daily recommended doses) were due to non-compliance with the individualized care approach postulated by [Joint National Committee (JNC7) on detection, prevention, evaluation and treatment of hypertension], lack of sound knowledge of drugs on the part of medical doctors and inability of pharmacists to effectively carryout pharmaceutical care which will improve the quality of life of patients [17,47] the few cases of IV drugs given in the study correlates also with WHO guideline that reserves parenteral antihypertensive drug to emergency cases only.[30]

Prescribing without signature is unethical as with 4.2% of the prescription papers that were not signed at all by the doctors.

It was also discovered that as the number of doctors that prescribe increased, number of medication error noted increased, which supports the fact that only the expert should be allowed to handle Hypertensive patients. Also the number of pharmacists have a direct relationship with quality of services given to patients since the hospital with least number of pharmacist recorded highest number of medication errors.

**SUMMARY/CONCLUSION**

The prescription frequency of formulation and prescription pattern of doctors tallied with WHO/ISH recommendation by the high frequency of Aspirin, calcium antagonist and ACEIs and low frequency of Beta blockers and IV drugs and also by use of combination therapy. Irrational prescribing was noted with the use of brand name in virtually all prescription and inability to sign all the prescription papers. It was also noted an addition of up to 3 classes of diuretic, digoxin, phenytion and IV fluid in treatment regimen of severely hypertensive patient. There was also no adverse event report system and scanty or none existing pharmaceutical care in the hospitals surveyed. We therefore conclude that the treatment protocol in the management of hypertension in the above Hospitals surveyed is yet to meet the desired standard

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**REFERENCES**

- (1) Stephanie L. (2004) *Br Med*, J 328: 593-594
- (2) Aguwa C. N, Hypertension. (2004) In therapeutic basic of clinical pharmacy in the tropic 3<sup>rd</sup> Ed SNAAP press Enugu, Nigeriapp102-104
- (3) Olatunbosun ST, Kaufman J.S., Cooper RS, Bella A.F, (2000), *J. human Hypertens* 14(4): 249-57
- (4) Cooper RS, Ataman S, Mc Gee D. (1997), *Am. J. Pub. Health*; 87: 160-168
- (5) Young WF: *Cardiol Revi.* 7.207 (1999)
- (6) Justin A Sattin, Justin A Zivin: (2007) *American Journal of therapeutics* Vol 14:291-298
- (7) Hoyert DL, Kung HC, Smith BL. Death: Preliminary Data for 2003. National vital statistics reports Vol 58 No 15 Hyattville MD: National centre for Health statistics: 2005
- (8) Kannel WB: 1996, *JAMA*, 275:1571.
- (9) Ajayi OE, Balogun MO, 2002: Abstraction of the ISHIB programme syllabus (PUBMED) .
- (10) Ugwu E,C, Ischemic Heart diseases in therapeutic basis for clinical pharmacy in the tropics 3<sup>rd</sup> Ed by C,N Aguwa P-145-150
- (11) Chobaman AV, Bakris JL, Black AR, Cushman WC, Green LA Izzo JL, (2003). *JAMA*; 289:25
- (12) Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. *Lancet* 2002; 360:1903
- (13) Gorden H. Willams , Hypertenstive Vascular Disease: In Harrison's principle of Internal Medicine 5th Ed, Braunwald, fauce, Kasper, Hamser, Loggo, Jameson (ed) 2001 p1414-1430
- (14) Sealy J.E Blumenfeld JD, Bell GM: 1988. *Hypertens* 6:763.
- (15) Hoffman B, Briam; Catecholamines, Sympathomimetic and Adrenergic Receptor Antagonist in Pharmacological basis of therapeutics 10th Ed p.878- 891
- (16) LPM Dapar, Wannang NN, AGUYI JC, Gyang SS, Banwat, SB Ladep NG: *Nigeria Journal of Pharm, Research* Vol5, No1 Pp62-70 (Step 2006)
- (17) Vollmer WM, Sacks FM, Ard J, Appel L J. Bray GA, Simons-Morton DG. (2001) *Ann intern. Med.*; 135:1019.
- (18) Lewis E J: (1993). *N. Engl J. med* 329: 1456
- (19) Quest JR.(1991) Effect of enalapril on survival of patients with left ventricular Ejection fraction and congestive Heart failure.
- (20) The sixth report of Joint National committee on prevention, Detection, Evaluation and Treatment of High blood pressure. *Arch intern. Med* 1997 p2413.
- (21) Evans W, Holt D, Chinton F (1994) *Therapeutic drug monitoring clinical guide* p6-14.
- (22) Harri D, Green J (1993) *Pathology and therapeutics for pharmacists* p75-91
- (23) Wald NJ, Law MR. (2003), *Br Med J.*; 326:1419-24
- (24) Rodgers A.. (2003), *Br Med. J:* 326: 1407-8
- (25) The assessment and management of cardiovascular risk Best practice evidence based guideline. Wellington, NZ; New Zealand guideline group 2003.
- (26) McCann. Andrew: *Aust. Prescriber* Vol.30 No4 Aug (2007) p.92
- (27) Anti-thrombotic Trialist Collaboration: collaborative Meta-analysis of Randomized trial of antiplatelet therapy for prevention of death, Myocardial infarction and stroke in High risk patients, *BMJ* 2002; 324. 71-86.
- (28) Derry S, Loke YK. *BMJ* 2000;321: 1183-7.
- (29) Aguwa , C N. (2002) the amazing Drug called Aspirin and its therapeutic uses: SNAAP press Enugu, Nigeria p8
- (30) WHO (2002) promoting rational use of medicine core components. WHO policy perspective on medicine No5 Geneva Switzerland.
- (31) Adigum A. Q, Ishola D,A, Akintomide A,O, and Ajayi AAL (2003):. *J Human Hypertens.* 17(4) 277-285.
- (32) Kazeem BY, Olumide B. (2003): *J. Pharm Pharmacies Sci* 8 (21): 235-42
- (33) Douglas J.G. Bakris GL. Epstein M. *Ann. Int. Med.* (2003)163(4). 1744-5
- (34) Morgan T, lauri J, Bertram, D, Anderson A. *AM J Hypertens* 2004; 17.118-23.
- (35) Lindholm LH carlberg B, Samuelsson O. *Lancet* 2005; 366: 1545.53.
- (36) Dahlof , Devereux RB, Kjeldsen SE, Julius S, Beevers G, de faure U, *Lancet* 2002; 359:995-1003.
- (37) UK National institute for clinical excellence (NICE). Hypertension. Management of the Hypertension in adults in primary care: partial update. <http://www.nice.org.uk/downland.aspx?o=CG034> fullguideline (Extracted from the internet on Jan 11, 2007).
- (38) Khan N, McAlister FA, *CMAJ* 2006; 174: 1737-42
- (39) Williams B, Lacy Ps. Thom SM, crmick Shank Stanton A, Collier D. *Circulation* 2006; 113: 1213-25
- (40) Elsik M, Krum H- *Aust Prescriber* 2007; 30:9 p5-7
- (41) Connor J, Rafter N, Rodgers A. *Bull. World Health org.* 2004; 82:935-9.
- (42) Kuijpers MA, van Marum RJ, Egberts AC, Jansen PA. *Br J Clin Pharmacol* 2003; 65:130-3
- (43) Steinman MA. Landfeld CS, Rosenthal GE, Benthenthal D, Sens S, Kabolic PJ.. *J Am. Geriatr SOC* 2006; 54: 1516-23.

- (44) Hassali A Stewart K, Kong D,. Aust Preser 2004, 27.80-1
- (45) Pearce GA, McLachlan AJ, Rramzan I. J. Pharm pract Res 2004; 34:195-200
- (46) Department of Health and Ageing Guiding principles for medication management in the community 2006. [http\www.health.Gov. am/internet/wcms/publishing.nsf/content/apac-publications-guiding](http://www.health.gov.au/internet/wcms/publishing.nsf/content/apac-publications-guiding) (cited 2007 march 6)
- (47) Aguwa CN Ukwe Chinwe V, Ekwunife OI: Pharm world Sci (2008)30: 107-110