**Research Article**

# A TEN YEAR STUDY OF THE PHARMACOTHERAPY OF HYPERTENSION AT A TERTIARY HOSPITAL IN SOUTH WESTERN NIGERIA

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## ABSTRACT

This study was carried out at the University College Hospital, (U.C.H) Ibadan.  Its primary purpose was to assess the Pharmaco-therapeutic approach to the management of Hypertension by comparing the antihypertensives  prescribed at the U.C.H during a period of 10 years (1997-2006) with the British ABCD aligorithm.

Two hundred and thirty (230) patients were selected randomly for the study with age bracket 25 to 85 years.  Age, gender, history of hypertension, general health status and regimen on which the patients were placed were used for data collection.

Average age of hypertensive patients was 51 $\pm$ 14.561 years.  The modal age was 52 $\pm$ 14.561 years. One hundred and thirty six (136) (59%) of the studied population were males while (94) (40.9%) were females. Seventy four (74) (37.2%) of the hypertensive patients had heart failure as comorbidity, followed by 59 (29.6%) with renal failure while 14 (7%) had diabetics mellitus. One hundred and thirty nine (139) (21.3%) were on monotherapy of calcium channel blockers being the commonest. This is followed by 122 (18.7%) on ACEIs, 120 (18.3%) on diuretics and 41 (6.3%) on beta-blockers. Twenty two (22) (6.9%) were on biotherapy of ACEIs + beta-blockers, 67 (21.2%) on ACEIs + calcium channel blockers, 74 (23.4%) on ACEIs + diuretics, 74 (23.4%) on calcium channel blockers + diuretics. Eighteen (18) (5.7%) were on triple therapy while 6 (1.9%) were on quadruple therapy.

The study indicated a close correlation in the choice of anti hypertensives prescribed and the British ABCD algorithm.

**Key Words:** Pharmacotherapy, Hypertension, Monotherapy, Bitherapy, Triple  therapy, Quadruple.

## INTRODUCTION

Hypertension prevalence increases as the population ages.  People who are normotensive at age 55 have 90% lifetime risk of developing hypertension (Anderson KM, et al (1991)). The Joint National Committee (JNC) on detection evaluation and treatment of hypertension reiterates that people who are older than 50 years with systolic blood pressure exceeding 140 mmHg are much more proned to risk factors for cardiovascular disease than those with elevated diastolic blood pressure. As blood pressure increases, the patient's chance of heart attack, heart failure, stroke and kidney disease also increases.  Across the entire BP range, among those ages 40 to 70, the risk of cardiovascular disease doubles with each increment of 20/10 mmHg, thus alerting health care practitioners as well as the general public to the potential dangers of prehypertension, with systolic blood pressure ranges between 120 and 139 mmHg diastolic blood pressure ranges between 80-89 mmHg primary goal of the JNC VI (Anderson KM, et al (1991),(Cutler J (1999), (L. Brian Cross, (2006)).

Hypertension is common throughout the world and it represents the single greatest risk factor for increasing cardiovascular mortality, and morbidity (Anderson KM, et al (1991),(Cutler J (1999)).  It has been estimated that as many as 58 million people in the United States have hypertension with prevalence increasing with age and it is more prevalent in blacks (Dickerson JE et al (1999), Eccles M et al (1998))

The current prevalence of hypertension in Nigeria is estimated as 30% of the total population. Therefore, more than 40 million people in Nigeria suffer from hypertension.  This figure was arrived at using the new universal hypertensive cut off point of 140/90 mmHg, which was adopted in Nigeria in 1999 (Hansson L et al (1999), (L. Brian Cross, (2006). In line with this universally adopted hypertensive cut off point for measuring blood pressure, any adult whose blood pressure is consistently 140/90 mmHg and above is hypertensive. The prevailing rampant cases of hypertension in Nigeria has been attributed to several risk factors such as excessive salt intake, smoking, lack of physical exercise, diabetic mellitus, family hereditary, old age and post menopause. Men and women of the same race are affected approximately equally and it is greater in people with less education.Anti-hypertensive treatment is accomplished by a reduction of high blood pressure relative to cardiovascular risks, a clear-cut benefit in terms of reduced incidence of major cardiovascular complications of hypertension

and overall mortality (Cutler J (1999), Hargreaves MR et al (1995), JNCVI (1997)). Most effective antihypertensive according to clinical trial results are Angiotensin Converting Enzyme Inhibitors (ACEIs-A), Beta-Blockers (BBS-B), Calcium Channel Blockers (CCBs-C) and Diuretics-D (Thiazide-type).

The study seeks to gain insight into the management of hypertension with different classes of antihypertensive agents and to compare the selection with the British ABCD algorithm which simplifies the selection of first line antihypertensives to be from angiotensin converting enzyme inhibitors (A), bata blockers (B), calcium channel blocker (C) and thiazide diuretics (D) with the goal of providing and promoting pharmaceutical care.

## METHODS

A ten-year retrospective cohort study of 230 case notes from medical records department of the University College Hospital, Ibadan in South west Nigeria was made.

Hypertensive patients' medical records containing the patient medical profile were reviewed in this study.  The records were randomly selected.

The study population included outpatients and inpatients at the cardiology unit who continuously registered at the University College Hospital, Ibadan between May 1997 and April 2006.  Each patient medical record was thoroughly studied.

The sixth report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNCVI) for classification of Blood pressure for Adults aged 18 years and above was used to define hypertension.

The past medical histories of the patients were used to determine the presence of prior hypertension, myocardial infarction, valvular disease, kidney disease, liver disease, diabetes mellitus and other co-morbidities.  The drug management was studied by taking note of the types of drugs prescribed, documentation of lifestyle modification such as restricted diet, and exercise programmes. Age, sex, marital status and occupation were part of the indices used for this study. Statistical analysis was done using the SPSS Microsoft version 11.0 software programme for frequency distribution and cross tabulation. The ethical committee of the University College Hospital (U.C.H) Ibadan granted the permission to conduct this study.

## RESULTS

230 case notes of patients diagnosed to have hypertension were studied. Co-morbidities reviewed showed that the highest number of patients had heart failure, 74 (37.2%), followed by 59 (29.6%) with renal failure.

14 (7.0%) patients had diabetes mellitus, 9 (4.5% patients had atrial fibrillation, 6 (3.0%) patients had chronic obstruction pulmonary disease (COPD), 6 (3.0%) had seizures, 4 (2.0%) had stroke, 4 (2.0%) had liver disease 4 (2.0%) had retinopathy, 3 (1.5%) had left ventricular hypertrophy, 3 (1.5%) had cancer, 3 (1.5%) had dementia and 3 (1..5%) had asthma. 2 (1.0%) had infection, 2 (1.0%) had ischemic heart disease and 1 (0.5%) patient had anemia, hepatitis, and parkinsonism each respectively. 139 (21.3%) of the study population were on monotherapy of calcium channel blockers, followed by 122 (18.7%) on ACE Inhibitors. 120 (18.3%) on diuretics and 41 (6.3%) on beta-blockers.

Twenty two (22) (6.9%) of the studied population were on biotherapy of ACEI + beta-blockers, 67 (21.2%) on ACEIs + calcium channel blockers, 74 (23.4%) on ACEI + diuretics, 74 (23.4%) on calcium channel blockers + diuretics as biotherapies. Eighteen (18) (5.7%) were on triple therapies of ACEIs + beta-blockers + calcium channel blockers, 6 (1.9%) of the studied population were on ACEI + beta-blockers + calcium channel blockers + diuretics as quadruple therapies.

## DISCUSSION

The basic therapeutic goal in the management of hypertension is lowering of blood pressure to 140/90 mmHg or below. Consistent increase in blood pressure predisposes occurrence of heart attack, heart failure, stroke and kidney disease secondary to hypertension. (Kadiri S et al (2000a), Kadiri S et al (2000b))

Data from the multiple risk factors intervention trial (MRFIT) study describe the combined effects for cardiovascular risk factors. In men less than 46 years of age, a diastolic blood pressure (DBP) greater than 90 mmHg increased deaths to a rate 1.6 times the rate for men without any risk factor (Thomas SHL (2007)).

In the study conducted, hypertension was observed to be higher in males than females with males being 136 (59.1%) and females being 94 (40.9%) (Table 1). More recent evidence shows a clear and significant risk of cardiovascular events from elevated systolic blood pressure (SBP) especially in patient above the age of 50 years (L. Brian Cross, (2006)). DBP is a more predictive of cardiovascular risk before the age 50 years with SBP more predictive thereafter. The age group that has the highest occurrence of hypertension were patients between 50 and 59 years with the mean, median and mode ages were 52.47, 51 and 50 years respectively (SD $\pm$ 14.56%). (Table 1) Mental and physical stress causes transient increases in blood pressure. This effect is not generally sustained and taking the

hypertensive individual out of the stress for environmental does not always result in a decreased blood pressure (E.M. Graham-Clarke B.S. Hebron (1999).

**Table 1:  Sex, Age, Marital status and occupation distribution of hypertensive patients.**

|  | Frequency (N) | % | Valid % | Cumulative % |
|---|---|---|---|---|
| **Sex** | | | | |
| Male | 136 | 59.1 | 59.1 | 59.1 |
| Female | 94 | 40.9 | 40.9 | 100.1 |
| **Total** | 230 | 100 | | |
| **Age group** | | | | |
| 20-20 | 13 | 5.7 | 5.7 | 5.7 |
| 30-39 | 27 | 11.7 | 11.7 | 17.4 |
| 40-49 | 53 | 23.0 | 23.0 | 40.4 |
| 50-59 | 60 | 26.1 | 26.1 | 66.5 |
| 60-69 | 49 | 21.3 | 21.3 | 87.8 |
| 70+ | 28 | 12.2 | 12.2 | 100 |
| **Total** | 230 | 100 | | |
| **Marital status** | | | | |
| Married | 162 | 70.4 | 87.1 | 87.1 |
| Single | 15 | 6.5 | 8.1 | 95.2 |
| Widowed | 8 | 3.9 | 4.8 | 100.0 |
| Not indicated | 44 | 19.1 | | |
| **Total** | 230 | 100 | | |
| **Occupation** | | | | |
| Traders | 92 | 40.0 | 42.2 | 42.2 |
| Civil servant | 49 | 21.3 | 22.5 | 64.7 |
| Pensioner/retired | 34 | 14.8 | 15.6 | 80.3 |
| Student/apprentice | 15 | 6.5 | 6.9 | 87.2 |
| Artisan | 28 | 12.2 | 12.8 | 100.0 |
| Not indicated | 12 | 5.2 | | |
| **Total** | 230 | 100r | | |

Hypertension was observed to be more prominent in the people who are married than other marital status as 162 (70.4%) of the hypertensive population studied were married in comparison with 15 (6.5%) singles. Occupation of hypertensive studied indicated that traders were more hypertensive than others as 92 (40.0%) of the studied population were traders while 49 (21.3%), 34 (14.8%), 15 (6.5%) and 28 (12.2%) were civil servants, pensioners or retirees, students or apprentice and artisan respectively. 12 (5.2%) of the studied population did not indicate their occupation. (Table 1)

Married people are subjected to stress than the single. Nature of occupation such as travelling is usually associated with stress. Below the age of 75 years men are at greater risk of hypertension than women (L. Brian Cross, (2006)). Table 2 shows that 34 (25.0%) males aged between 60 and 69 years had the highest occurrence of hypertension while 28 (29.8%) females aged between 40 and 49 years had the highest occurrence of hypertension.

**Table 2:  Hypertensive Patients by age as related to sex group.**

| Age groups | Male N (%) | Female N (%) | Total | $X^2$ | P |
|---|---|---|---|---|---|
| 20-29 | 9 (6.6) | 4 (4.3) | 13 (5.7) | | |
| 30-39 | 16 (11.8) | 11 (11.7) | 27 (11.7) | | |
| 40-49 | 25 (18.4) | 28 (29.8 | 53 (23.0) | 7.126 | 0.211 |
| 50-59 | 33 (24.3) | 27 (28.7) | 60 (26.1) | | |
| 60-69 | 34 (25.0) | 15 (16.0) | 49 (21.3) | | |
| 70+ | 19 (14.0) | 9 (9.6) | 28 (12.2) | | |

However, since p = 0.05, there is no significant statistical difference between age and sex. Compelling indications for individualize drug classes includes heart failure, chronic kidney disease and diabetes mellitus. Among the comorbidities reviewed in the study, it was clear that hypertension predisposed patients more to Congestive Heart Failure (CHF) as CHF accounted for 74 (37.2%) of co-morbidities. This is supported by previous studies. (Kannel WB (2000), Kannel WB et al (1986)) This was followed by Renal Failure which accounted for 59 (29.6%) and Diabetes Mellitus which accounted for 14 (7.0%). (Table 3) Additional precipitating factors

for hypertension include Infection, Anaemia and Seizures. These were shortly resolved after removing the precipitating factors (Table 3). There is need for aggressive treatment to achieve sustained control of blood pressure through the use of right single antihypertensive or combinations of antihypertensives. The choice of drugs depends on the initial systolic blood pressure and how well the patient tolerates the drug (Kumar and Clark (2000)). Determination of the need for drug therapy is based on combined assessment of blood pressure level and the absolute risks of cardiovascular disease (L. Brian Cross, (2006)).

**Table 3: Co-morbidities documented from the case note of hypertensive patients.**

| Co-morbidity | Frequency | Percentage % |
|---|---|---|
| Left Ventricular hypertrophy | 3 | 1.5 |
| Renal failure | 59 | 29.6 |
| Diabetics | 14 | 7.0 |
| Heart failure | 74 | 37.2 |
| Stroke | 4 | 2.0 |
| Ischemic Heart failure | 2 | 1.0 |
| Seizures | 6 | 3.0 |
| Liver disease | 4 | 2.0 |
| Cancer | 3 | 1.5 |
| Infection | 2 | 1.0 |
| Chronic obstructive pulmonary disease | 6. | 3.0 |
| Dementia | 3 | 1.5 |
| Retinopathy | 4 | 2.0 |
| Atrial fibrillation | 9 | 4.5 |
| Parkinsonism | 1 | 0.5 |
| Asthmatic | 3 | 1.5 |
| Hepatitis B | 1 | 0.5 |
| Anaemia | 1 | 0.5 |
| **Total** | **199** | **100** |

Patients with stage 1 hypertension with systolic blood pressure reading antihypertensive therapies accounted for 64.6% of the British ABCD algorithm, with 34.3% accounting for other antihypertensives and comcommitant drugs prescribed.

**Table 4:Drug Regimen Prescribed for the hypertensive patients.**

| Drugs | Frequency | Percentage % |
|---|---|---|
| Diuretics | 19 | 2.7 |
| Moduretic | 82 | 11.7 |
| Aspirin | 21 | 3.0 |
| Plendil | 6 | 0.9 |
| Lisinopril | 89 | 12.7 |
| Digoxin | 27 | 3.9 |
| Nifedipine | 112 | 15.9 |
| Atenolol | 26 | 3.7 |
| Aldomet | 99 | 14.1 |
| Amlodipine | 22 | 3.1 |
| Anxiolytic | 5 | 0.7 |
| Brinerdine | 3 | 0.4 |
| Ramipril | 28 | 4.0 |
| Laxix | 87 | 12.4 |
| Propranolol | 9 | 1.3 |
| Spironolactone | 29 | 4.1 |
| Slow K | 17 | 2.4 |
| Isosorbide dinitrate | 5 | 0.7 |
| Lisinopril | 8 | 1.1 |
| Felodipine | 4 | 0.6 |
| Hydrallazine | 3 | 0.4 |
| **Total** | **701** | **100** |

Triple antihypertensives therapies indicate 18 (5.7%) patients on A + B + C. while 6 (1.9%) patients combined four antihypertensives of

A+B+C+D, indicating that within the ABCD of British algorithm, antihypertensives can be combined either as bitherapies, tritherapies and quadruple therapies. The rational for ABCD has been established by various antihypertensives studies. The Captopril prevention project (CAPP) trial found Captopril to be equal to

Diuretics and ß Blockers in preventing cardiovascular morbidity and mortality (Midgley JPet al (1996)). For patients who do not respond to initial ACE inhibitor therapy, adding low dosages of a thiazide diuretic controls blood pressure in up to 85% of the patients by working synergistically with ACE inhibitors therapy (Peter C. Gazes (1990), Prisant LM et al (1995)). ACE inhibitors are also synergistic with Calcium Entry Blockers and additive with ß Blockers (Rang HP et al (1996)).

Table 5 indicates the drug combination therapies with 74 (23.4%) patients on A+D, 74 (23.4%) patients on C+D, 22 (6.9%) patients on A+B, 67 (21.2%) patients on A+C, 32 (10.1%) patients on B+C and 23 (7.3%) patients on B+D, indicating the agreement of the prescribed antihypertensives combination with British ABCD algorithm with bitherapies.

**Table 5: Drug combination prescribed for the hypertensive patients.**

| Class of Drugs | Frequency (N) | Percentage % |
|---|---|---|
| A+B | 22 | 6.9 |
| A+C | 67 | 21.2 |
| A+D | 74 | 23.4 |
| B+C | 32 | 10.1 |
| B+D | 23 | 7.3 |
| C+D | 74 | 23.4 |
| A+B+C | 18 | 5.7 |
| A+B+C+D | 6 | 1.9 |
| **Total** | **316** | **100** |

Table 6 indicates the comcommitant drugs prescribed to be 69 (20%) Antibiotics, 34 (8.1%) Anxiolylitics, 31 (7.2%) Anticoagulants, 28 (7.1%) Analgesics while oral Hypoglycemic agents and Insulin accounted for 24 (6.1%) and 14 (3.6%) respectively, indicating Infections, Arthritis, and Diabetic Mellitus as important comorbidites in Hypertension (Kannel WB (2000)).

**Table 6: Concomitant Drugs Prescribed for the hypertensive patients.**

| Drugs | *Frequency (N) | Percentage |
|---|---|---|
| Anxiolytics | 34 | 10.9 |
| Antibiotics | 69 | 22.2 |
| Oral hypoglycemic agents | 24 | 7.7 |
| Insulin | 14 | 4.5 |
| Anticoagulant | 31 | 10.0 |
| Analgesics | 28 | 9.0 |
| Antiemetics | 13 | 4.3 |
| Antimalaria | 5 | 1.7 |
| Antidepressant | 17 | 5.4 |
| Insulin | 14 | 4.5 |
| Antiplatelets | 21 | 6.7 |
| Others | 41 | 13.0 |
| **Total** | **311** | **100** |

**Table 7: Various classes of Hypertension with associated comorbidities.**

| | High normal N (%) | Stage 1 N (%) | Stage 2 N (%) | Stage 3 N (%) | Total |
|---|---|---|---|---|---|
| Left ventricular | 0 (0.0) | 2 (100.0) | 0 (0.0) | 0 (0.0) | 2 (6.3) |
| Renal failure | 1 (6.3) | 4 (25.0) | 2 (12.5) | 9 (56.3) | 16 (50.0) |
| Diabetics | 0 (0.0) | 0 (0.0) | 2 (100.0) | 0 (0.0) | 2 (6.3) |
| Heart failure | 1 (6.7) | 5 (33.3) | 3 (20.0) | 6 (40.0) | 15 (46.9) |
| Seizures | 0 (0.0) | 1 25.0) | 3 (75.0) | 0 (0.0) | 4 (12.5) |
| COPD | 0 (0.0) | 1 (100.0) | 0 (0.0) | 0 (0.0) | 1 (3.1) |
| Dementia | 0 (0.0) | 1 (50.0) | 1 (50.0) | 0 (0.0) | 2 (6.3) |
| Retinopathy | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (100.0) | 1 (3.1) |
| Atrial fibrillation | 0 (0.0) | 2 (100.0) | 0 (0.0) | 0 (0.0) | 2 (6.3) |

Table 7 shows various classes of hypertension with comorbidites, with renal failure and Heart failure occurring most in stage 3 hypertension as comorbidities. This indicates that progression of target organ damage occurred most in stage 3 hypertension. 106 (76.8%) of the hypertensive patients of the studied population have normal blood pressure along with comorbidities with stage 1 hypertension having 12 (8.7%) comorbidities, stage 2 hypertension having 7 (5.1%) comorbidities and stage 3 hypertension having 12 (8.7%) comorbidities.

The British Hypertension society recommends a treatment algorithm based on the ABCD rule to checkmate substantial under diagnosis, under treatment and poor rates of blood pressure control.Many hypertensive patients who are hospitalized could return to a modified version of their everyday routine within weeks or months, depending upon the severity of their condition. Regardless of the nature and severity of the hypertension, non-pharmacological treatment should be employed along with pharmacological ABCD hypertensive treatment algorithm (Robert T. Welbert (2000)). Each patient is encouraged to avoid physical and emotional stress as much as possible. Bed rest and physical exercise could be beneficial to certain patients. The use of one or combination agent known to prevent the initiation and progression of Congestive Heart Failure (CHF), Renal failure, Hypertensive retinopathy secondary to Hypertension should be encouraged.

To enhance compliance, once daily dosing regimen is preferred. Where possible, appropriate substitution or combination should be made for the antihypertensive, instead of giving up to four agents at the same time (Thomas SHL (2007)).

Adverse effects should be monitored so as to determine the extent the patients tolerates the antihypertensive agents prescribed.

## CONCLUSION

In initiating drug therapy for hypertension, it is important to remember that hypertension is a disease of decades. Unless hypertension is severe, it is important to start a simple drug regimen that minimizes side effects and encourage long term compliance. A continuing principle is that clinical drug therapy should be based on well tested drugs that have been shown to prevent cardiovascular disease and reduce mortality (Robert T. Welbert (2000)). These agents are best selected from ABCD algorithm therapy.

## ACKNOWLEDGEMENTS

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