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Effect of Anti-Hypertensive Drugs on Blood Pressure Lowering and Renal Function

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Authors' contributions

This work was carried out in collaboration among all authors. Author OMA designed the study, wrote the protocol and supervised field work. Author OHA wrote the draft of the manuscript and supported field work. Authors BWA and IOU managed the field work. Author BWA managed the literature searches and performed the statistical analysis. All authors read and approved the final manuscript.

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ABSTRACT

Aim: Study aimed at evaluating blood pressure (BP) lowering effect of antihypertensive medications and their effect on renal function.
Study Design: This was a progressive observational study, evaluating the lowering effect of selected antihypertensive agents on BP and renal functions of hypertensive patients.
Study Location: The study involved moderately hypertensive patients who attended Cardiology clinic and were already receiving antihypertensive drug regimen at the University of Uyo Teaching Hospital, Uyo, Akwa-Ibom state, Nigeria. University of Uyo Teaching Hospital is a tertiary healthcare facility that was established in 1999.
Methods: Seventy hypertensive patients who received antihypertensive medications for at least 6

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months were recruited for the study. The recruited participants were advised on adherence and were given adherence chart to record time of medication used. A 3 ml blood was collected and Omron digital BP meter was used to take three separate BP readings and the average was recorded. The blood samples were analysed in the laboratory for serum creatinine (Scr) by using Randox's Scr and blood urea nitrogen (BUN) kits. The Scr was used to calculate the creatinine clearance (CrCl) by using Corkcroft-Gault equation. Participants were followed-up for three months consecutively. Statistical analysis was considered significant at p=.05. SPSS version 20 was used for the analysis.

Results: Systolic blood pressure (SBP) reduced from 130±2.64 mmHg in phase 1 to 120±1.13 mmHg in phase 3 while CrCl increased from 82.01±4.49 ml/min to 91.62±4.35 ml/min respectively. Both SBP and BUN were higher in females (131±3.30 mmHg and 2.67±0.19 µmol/l) while CrCl was higher in males (102.06±8.91 ml/min). Amlodipine (AM) reduced SBP by 9 mmHg, Lisinopril+Hydrochlorothiazide (LH) reduced SBP by 7 mmHg and Lisinopril+Amlodipine+Hydrochlorothiazide (LAH) reduced SBP by 22 mmHg. CrCl decreased among participants on AM, LH and LAH by 0.89 ml/min, 0.01 ml/min and 8 ml/min respectively.

Conclusion: Antihypertensive medications reduced SBP especially in three-drug combinations but worsened renal function.

Keywords: Antihypertensives; blood pressure; creatinine clearance; blood urea nitrogen.

1. INTRODUCTION

Cardiovascular diseases are a major public health challenge, representing 10% of the global burden of disease [1]. The annual number of deaths caused by cardiovascular disease is expected to rise by more than 33% over the next three decades [2]. Hypertension is among the most important modifiable risk-factors for cardiovascular diseases [3]. Meta-analyses of placebo-controlled trials of anti- hypertensive medication have shown that such treatment can prevent, or postpone myocardial infarction and stroke [4]. But the key question remains: Which of the many available types of blood pressure lowering drugs is the better choice as first-line medication? Several clinical trials and systematic reviews have addressed this issue, but have failed to convincingly show that one or more drug-classes are superior to the others [5-9]. Still, controversy remains about possible important differences between the various drugs. The findings from the alpha-blocker arm of the ALLHAT-trial a decade ago [10], and reviews in recent years assessing the effectiveness of beta-blocking agents [11,12] cast doubt about the assumption that all antihypertensive drugs are equally effective with regards to cardiovascular disease prevention. Also, recent systematic reviews have found potentially important differences regarding their effectiveness for some specific outcomes [13,14]. Systematic reviews of randomized controlled trials comparing different drugs provide evidence for decisions about choice of antihypertensive medication. Unfortunately, direct comparative studies are lacking for many of the competing drug-classes. Conventional meta-analyses of antihypertensive medication, therefore, typically provide comparative effectiveness estimates for only some drug-comparisons, that is, those that have been tested head-to-head in clinical trials. However, a decision maker would want to have effect-estimates for as many comparisons as possible, preferably with a ranking of the various drugs. Multiple treatments (network) meta-analyses provide this by utilizing indirect comparisons, making it possible to estimate the comparative effectiveness of drugs that have not been tested directly in clinical trials [8,13,14]. The most recent systematic review addressing several of the most clinically important outcomes and using multiple treatments meta-analysis of antihypertensive drug therapy was published by Psaty and colleagues in 2003 [8]. An update is warranted to reflect the current evidence-base in the field and to address some short- comings of the earlier review, for example, that the authors neither explicitly assessed the risk of bias in the included studies, nor graded the quality of the overall body of evidence.

Blood pressure is quantified as diastolic and systolic pressures measured in millimeters of mercury (mmHg). The diastolic pressure represents the pressure during ventricular relaxation in diastole whereas the systolic pressure represents the peak pressure due to ventricular contraction during systole. Either or both pressures have specified upper limits of normal and elevation in either or both pressures are used to define hypertension [15].

Blood pressure is normally distributed in the population and there is no natural cut-point above which "hypertension" definitively exists and below which, it does not. Epidemiological studies demonstrate that the aforementioned disease risk associated with blood pressure is a continuous relationship and above blood pressures of 115/70 mmHg, the risk of cardiovascular events doubles for every 20/10mmHg rise in blood pressure. The threshold blood pressure determining the presence of hypertension is defined as the level of blood pressure above which treatment has been shown to reduce the development or progression of disease. Primary hypertension was previously termed “essential hypertension” because of a long-standing view that high blood pressure was sometimes “essential” to perfuse diseased and sclerotic arteries. It is now recognized that the diseased and sclerotic arteries were most often the consequence of the hypertension and thus the term “essential hypertension” is redundant and the “primary hypertension” is preferred. Primary hypertension refers to the majority of people with sustained high blood pressure of which about 90% encountered in clinical practice, for which there is no obvious, identifiable cause. The remaining 10% are called "secondary hypertension" for which specific causes for the blood pressure elevation can be determined such a Conn's adenoma, renovascular disease, or phaeochromocytoma [15].

Primary hypertension is remarkably common in the UK population and the prevalence is strongly influenced by age and lifestyle factors. Systolic and/or diastolic blood pressures may be elevated. Systolic pressure elevation is the more dominant feature of hypertension in older patients and diastolic pressure more commonly elevated in younger patients, such as those less than 50 years of age. At least one quarter of the adult population of the UK have hypertension with blood pressure ≥140/90 mmHg and more than half of those over the age of 60 years. As the demographics of the UK shifts towards an older, more sedentary and obese population, the prevalence of hypertension and its requirement for treatment will continue to rise [15].

Hypertension is reported to be the second leading cause of end-stage renal disease (ESRD) [16]. African Americans are 6 times more likely to develop ESRD from hypertension than whites [17]. Observational studies show a direct relationship between the level of blood pressure (BP) and renal disease progression [18,19].

Several studies document that African Americans with chronic kidney disease have faster declines in renal function compared with whites with similar BPs [20]. In the first trial to randomize patients to different BP levels and examine the outcome on kidney disease progression, the Modification of Diet in Renal Disease trial, a benefit of the lower BP goal (92 mmHg) was suggested in the small subgroup of 53 African Americans [21]. However, whether a lower BP goal actually retards progression of renal disease in African Americans is uncertain [22-26]. In trials that enrolled individuals with renal disease from diabetes and other etiologies, angiotensin-converting enzyme inhibitors significantly reduce progression of kidney disease. However, few African Americans were included in such trials [27-30].

The study aimed to evaluate lowering effects of different antihypertensive drugs and renal functions of participants on antihypertensive agents.

2. METHODS

2.1 Materials

The following items were used in the course of the study such as weighing scale, metre rule, Omron digital sphygmomanometer, 5 ml syringes, plain sample tubes, methylated spirit, disposable hand gloves, cotton wool, creatinine kit and blood urea nitrogen kit.

2.2 Study Design

This was a progressive observational study evaluating the relative lowering effect of selected antihypertensive agents on blood pressure and monitoring of renal functions of antihypertensive patients on medication.

2.3 Study Location

The study was involved moderately hypertensive patients who attended Cardiology clinic and were already receiving antihypertensive drug regimen at the University of Uyo Teaching Hospital, Uyo, Akwa-Ibom state, Nigeria. University of Uyo Teaching Hospital is a tertiary hospital that was established in 1999.

2.4 Study Population

The study involved seventy patients aged 18 years and above who were diagnosed with hypertension and had commenced antihypertensive agents. Participants' drug adherence was monitored by a specially designed chart after prior counselling on drug adherence.

2.5 Sample Size

Purposive-convenience sampling was used for recruitment of participants into the study. We obtained a sample size of seventy patients because this was an observational study which excluded patients with other chronic diseases that could interfere with the results of the study. This study focused on biochemical parameters such as blood pressure, serum creatinine, BUN and creatinine clearance. Thus the effect on these parameters would represent the effect on the parameters of the general population.

2.6 Data Collection

Three sets of blood pressure reading were taken on each participant during each hospital visit with Omron blood pressure digital device. Confounding factors ranging from patient selection, precise digital device reading and chronic diseases were adequately prevented from the study. A 3ml blood sample was collected from participant at each hospital visit. The blood samples were then analysed in the laboratory for serum creatinine with serum creatinine kit manufactured by Randox®. The procedure for laboratory evaluation of serum creatinine was described in previous study [31]. The creatinine clearance was calculated from the serum creatinine by using Cockcroft-Gault formula as shown below:

$$Creatinineclearance = \{(140 - age) * weight\} / (72 * serumcreatinine)$$

Each study participants was followed up for three months.

2.7 Inclusion Criteria

The study involved participants aged 18 years to 70 years including males and females that had been diagnosed with hypertension and had commenced antihypertensive medication.

2.8 Exclusion Criteria

Any hypertensive patients aged under 18 years and adult hypertensive patients on renal dialysis were excluded from the study. Participants with diabetes mellitus any other chronic illnesses, pregnant and lactating women were excluded from the study.

2.9 Data Analysis

SPSS software package version 21 was used. Descriptive statistical tool such as mean was used for the data. Data obtained from participants on single antihypertensive medication and those on combination medication were compared by using T-test analysis. Reduction of blood pressure caused by combined antihypertensive medication was assessed by the single antihypertensive medication's reduction of blood pressure. Level of significance was considered at P=.05. The blood pressure lowering effect of various antihypertensive agents was compared by using statistical tool called analysis of variance (ANOVA).

3. RESULTS

The results showed that that the mean ages of the participants were 53±1.42 years. Fifty-one (73%) participants were females while nineteen (27%) were males. Twenty-two (31%) participants had normal weight, twenty-seven (39%) were overweight while twenty-one (30%) were obese. Among the recruited participants, sixteen (23%) participants had received treatment for less than one year; twenty-five (36%) participants had received treatment within1-5 years while forty-nine (41%) participants had received treatment for more than 5 years. Nine (14%) participants were on single drug, twenty (28%) participants were on two-drug combinations, 28 (40%) participants were on three-drug combinations and thirteen (17%) participants were on four-drug combinations. In phase 1 of the study, sixty-eight percent (68%) of the participants adhered to their medications while eighty-eight percent (88%) and ninety-seven percent (97%) adhered in Phases 2 and 3 respectively.

The participants at Phase 1 of the study had a systolic blood pressure (130±2.64 mmHg) which was higher than the systolic blood pressure (SBP) at Phase 2 (124±1.9 mmHg) and Phase

3 (120±1.31 mmHg) but the diastolic blood pressure (DBP) of the participants at Phase 1 (74±1.36 mmHg) was lower than the DBP of the participants at Phase 2 (76±1.03 mmHg) and Phase 3 (77±1.82 mmHg). The creatinine clearance of participants in the study at Phase 1, 2 and 3 were 82.01±4.49 ml/min, 82.46±3.98 ml/min and 91.62±4.35 ml/min respectively (Table 1).

A comparison of obtained data at Phase 1 and Phase 2 showed a significant variation for SBP (*P*=.05) and DBP (*P*= .01). A comparison of obtained data at Phases 1 and 3 also showed a significant variation for SBP (*P*=.00). The female participants had a higher SBP (131±3.30 mmHg) than the male participants (129±4.79 mmHg) and a lower DBP (76±1.64 mmHg) than the male participants (77±2.79 mmHg). There was a significant variation for both the serum creatinine (*P*=.02) and creatinine clearance (*P*=.01) (Table 2).

Classification of participants into normal weight, overweight and obese showed that the systolic blood pressure was significantly higher in the normal weight participants (Table 3).

Considering the duration of therapy, the participants who had received antihypertensive drug regimen for more than five years had a significantly reduced SBP than those who were on therapy for less than a year and those who had received therapy between one year and five years. Similarly, the participants who had received therapy for more than five years had BUN that was significantly varied from participants who received therapy for less than a year and those who received therapy between one year and five years. The participants on antihypertensive therapy for more than five years had the poorest renal output (Table 4).

Evaluating the performance of single antihypertensive agent with that of 2-drug combination therapy showed that both therapies could not reduce the SBP to the target goal of 120mmHg but the 2-drug combination therapy reduced SBP by 4mmHg lower than the single therapy. Serum creatinine was significantly varied between participants on single therapy and those on 2-drug combination therapy. Both creatinine clearance and BUN were outside the normal range for participants on 2-drug combination (Table 5).

Evaluating the performance of single antihypertensive therapy with 3-drug combination therapy showed that the participants on 3-drug combination had SBP higher than participants on single drug therapy by 6 mmHg. Serum creatinine was significantly lowered in 3-drug combination than the single drug therapy. The creatinine clearance and BUN of the participants on 3-drug combination were not in the normal range. The result also showed that DBP was significantly higher in 3-drug combination therapy than the 2-drug combination therapy by 6 mmHg (Table 5).

The results showed that amlodipine as single drug therapy reduced SBP in phases 2 and 3 by 5 mmHg and 4 mmHg respectively. A 2-drug combination such as Lisinopril + Hydrochlorothiazide was shown to reduce SBP in phases 2 and 3 by 3 mmHg and 4mmHg respectively. A 3-drug combination like Lisinopril + Amlodipine + Hydrochlorothiazide reduced SBP in phases 2 and 3 by 14 mmHg and 8 mmHg respectively. Participants on single therapy, amlodipine (98.71±11.0 mmHg) had better creatinine clearance than 2-drug combination (81.10±8.09 mmHg) and 3- drug combination therapy (63 mmHg) (Table 6).

Evaluation of participants on 2-drug combination as Lisinopril + Hydrochlorothiazide and 3-drug combination as Lisinopril + Amlodipine + Hydrochlorothiazide showed that both SBP and DBP of participants on Lisinopril + Hydrochlorothiazide varied significantly with the SBP and DBP of participants on Lisinopril + Amlodipine + Hydrochlorothiazide. Participants on Lisinopril + Amlodipine + Hydrochlorothiazide therapy had higher creatinine clearance than participants on Lisinopril + Hydrochlorothiazide therapy. The mean BUN of participants on Lisinopril + Hydrochlorothiazide therapy was outside the normal range (Table 7).

4. DISCUSSION

The participants that were recruited in the study were mostly middle aged individuals who were not diagnosed with renal injury as a result of chronic disease, thus, they were very relevant to the study. This is in consonance with the study conducted by Borzecki which revealed that study participants aged 48 to 70 years had a better blood pressure control compared to those aged 70 years and above who had received antihypertensive agents [32].

Table 1. Profile of participants' parameters

Description	Number of participants	Age (years)	BMI (Kgm^2)	Pulse (mins)	SBP (mmHg)	DBP (mmHg)	Serum creatinine (mg/dl)	Creatinine clearance (ml/min)	BUN (µmol/l)
Normal range			18.5-24.5	60-100	90-120	60-80	0.6-1.2	*97-137 **88-128	3.6-7.1
Phase 1	70	53±1.42	27.14±0.64	75±1.61	130±2.64	74±1.36	1.02±0.12	82.01±4.49	2.66±0.15
Phase 2	70	53±1.42	27.48±0.64	72±1.12	124±1.97	76±1.03	0.98±0.05	82.46±3.98	3.97±2.13
Phase 3	70	53±1.42	27.02±0.61	71±1.15	120±1.31	77±1.82	0.85±0.05	91.62±4.35	1.71±0.1
***P*-value**		.09	.9	.87	.00	.34	.31	.20	.43

**male value, **female value, SBP= systolic blood pressure, DBP= Diastolic blood pressure, BUN= Blood urea nitrogen*

Table 2. Effect of therapy

Description	Number of participants	Age (years)	BMI (Kgm^2)	Pulse (mins)	SBP (mmHg)	DBP (mmHg)	Serum creatinine (mg/dl)	Creatinine clearance (ml/min)	BUN (µmol/l)
Normal range			18.5-24.5	60-100	90-120	60-80	0.6-1.2	97-137 88-128	3.6-7.1
Phase 1	70	53±1.42	27.14±0.64	75±1.61	130±2.64	74±1.36	1.02±0.12	82.01±4.49	2.66±0.15
Phase 2	70	53±1.42	27.48±0.64	72±1.12	124±1.97	76±1.03	0.98±0.05	82.46±3.98	3.97±2.13
P-value		1.00	1.00	.11	.05	.012	.7	.92	.55
Phase 1	70	53±1.42	27.14±0.64	75±1.61	130±2.64	74±1.36	1.02±0.12	82.01±4.49	2.66±0.15
Phase 3	70	53±1.42	27.02±0.61	71±1.15	120±1.13	77±1.82	0.85±0.05	91.62±4.35	1.71±0.1
P-value		1.00	.57	.07	.00	.51	.18	.122	.00
Phase 2	70	53±1.42±	27.14±0.64	72±1.12	124±1.97	76±1.03	0.98±0.05	82.46±3.98	3.6±7.1
Phase 3	70	53±1.42	27.02±0.61	71±1.15	120±1.31	77±1.82	0.85±0.05	91.62±4.35	1.71±0.10
P-value		1.00	.55	.87	.07	.14	.04	.08	.29
Female	51	53±1.58	27.54±0.81	74.76±1.98	131±3.30	76±1.64	1.09±0.16	74.39±4.59	2.67±0.19
Male	19	53±3.14	26.07±0.99	77.74±2.64	129±4.79	77±2.79	0.84±0.06	102.06±8.91	2.54±2.08
P-value		1.00	.87	.37	.75	.71	.02	.01	.70

**male value, **female value, SBP= systolic blood pressure, DBP= Diastolic blood pressure, BUN= Blood urea nitrogen*

Table 3. Effect of BMI on treatment efficacy

Parameters	Normal range	Comparison between normal weight and obese			Comparison between normal weight and overweight		
		Normal weight	Obese	*P*-value	Normal weight	Overweight	*P*-value
Number of participants		22	21		22	27	
Age (years)		50.86	51.05	.15	50.86	55.78	1.00
BMI (kgm^{-2})	18.5-24.5	21.88	42.61	.00	21.88	27.37	1.00
Pulse (min^{-1})	60-100	76.14	78.00	.66	76.14	73.70	.52
Systolic BP	90-120	134.77	122.85	.04	134.77	131.43	.64
Diastolic BP	60-80	75.82	75.59	.92	75.82	80.29	.22
Serum creatinine (mg/dl)	0.6-1.2	0.01	0.84	.37	0.01	1.25	.33
Creatinine clearance (ml/min)	*97-137 **88-128	78.32	83.08	.68	78.32	86.67	.48
BUN (µmol/l)	3.6-7.1	2.70	2.53	.67	2.7	2.69	.99

**male value, **female value, SBP= systolic blood pressure, DBP= Diastolic blood pressure, BUN= Blood urea* nitrogen

Table 4. Effect of treatment duration on treatment efficacy

Duration of therapy	Number of participants	Age (years)	BMI (kgm^{-2})	Pulse (min^{-1})	SBP (mmHg)	DBP (mmHg)	SCr (mg/dl)	Creatinine Clearance	BUN (µmol/l)
Normal range			18.5-24.5	60-100	90-120	60-180	0.6-1.2	*97-137 **88-128	3.6-7.1
Less than 1 year	16	44.56	26.52	74.25	135	76	0.87	87.52	2.36
1-5 years	25	53.08	27.24	73.88	133	77	0.99	85.64	2.32
Greater than 5 years	29	57.34	29.25	71.83	119	71	0.98	81.84	2.41
P-value			.21	.70	.02	.19	.58	.88	.002

**male value, **female value, SBP= systolic blood pressure, DBP= Diastolic blood pressure, BUN= Blood urea nitrogen, SCr= Serum creatinine*

Table 5. Effect of mode of therapy on blood pressure reduction

Parameters	Normal range	Single drug versus 2-drug combination			Single drug versus 3-drug combination			2-drug versus 3-drug combinations		
		Single drug	Two drugs	P-value	Single drug	Three drugs	P-value	Two drugs	Three drugs	P-value
Number of participants		9	20		9	28		20	28	
Age (years)		45±5.74	56±2.19	.03	45±5.74	50±2.23	.29	56±2.19	50±2.23	.17
BMI (kgm^{-2})	18.5-24.5	24±1.15	27±0.87	.23	24±1.15	28±1.65	.15	27±0.87	28±1.65	.82
Pulse (min^{-2})	60-100	70±5.13	72±2.06	.65	70±5.13	79±2.75	.06	72±2.06	79±2.75	.06
Systolic BP (mmHg)	90-120	128±8.23	124±4.44	.64	128±8.23	134±4.67	.5	124±4.44	134±4.67	.13
Diastolic BP (mmHg)	60-80	70±4.92	72±2.50	..44	70±4.92	78±1.77	.40	72±2.50	78±1.77	.04
Serum creatinine (mg/dl)	0.6-1.2	1.81±0.89	0.92±0.91	.05	1.81±0.89	0.90±0.68	.04	0.92±0.91	0.90±0.68	1.00
Creatinine clearance (ml/min)	88-128	84±17	82±8	0.18	84±17	85±7	0.92	82±8	85±7	.74
BUN (µmol/l)	3.6-7.1	3.13±0.6	2.39±0.26	.89	3.13±0.60	2.57±0.24	.28	2.39±0.26	2.57±0.24	.66

**male value, **female value, SBP= systolic blood pressure, DBP= Diastolic blood pressure, BUN= Blood urea nitrogen*

Table 6. Comparative analysis of some selected drugs

Parameters	*male value	Amlodipine only				Lisinopril + Hydrochlorothiazide				Lisinopril + Amlodipine + Hydrochlorothiazide			
		Phase 1	Phase 2	Phase 3	*P*-value	Phase 1	Phase 2	Phase 3	*P*-value	Phase 1	Phase 2	Phase 3	*P*-value
No of participants		9	9	9		4	4	4		4	4	4	
Age (year)		45±6.35	45±6.35	45±6.35	1.00	58±2.35	58±2.35	58±2.35	1.00	63	63	63	1.00
BMI (kgm^{-2})	18.5-24.5	24.02±1.01	23.86±1.05	23.70±1.00	.93	26.89±1.43	26.96±1.35	26.48±1.21	.96	27.29	27.31	27.43	.96

Parameters	*male value	Amlodipine only				Lisinopril + Hydrochlorothiazide				Lisinopril + Amlodipine + Hydrochlorothiazide			
		Phase 1	**Phase 2**	**Phase 3**	***P*-value**	**Phase 1**	**Phase 2**	**Phase 3**	***P*-value**	**Phase 1**	**Phase 2**	**Phase 3**	***P*-value**
Pulse (min^{-1})	60-100	68±4.09	66±2.03	66±2.18	.83	68±6.75	66±4.64	64±4.60	.90	74	64	68	.70
Systolic BP (mmHg)	90-120	125	120	116	.29	124	121	117	.67	148	134	126	.1
Diastolic BP (mmHg)	60-80	70	74	72	.67	67	69	69	.95	83	72	96	.7
Serum creatinine (mg/dl)	0.6-1.2	0.91±0.11	93.57±8.64	98.71±11.09	.91	0.83±0.16	1.23±0.31	1.29±0.36	.51	1.00	0.97	1.40	.47
Creatinine clearance (ml/min)	97-137 88-128	99.60±18.47	93.57±8.64	98.71±11.09	.94	81.11±16.83	81.12±8.64	81.10±8.09	1.00	71.6	80.48	63	.64
BUN (µmol/l)	3.6-7.1	2.68±0.51	1.59±0.17	1.58±0.17	.94	3.19±0.71	3.19±0.71	1.84±0.33	.05	2.65	1.66	1.96	.29

**male value, **female value, SBP= systolic blood pressure, DBP= Diastolic blood pressure, BUN= Blood urea nitrogen*

Table 7. Comparison between combination drugs

Therapy	Number of participants	Age (years)	BMI (kgm^{-2})	Pulse (min^{-1})	SBP (mmHg)	DBP (mmHg)	Serum creatinine (mg/dl)	Creatinine clearance (ml/min)	BUN (µmol/l)
Normal range			18.5-24.5	60-100	90-120	60-80	0.6-1.2	97-137 88-128	3.6-7.1
Lisinipril + Amlodipine + Hydrochlorothiazide	4	58±4.9	26.95±2.70	68±13.50	126	76	0.84±0.31	81.11±33.68	3.19±1.42
Lisinopril + Hydrochlorothiazide	4	63±2.06	27.29±4.47	75±26.70	117	69	1.00±0.26	71.60±9.38	2.65±1.04
P-value			.9	.66	.00	.03	.45	.61	.56

**male value, **female value, SBP= Systolic Blood Pressure, DBP= Diastolic Blood Pressure, BUN= Blood Urea Nitrogen*

Only a few participants in the study were obese and their response to antihypertensive therapy was not affected by their obesity at the start of the study. This observation contradicted earlier findings by Sebaka et al., who evaluated the effect of body weight loss and gain on arterial hypertension control. Their study indicated that weight increase was directly proportional to poor hypertension control in obese and overweight participants [33]. The difference in observation could be due to the difference in the period of observation in the two studies.

The intervention of the principal investigation was focused on the medication adherence of the participants which was observed in the progressive improvement of participants' medication adherence as the study progressed. It was observed that there was a consistent progressive improvement on the systolic blood pressure which was significantly reduced at day 60 of the drug monitoring. This observation was profoundly due to the intervention of the investigator and the medication used by the participants. A study conducted in Malaysia by Ramli et al., on medication adherence among hypertensive patients attending primary healthcare facility. Their study indicated that medication adherence among hypertensive patients attending primary healthcare facility was poor and it affected the blood pressure control negatively [34]. Consequently, multidisciplinary interventions implementation was advised to ensure improvement of drug adherence and consequently improvement of blood pressure control.

The BMI of the participants within the normal range was significantly varied with the BMI of obese participants. The systolic blood pressure of the normal weight participants also varied significantly with the systolic blood pressure of the obese participants. Therefore, it was suggested that the variation in the BMI of the normal weight participants and the obese participants was responsible for the variation in the systolic blood pressure of the two groups. This observation was in agreement with the study of Jones et al., which suggested that weight loss appeared to be a useful tool in blood pressure control in patients who required antihypertensive agents to control their blood pressure [35].

It was also observed that those who received antihypertensive medication for less than one year had greater systolic blood pressure and blood urea nitrogen than those who received antihypertensive agents for 1-5 years. The significant variation of this systolic blood pressure suggested that continuous use of antihypertensive agents resulted in controlled blood pressure. Previous study had suggested that persistent use of antihypertensive agents had resulted in both direct and indirect benefits such as reduction of risks of morbidity and mortality [36].

Administration of two antihypertensive agents was more effective in controlling the systolic blood pressure of hypertensive participants than those participants who received single antihypertensive agent. Previous study suggested that combination antihypertensive drugs regimens are more effective at controlling hypertension than single antihypertensive agent [37].

Antihypertensive medication used such as single-drug therapy, two-drug therapy and three-drug therapy were observed to reduce systolic blood pressure effectively depending on the previously elevated level of the blood pressure. Single therapy such as Amlodipine, two-drug therapy such as Lisinopril + Hydrochlorothiazide and three-drug therapy such as Lisinopril + Amlodipine + Hydrochlorothiazide reduced systolic blood pressure by 9 mmHg, 7 mmHg and 22 mmHg respectively in 90 days suggested their effectiveness. Previous study had indicated that combination therapy would result in greater blood pressure reduction, reduced side effect and improved medication adherence [38]. Similarly, Munger et al., concluded in their study that combination therapy could achieve greater blood pressure reduction than single antihypertensive agent and could also enhance safety and adherence to medication [39].

On renal function, only the male participants had adequate renal function but the female renal function was not adequate. The renal function of the total population of participants in the study was not adequate even with the use of antihypertensive medications. Participants with three-drug antihypertensive combination had a better but inadequate renal function than those who received either two-drug antihypertensive combination or single antihypertensive medication. Previous study had revealed that antihypertensive drugs had a disparate effect on renal haemodynamics, tubular function, plasma electrolytes and hormonal responses. Both calcium channel blockers and angiotensin

converting enzymes inhibitors were found to increase glomerular filtration rate and renal blood flow in hypertensive patients. In spite of adequate control of systolic blood pressure and unchanged plasma creatinine, progressive kidney damage in the stenotic kidney occurred with the use of antihypertensive agents [40]. A recent study suggested that decline in glomerular filtration rate during intensive blood pressure reduction was associated with patients with risks of adverse reaction [41]. In this study, renal function of female participants was not adequate which might be an indicator for future end stage renal disease.

However, it is pertinent to include other supportive measures in addition to medication in order to achieve the goal of successful blood pressure control in hypertensive patients. These measures include diet, exercise, adequate rest and lifestyle modification. Eight Joint National Committee guidelines on hypertension had recommended healthy eating, weight management and appropriate physical activity were essential for the management of high blood pressure in adults as their lifestyle modification influenced improvement of blood pressure control [42].

5. CONCLUSION

The various modes of antihypertensive therapies such as single drug therapy, two-drug combination therapy and especially three-drug combination therapy effectively reduced SBP of study participants. However, renal functions of participants were most worsened among participants on three-drug combination therapy such as LAH.

6. RECOMMENDATION

Renal function test is hereby recommended for patients receiving antihypertensive agents on regular interval.

CONSENT

Informed consent was obtained from participants before they were recruited to the study.

ETHICAL APPROVAL

Ethical approval for this study was granted by the Research and Ethical committee of University of Uyo Teaching Hospital.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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