International Journal of TROPICAL DISEASE & Health
11(4): 1-11, 2016, Article no.IJTDH.20176
ISSN: 2278–1005, NLM ID: 101632866

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Effects of Thiazide Diuretic in Combination with Amiloride versus Hydrochlorothiazide Alone, on Plasma Glucose and Electrolytes in Hypertensive Nigerians: A Community Based Study

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Authors' contributions

This work was carried out in collaboration between all authors. Author OA did the study design, analyzed the data and wrote the manuscript. Author FO did most of the experimental analysis and literature searches. Authors MA and AA recruited the patients and collected clinical data while author OSO contributed to the statistical analyses and preliminary preparation of manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJTDH/2016/20176
Editor(s):
(1) Akihiro Asakawa, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan.
Reviewers:
(1) Mra Aye, Melaka Manipal Medical College, Malaysia.
(2) Anonymous, Hospital "F. Perinei"–Altamura (Bari), Italy.
(3) Hassan Ali Abdelwahid, Suez Canal University, Egypt.
Complete Peer review History: http://sciencedomain.org/review-history/11845

Original Research Article

Received 14th July 2015
Accepted 19th September 2015
Published 16th October 2015

ABSTRACT

Background: Diuretics are known to be the most effective antihypertensive medicines in Black Africans and people of African origin. Hydrochlorothiazide (HCT) and Amiloride-HCT(Amiloride combined with-Hydrochlorothiazide (Amiloride-HCT) used either as a single medicine or in combination with other antihypertensive medicines, are the two diuretics commonly used in the management of high blood pressure in Nigeria.

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Aim: The present study aimed at comparing the metabolic effects of the Hydrochlorothiazide (HCT) and Amiloride-HCT in Nigerian hypertensive population.
Methods: Participants who gave their consent were recruited through a community based hypertension screening programme. One hundred newly diagnosed hypertensive patients aged 30 - 70 years were recruited and randomly assigned to use either Amiloride-HCT or HCT. A cohort of two groups of patients consisting of 50 patients per group was studied. Each group of patient was followed up for a period of 6 weeks after commencing diuretic antihypertensive medicines. Fasting plasma glucose, serum electrolytes and lipids were assessed at baseline and at two (2) weeks interval after commencing antihypertensive therapy.
Results: HCT and Amiloride-HCT significantly reduced blood pressure in mild to moderate hypertension after six (6) weeks of treatment and this reduction was similar in the two groups. Although, moduretic appears to have more pronounced effect on K^+, Ca^{2+} and HDL-C, this metabolic effect was not significantly different from the observed pattern in HCT group.
Conclusions: Amiloride-HCT and HCT commonly used in the management of hypertension in Nigeria remain effective and achieve similar reduction in blood pressure. They both also cause similar derangement in metabolic profile in the newly diagnosed hypertensive subjects at least in the short-term.

Keywords: Hypertension; hydrochlorothiazide; Amiloride-Hct; glucose; lipids; electrolytes; Nigerians.

1. INTRODUCTION

The main aim of antihypertensive therapy is to achieve optimal blood pressure control with minimal adverse effects as well as cost benefit. This optimal goal is at most times difficult to achieve. Selection of appropriate antihypertensive medicines is often very challenging to physicians since the medicines are often associated with adverse effects [1]. Diuretics are known to be a very effective antihypertensive medicine in black Africans and people of African origin in the western world [2–5]. The antihypertensive efficacy of diuretics therapy has been shown in major landmark trials to be an effective first line therapy for controlling high blood pressure [6] and for significant reductions of cardiovascular morbidity and mortality [7]. However, data from the same clinical studies also showed that diuretics (and *β*-blockers) can cause abnormalities in carbohydrate, electrolyte, and lipid metabolism and also may influence quality of life [7]. Hence, their effectiveness is limited by possible adverse metabolic effect such as hypocalcaemia, hypomagnesaemia, impaired glucose tolerance and dyslipidemia.

The ALLHAT study demonstrated the efficacy of thiazide diuretics as first line drug therapy in hypertension especially in Africans. Thiazide diuretics have also been shown to be the commonest medicines prescribed to hypertensive patients in Nigeria [2,5,8]. However, their effect on blood pressure is related to natriuresis and volume depletion. Thiazide also fails to increase free water clearance and in some instances reduce it. This may result in the excretion of hypertonic urine and may contribute to dilutional hyponatraemia. Consequence to increased delivery of sodium to the distal nephron, $Na^+ – K^+$ ion exchange is enhanced, and kaliuresis may result. Few reports have recorded the possibility of Thiazide-induced glucose intolerance and insulin resistance [9-11]. Amiloride-HCT is a product containing a combination of HCT (50 mg) and potassium sparing Amiloride (5 mg).

Although, Amiloride-HCT and HCT are two diuretics commonly used in the management of high blood pressure in Nigeria [8], there is paucity of data comparing the metabolic effects of these two drugs in newly diagnosed hypertensive Nigerians. The present study was designed to compare the metabolic effects of these two drugs in a Nigeria hypertensive population.

2. METHODOLOGY

2.1 Study Population and Design

The study was a randomized, open-labelled, parallel treatment study design. The target population are newly diagnosed hypertensive patients recruited from a community based screening programme of the University College Hospital, Ibadan, Nigeria. The recruitment location was at Yemetu area of Ibadan, South Western Nigeria. All the biophysical measurements were done at the site. Biochemical analyses were carried out at the Department of Chemical Pathology, University College Hospital, Ibadan. One hundred newly

diagnosed hypertensive patients aged 30 to 70 years were recruited into the study. The patients were divided into 2 groups consisting of fifty (50) participants each. The study was 90% powered to detect a difference of 0.7 meq/L in the mean serum potassium of subjects treated with HCT and Amiloride-HCT group and at an alpha error of 5%. The estimated minimum sample size was twenty seven (27) subjects per group. However, 50 patients were recruited in each group in order to make provision for fall out and withdrawal. Hypertension was diagnosed in subjects having systemic blood pressure ≥ 140 mmHg or diastolic ≥ 90 mmHg on at least two occasions. Ethical clearance was obtained from the Ministry of Health, Oyo State, Nigeria. Informed consent was obtained from all the participants. The participants were randomized by randomly selecting a number to assign the patient into corresponding treatment group, either to HCT or Amiloride-HCT which contain a combination of 5mg amiloride and 50mg HCT. Each participant was then followed up for a period of 6 weeks. The biochemical parameters of interest were assessed at baseline and at two (2) weeks interval for 6 weeks following the commencement of antihypertensive therapy.

No side effect of the medicine that may warrant discontinuation of treatment was observed in this study. The most common complaint by participants were excessive urination and feeling light. One subject discontinued treatment because of critically high blood glucose value. Eight subjects in the HCT group and five subjects in the Amiloride-HCT group did not complete the follow up programme (compliance failure). Hence, they were not included in the final analysis. Forty five (45) apparently normal individuals with no history of cardiovascular or metabolic disorder were recruited as controls. The controls were sex and age matched with the study population.

2.2 Inclusion and Exclusion Criteria

Subjects were included into the study if they had primary hypertension in the mild to moderate range. The exclusion criteria included, subjects on diuretic therapy, metabolic abnormalities e.g. morbid obesity, diabetes mellitus, and Cushing's syndrome, subjects known to have secondary cause of hypertension that can affect potassium homeostasis e.g. Conn's syndrome, those with co-existing congestive heart failure, renal failure, cardiomyopathy and valvular heart disease. Also, subjects who did not give their consent were excluded.

2.3 Clinical Evaluation

Baseline clinical and demographic characteristics were obtained from the participants. These included age, gender, weight and height. Blood pressure measurements were obtained by conventional method using a mercury sphygmomanometer (Accosson, London). Systolic and diastolic blood pressures were measured at Korotkoff sounds phases I and V, respectively. Blood pressure was measured at the right arm three (3) times after a 5 minutes rest. Blood pressure 140/90 and above was taken as hypertension. Participants were weighed without shoes and in light clothing on and height measured to the nearest centimeter with conventional methods. Body mass index (BMI) was calculated using the formula: BMI = Weight (kg) / Height ^{2}(m^2). Body surface area (BSA) was calculated using the Dubois and Dubois formula [12].

2.4 Sampling and Analytical Methods

After an overnight fast of 12 hours, venous blood was drawn from the antecubital vein, using a sterile syringe and needle, into fluoride oxalate (FO) bottle, ethylene diaminetetra acetic acid (EDTA) and plain bottles. The samples were spun with a bench centrifuge at 4000 Rpm for 10 minutes. Plasma and serum were separated into plain bottles and stored at -20℃ until analysis.

Blood urea, creatinine, calcium and magnesium, glucose and lipids were measured with conventional colorimetric method using Hitachi 902 autoanalyzer (Roche Diagnostics Germany). However, Low-density lipoprotein-cholesterol (LDL-C) was calculated using the formula of Friedwald et al. [13]. While sodium and potassium were measured with conventional flame emission photometry, chloride and bicarbonate were measured with titrimetric methods.

2.5 Data Management and Statistical Analysis

SPSS software version 14.0 (SPSS Inc Chicago, Ilinois) was used for statistical analysis. All randomized subjects who completed the study were included in the analysis. The changes from randomization to after six weeks (every 2 weeks) of treatment in heart rate, blood pressure and biochemical variables were evaluated using a two-way analysis of variance to test for differences within and between groups with treatment group and time as factors. Student "t"

test was used to compare difference between two groups. Pair wise comparisons were used to test for statistically significant results. Continuous variables were expressed as mean ± SD (standard deviation) and categorical variables were expressed as percentages. A two-tailed value < 0.05 was considered as statistically significant.

3. RESULTS

Biophysical characteristics of the hypertensive patients and normal controls are shown in Table 1. Body weight and waist-hip ration were significantly higher in hypertensive groups compared with controls (P < 0.05). While HDL-C was significantly higher in the control group (P < 0.001), LDL-C and 2 hours post prandial plasma glucose (2HPPG) were higher in the hypertensive subjects (P < 0.001). Also, while blood urea and creatinine were significantly higher (P < 0.01), bicarbonate and sodium are lower (P < 0.05) in hypertensive subjects compared with controls. Table 2 shows the comparison of the biophysical and biochemical parameters of the two hypertensive groups, at baseline and 6 weeks post-intervention. These parameters were similar in the two groups both before commencement and 6 weeks of anti-hypertensive therapy (P > 0.05). The changes in the blood pressure of the HCT and Amiloride-HCT groups over the six weeks period are shown in Tables 3 and 4. The reduction in blood pressure after 6 weeks of treatments was statistically significance in both groups (P < 0.001) compared with baseline. Tables 3 and 4 also show the changes in biochemical and metabolic parameters of the subjects from baseline to six weeks after treatment. Amiloride-HCT caused a significant fall in serum potassium (P = 0.023) with the mean change of 0.46 mmol/L. And caused significant increase in the levels of bicarbonate (P = 0.044), urea (P < 0.0001), creatinine (P = 0.027) and HDL cholesterol (P = 0.009). Amiloride-HCT also caused significant reduction in serum magnesium with mean change of 0.340 mg/dl (P= 0.027). HCT on the other hand, caused significant increase in only serum HCO_3 and creatinine with mean change 2 mmol/L (P<0.001) and 1.75 mg/dl (P = 0.037) respectively. HCT also causes significant reduction in serum calcium concentration with mean deference of 0.340 mg/dl (P = 0.027) but the reduction in serum potassium after 6 weeks treatment with HCT was not statistically significant (P = 0.077). However, comparison of all these biochemical changes between the two groups, did not reach statistical significant level. The distributions of these parameters were presented in Figs. 1 and 2.

4. DISCUSSION

Several notable observations were recorded in this study. This study include: - (1) Hypertensive subject have higher body mass index, waist hip ratio and pulse rate compared with age and sex-matched apparently normal subjects. (2) Serum Na^+, K^+, Cl^-, Ca^{2+} and Mg^{2+} were relatively higher in normotensive participants than in hypertensive patients, while serum HCO_3 was higher in the hypertensive patients. (3) Glucose and lipids were also higher in hypertensive patients than normotensive participants. (4) HCT and Amiloride-HCT significantly reduced blood pressure in mild to moderate hypertension after six (6) weeks of treatment and this reduction was similar in the two groups. (5) Both medicines have similar comparative effects on serum electrolytes, $Ca^{2+}$and Mg^{2+}, glucose and lipids. Hence, the use of potassium sparing diuretic Amiloride with HCT does not appear to have added advantage over HCT alone at least in the short term therapy.

Thiazide diuretics are generally indicated for the management of mild to moderate hypertension and the efficacy especially in Blacks has been well established. It is not surprising therefore that in this study significant blood pressure reduction was achieved after 6 weeks of treatment. The fact that HCT alone and HCT/Amiloride combination achieved similar blood pressure reduction may be because similar dose of HCT was used. Addition of Amiloride did not show any added advantage of Moduretic over HCT alone.

The antihypertensive effects of diuretics are well established especially in Africans and people of African origin. However, they are fraught with adverse metabolic effects such as impaired glucose tolerance, dyslipidaemia, hypocalcaemia, and hypomagnesaemia. Adedeji and Onitiri [14] reported higher plasma total cholesterol, triglyceride and low-density lipoprotein in hypertensive patients as compared with normal controls. HDL levels were generally lower in the hypertensive groups than the normotensive control [15]. It is also well documented that diuretics increase serum LDL and TG levels. Although LDL and VLDL cholesterol have been demonstrated to increase following diuretic treatment, HDL was reported to be virtually unaffected [16,17]. Our study

Table 1. Comparison of biophysical characteristics of the hypertensive subjects and normal controls

Parameter	Hypertensives	Controls	P-value
Age (years)	48.0 (15.2)	47.5 (16.8)	0.860
Gender (male/female)	42/45	21/24	0.938
Body weight (kg)	68.3 (14.5)	60.7 (12.9)	0.011
Height (cm)	162.1 (9.6)	163.3 (8.0)	0.640
Body mass index (kg/m^2)	26.1 (5.9)	24.7 (5.1)	0.078
Body surface area (m^2)	1.72 (0.19)	171.0 (0.16)	0.714
Waist circumference (cm)	90.3 (10.8)	85.2 (8.3)	0.017
Hip circumference (cm)	97.6 (11.7)	93.1 (10.4)	0.050
Waist-Hip ratio	0.93 (0.05)	0.82 (0.25)	0.0001*
Pulse rate (beats/min)	82.0 (20.0)	74.4 (19.9)	0.060
Systolic blood pressure (mmHg)	153.7 (15.7)	124.1 (11.0)	<0.0001*
Diastolic blood pressure (mmHg)	92.3 (11.6)	79.7 (9.1)	<0.0001*
Sodium (mmol/L)	138.4 (6.8)	140.8 (5.2)	0.039*
Potassium (mmol/L)	4.01(0.57)	4.04 (0.42)	0.779
Chloride (mmol/L)	105.7 (4.86)	108.2 (13.3)	0.113
Bicarbonate (mmol/L)	20.4 (1.84)	22.5 (1.96)	<0.0001*
Urea (mg/dl)	26.2 (8.70)	16.8 (5.30)	<0.0001*
Creatinine (mg/dl)	0.96 (0.35)	0.80 (0.19)	0.0032*
Calcium (mg/dl)	8.87(0.85)	9.06 (0.65)	0.187
Magnesium (mg/dl)	1.89 (0.73)	2.02 (0.22)	0.187
FBG (mg/dl)	93.8 (7.3)	88.6 10.1	0.330
2HPPG(mg/dl)	106.5 (20.8)	93.8 7.3	0.0001*
Total cholesterol (mg/dl)	166.5 27.9	160.4 39.1	0.350
Triglyceride (mg/dl)	107.3 29.9	95.0 47.5	0.111
HDL (mg/dl)	38.8 10.8	53.0 13.2	<0.0001*
LDL (mg/dl)	105.4 34.4	82.7 21.3	<0.0001*

*Values expressed as mean ± SD. *statistically significant (Students "t" test)*

confirms these findings and in addition, shows increase in the level of HDL cholesterol after 6weeks of treatment with HCT and Amiloride-HCT. This increase was more pronounced in patients on Amiloride-HCT. This probably suggests that diuresis, especially; HCT/Amiloride combination may be beneficiary to the deteriorating effect of hypertension on lipid metabolism. However, the mean differences comparing the HCT with Amiloride-HCT did not reach statistical significance. This implies that this possible advantage of Amiloride-HCT compared with HCT alone is not pronounced in short time therapy.

Both medicines caused increase in fasting blood glucose. However, 2HPPG only increased in the Amiloride-HCT group. The mean increase reported in the literature is 2-9 mgldL [9]. This was similar to the mean changes of 3 – 8 mg/dl in our study (3.33.mgldl for HCT and 7.27 mg/dl for Amiloride-HCT group). It is well established that thiazide diuretics can induce glucose intolerance [9,10,18]. Major decline in insulin mediated glucose disposal has been implicated [11]. Although, the mechanism of action is not clear, some workers have implicated potassium depletion as a possible culprit [10].

It is noteworthy that both Amiloride-HCT and HCT caused reduction in plasma potassium after 6 weeks of treatment compared with baseline value. This different was statistically significant in the Amiloride-HCT group. The reductions in serum potassium were 0.33 and 0.46 mmol/L in HCT and Amiloride-HCT groups respectively. This may be because the baseline mean of serum potassium of subjects in the Amiloride-HCT group was relatively lower than those in the HCT group, although not statistically significant.

In addition, it is known that diuretic may cause reduction in serum potassium [7]. Our results was similar to an average decline of 0.2 – 0.7 mmol/L in serum potassium in patients receiving 50 mg of HCT as reported previously in some studies [19-21]. This effect is supposedly ameliorated by potassium sparing agent such as Amilioride. Our finding simply shows that this effect is not pronounced or effective at short time intervention. Our finding of no significant difference in the values between the two groups, substantiate that addition of Amiloride to HCT does not appear to have an intended potassium saving effect in hypertensive in a short time therapy.

Table 2. Comparison of the biochemical variables of the HCT and moduretic groups before (Baseline) and after 6 weeks of treatments

Parameter	HCT baseline	Moduretic values	Difference in mean	HCT 6 weeks	Moduretic values	Difference in mean
Heart rate (beats/min)	79.8 (12.1)	83.7 (24.9)	3.44	80.8 (13.5)	85.9 (14.0)	5.1
Systolic blood pressure (mmHg)	157.5 (17.6)	150.9 (13.9)	6.6	129.5 (24.3)	123.7 (12.7)	5.8
Diastolic blood pressure (mmHg)	92.5 (15.4)	92.1 (7.9)	0.04	77.0 (14.4)	76.1 (9.8)	0.9
Potassium (mmol/L)	4.05 (0.55)	4.04 (0.61)	0.1	3.73 (0.66)	3.54 (0.55)	0.19
Chloride (mmol/L)	107.3 (5.8)	104.4 (3.8)	2.9	105.8 (4.3)	101.5 (7.70)	4.3
Bicarbonate (mmol/L)	20.3 (0.78)	20.5 (2.5)	0.2	22.3 (1.07)	22.3 (1.16)	0
Urea (mg/dl)	19.0 (5.1)	15.1 (5.4)	3.9	21.1 (5.6)	21.2 (5.83)	0.1
Creatinine (mg/dl)	0.99 (0.41)	0.93 (0.29)	0.5	1.18 (0.38)	0.95 (0.20)	0.23
Calcium (mg/dl)	8.98 (0.86)	8.59 (1.23)	0.39	8.86 (0.67)	8.65 (0.63)	0.21
Magnesium (mg/dl)	2.17 (0.96)	1.67 (0.39)	0.5	1.81 (0.38)	1.56 (0.50)	0.25
FBG (mg/dl)	91.7 (12.2)	88.4 (10.6)	3.3	95.0 (8.7)	95.8 (21.9)	0.8
2HPPG (mg/dl)	106.2 (25.1)	106.3 (16.7)	0.1	104.3 (54.6)	107.4 (33.4)	3.1
TCHOL (mg/dl)	157.2 (31.3)	163.7 (46.8)	6.5	161.4 (39.6)	177.7 (32.7)	16.3
Triglyceride (mg/dl)	100.35 (30.3)	85.8 (46.8)	14.55	102.6 (51)	92.1 (45.7)	10.5
HDL (mg/dl)	38.8 (7.5)	38.7 (13.9)	0.1	42.4 (6.2)	43.0 (13.8)	0.6
LDL (mg/dl)	97.7 (26.1)	113.3 (40.3)	15.6	99.1 (34.5)	118.1 (34.1)	19

Values expressed as mean ± SD. No significant difference in all the parameters

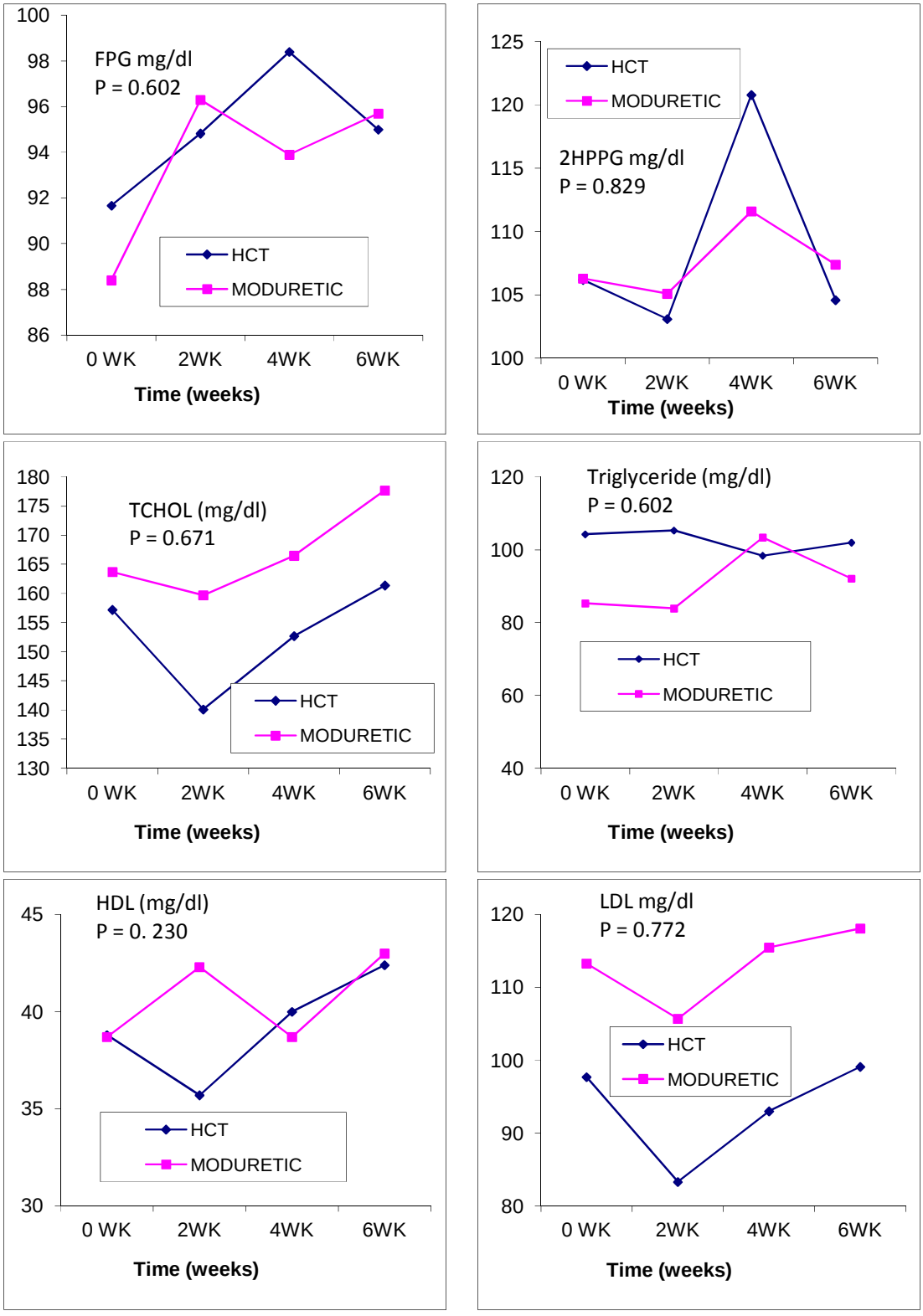

Fig. 1. Line chart showing changes in glucose and lipids at baseline and 6-weeks after treatment

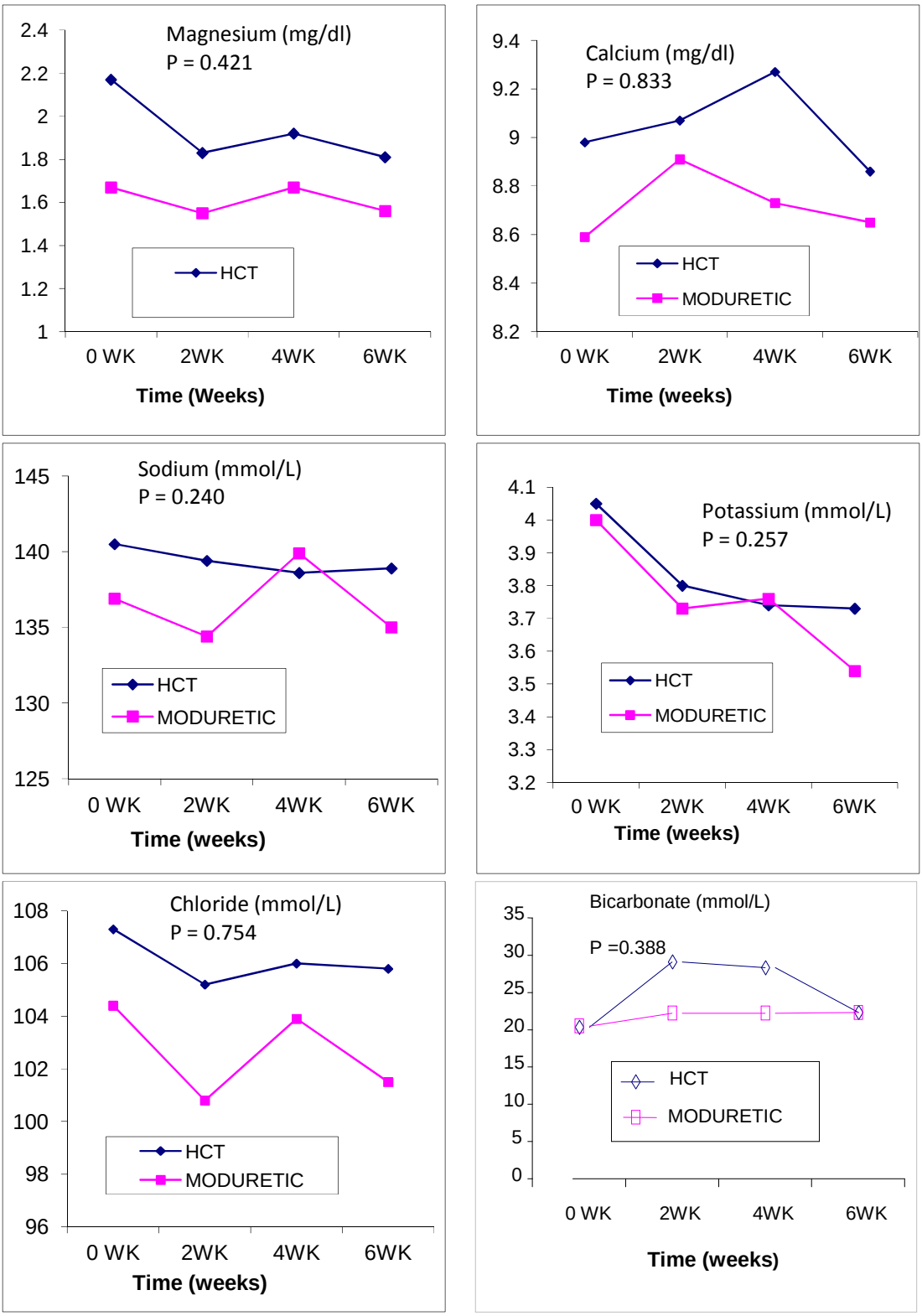

Fig. 2. Line chart showing changes in electrolytes at baseline and 6-weeks after treatment

Table 3. Comparison of baseline variables and six weeks after treatment with hydrochlorothiazide (HCT)

Parameter	Baseline	Six (6) weeks after	Difference in mean	P-value
Heart rate (beats/min)	79.8 (12.1)	80.8 (13.5)	0.920	0.370
Systolic BP (mmHg)	157.5 (17.6)	129.5 (24.3)	-28.0	0.002*
Diastolic BP (mmHg)	92.5 (15.4)	77.0 (14.4)	-15.5	0.004*
Sodium (mmol/L)	140.5 (9.6)	138.9 (5.1)	-1.58	0.669
Potassium (mmol/L)	4.05 (0.55)	3.73 (0.66)	-0.33	0.077
Chloride (mmol/L)	107.3 (5.8)	105.8 (4.3)	-1.58	0.268
Bicarbonate (mmol/L)	20.3 (0.78)	22.3 (1.07)	2.00	<0.0001*
Urea (mg/L)	19.0 (5.1)	21.1 (5.6)	2.08	0.158
Creatinine (mg/dl)	0.99 (0.41)	1.18 (0.38)	1.75	0.037*
Calcium (mg/dl)	8.98 (0.86)	8.86 (0.67)	-0.340	0.027*
Magnesium (mg/dl)	2.17 (0.96)	1.81 (0.38)	-0.120	0.646
FBG (mg/dl)	91.7 (12.2)	95.0 (8.7)	3.33	0.329
2HPPG (mg/dl)	106.2(25.1)	104.3 (54.6)	-1.58	0.856
TCHOL (mg/dl)	157.2 (31.3)	161.4 (39.6)	4.25	0.547
Triglyceride (mg/dl)	157.2 (31.3)	102.6 (51)	-2.25	0.855
HDL (mg/dl)	38.8 (7.5)	42.4 (6.2)	3.68	0.069
LDL (mg/dl)	97.7 (26.1)	99.1 (34.5)	1.42	0.866

*Values expressed as mean ± SD. *statistically significant (Students "t" test)*

Table 4. Comparison of baseline variables and six weeks after treatment with moduretics

Parameter	Baseline	Six (6) weeks after	Difference in mean	P-value
Heart rate (beats/min)	83.7 (24.9)	85.9 (14.0)	2.20	0.755
Systolic BP (mmHg)	150.9 (13.9)	123.7 (12.7)	-26.9	<0.0001*
Diastolic BP (mmHg)	92.1 (7.9)	76.1 (9.8)	-16.0	<0.0001*
Sodium (mmol/L)	136.9 (3.4)	135.0 (7.5)	-1.93	0.390
Potassium (mmol/L)	4.04 (0.61)	3.54 (0.55)	-0.46	0.023
Chloride (mmol/L)	104.4 (3.8)	101.5 (7.70)	-2.87	0.214
Bicarbonate (mmol/L)	20.5 (2.5)	22.3 (1.16)	1.73	0.044
Urea (mg/L)	15.1 (5.4)	21.2 (5.83)	6.13	<0.0001*
Creatinine (mg/dl)	0.93 (0.29)	0.95 (0.20)	0.027	0.027*
Calcium (mg/dl)	8.59 (1.23)	8.65 (0.63)	0.107	0.107
Magnesium (mg/dl)	1.67 (0.39)	1.56 (0.50)	0.067	0.067
FBG (mg/dl)	88.4 (10.6)	95.8 (21.9)	7.27	7.27
2HPPG (mg/dl)	106.3 (16.7)	107.4 (33.4)	1.07	0.871
TCHOL(mg/dl)	163.7 (46.8)	177.7 (32.7)	14.00	0.136
Triglyceride (mg/dl)	85.8 (46.8)	92.1 (45.7)	6.27	0.665
HDL (mg/dl)	38.7 (13.9)	43.0 (13.8)	4.27	0.009*
LDL (mg/dl)	113.3 (40.3)	118.1 (34.1)	4.80	0.338

*Values expressed as mean ± SD. *statistically significant (Students "t" test)*

In addition to hypokalemia observed in our study, we also observed low serum sodium, calcium and magnesium even in the absence of acidosis or alkalosis. This is in accord with previous findings [22,23]. However, It has been postulated that the abnormal potassium seen in newly diagnosed hypertensive Nigerians may be related to renal dysfunction, which appears early in Africans, compared to Caucasians [24]. Our finding of generally high serum urea and creatinine levels of the hypertensive subjects compared to normal controls support this possibility. Another plausible explanation for hypocalcaemia in these patients could be hypercorticolism. This may also be associated with low plasma phosphate and increased urinary phosphate, which were not measured in this study. However in a similar study carried out in Benin City, Nigeria, serum cortisol was not elevated in hypertensive subjects [24].

5. CONCLUSION

This study shows that, at least in the short term, thiazide diuretic (HCT) combined with a potassium sparing agent (Amiloride) does not appear to have advantage over HCT alone in the metabolic effects and blood pressure reduction. Both Amiloride-HCT and HCT commonly used in the management of mild to moderate hypertension achieve similar reduction in blood pressure. Both also cause similar derangement in most metabolic profile of newly diagnosed hypertensive subjects at least in the short-term.

ACKNOWLEDGEMENTS

The authors wish to acknowledge the subjects who voluntarily participated in the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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