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Full Length Research Paper

Electrolyte profiles in Nigerian patients with essential hypertension

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Information is inadequate on the serum and urine electrolyte profiles in Nigerians with mild to moderate essential hypertension. We, therefore, measured the levels of Na^+, K^+ and Cl^- in 40 adult Nigerians with untreated uncomplicated mild to moderate hypertension and compared these values with those obtained from age and sex-matched normotensives. Electrolytes were measured using ion-selective electrolyte analyzer. Mean arterial pressure (MAP) was 127.20 ± 4.20 mmHg in the hypertensives as compared to 92.27 ± 6.25 mmHg in the normotensives. Both groups of subjects had comparable weight and body mass indices. Results show that in the hypertensives serum, levels of Na^+ (152.8 ± 2.14 mmol l^{-1}) and Cl^- (115.4 ± 2.62 mmol l^{-1}) were significantly higher than in the normotensives (Na^+: 136.0 ± 3.23; Cl^-: 102.2 ± 2.52 mmol l^{-1}). Serum K^+ levels were significantly lower in the hypertensives than in the normotensives (4.01 ± 0.08 vs 4.82 ± 0.03 mmol l^{-1}). The hypertensives excreted more Na^+ (300.9 ± 41.30 mmol l^{-1}) and Cl^- (278.6 ± 4.39 mmol l^{-1}) than the normotensives (Na^+: 147.10 ± 1.10, Cl^-: 126.40 ± 1.51 mmol l^{-1}). Urinary K^+ level in the hypertensives was significantly higher than in the normotensives (73.70 ± 0.73 vs 55.60 ± 0.63 mmol l^{-1}). We conclude that mild to moderately hypertensive Nigerians show significant differences in their levels of serum and urinary Na^+, K^+ and Cl^- from their normotensive counterparts. The relatively higher serum Na^+ and Cl^- concentrations and the corresponding lower serum K^+ may indicate their roles in the pathogenesis of hypertension in these patients.

Key words: Electrolytes, mild to moderate hypertension, Nigerians.

INTRODUCTION

Hypertension is a global health problem that cuts across rich and poor societies although with differing pathogenetic basis (Amory and Strouser, 1996; Fuentes et al., 2000; Van den Hoogen et al., 2000; Kearney et al., 2005). Nigerians are particularly susceptible to hypertension and its complications such as disabling and fatal strokes which remain a major cause of morbidity and mortality (Nwosu et al., 1992; Iman and Olorunfemi, 2002; Akinkugbe, 2003). Aetiologically, it is regarded as a multi-factorial disease condition in which a myriad of physiological mechanisms participate to elevate and maintain blood pressure (BP) (Kaplan, 1994; Beevers et al., 2001). In spite of the many hypotheses that have been advanced in respect of the possible mechanisms for essential hypertension, it is not clear whether the kidney provides the causative factors or bears the brunt of the vascular disease (Coleman et al., 1981; Feig et al., 2004). Even though the supporting evidence associating essential hypertension with obvious renal disease is not fully persuasive, there remains the possibility that subtle renal defects, whether primary or secondary, may adversely affect electrolyte and water balance leading to hypertension (Blaustein et al., 1991; Beevers et al., 2001; Vikrant and Tiwari, 2001).

Thus the role of electrolytes in the pathogenesis and

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maintenance of essential hypertension has received considerable attention, debate and study (Blaustein and Hamlyn, 1991; Haddy, 1991; Kuller, 1997; Milan et al., 2002). These studies have implicated Na^+, K^+, Cl^- and other ions like Ca^{2+} and Mg^{2+}. It has also been shown by these studies that in both caucasians and blacks, intracellular and plasma (or serum) Na^+ and Cl^- concentrations are significantly higher in hypertensives than normotensives. Aderounmu and Salako (1979) and Worthington et al. (1993) reported that these values are even higher in black hypertensives. Human and animal models of hypertension have shown that Na^+ and Cl^- must act in concert to induce blood pressure rise (Whitescarver et al., 1986). In various human populations K^+ is an important predictor of mean arterial pressure (MAP) because hypertensives have been reported to have lower plasma (or serum) and total body K^+ as well as lower urinary K^+ excretion levels than normotensives (Kurtz et al., 1987; Morton and Abraham, 1987; Krishna et al., 1989).

Table salt is a popular seasoning agent and consumption of potassium-rich food especially in the rural and sub-urban areas is not a regular feature in Nigerian diets. These factors may affect electrolyte balance. That the observed susceptibility of Africans nay Nigerians to hypertension and its complications may be due to electrolyte abnormalities is a possibility which has not been properly evaluated (Ukoh and Obasohan, 1992).

There exists considerable discrepancies in the reported serum (or plasma) and urinary electrolyte values obtained from Nigerians because earlier workers (Aderounmu and Salako., 1979; Ekpo et al., 1989; Adegoke et al., 1990; Ukoh and Obasohan, 1992) used different age-groups and criteria in urban areas. Therefore, following a standard protocol, we have studied serum and urinary electrolytes in sub-urban Nigerian patients with essential hypertension.

MATERIALS AND METHODS

Study setting

Auchi is a sub-urban cosmopolitan town located in Edo State in the Niger Delta area of the South-South Zone of Nigeria. Apart from a few artisans, government workers and teachers, the people are predominantly farmers.

Patients

Those who were eligible for inclusion into the study were patients attending Osigbemhe Hospital, Auchi (20 males and 20 females), aged 32-80 years, with untreated mild to moderate uncomplicated essential hypertension (BP>160/95 mmHg and ≤ 180/110 mmHg). A standardized pretested questionnaire was used to elicit background information such as demographic data, family history of hypertension, current drug use if any, educational and social status as well as dietary habits. Pregnant women were excluded from the study, as well as patients with concurrent medical conditions including cardiac, renal, hepatic, gastrointestinal or endocrinologic (e.g.diabetes) diseases, following clinical examination and urinalysis. Also excluded were patients using any concomitant medications such as monoamine oxidase inhibitors, antiarrhythmic drugs, digitalis, sedative-hypnotics, minor tranquilizers, psychotropic drugs or non-steroidal anti-inflammatory drugs that might interfere with BP or renal function.

Control subjects

These were 40 age and sex-matched healthy normotensives. All the subjects signed an informed-consent form according to the protocol approved by the Medical Ethics Committee of Ambrose Alli University College of Medicine. The study was conducted in an outpatient setting and none defaulted. All subjects were advised to maintain their usual diet, to avoid foods excessively high in salt and undue stress.

Height and weight

In all the participants, a standard scale (Seca model, UK) was used to determine height (no shoes on) and a beam balance (Hackman, UK) was used for measuring weight (on light clothing) by the same trained observer.

Body mass index (BMI)

This was calculated from the formula BMI = Weight (kg) / Height (m^2).

BP measurements

Maintaining a standard protocol using phases I and V of Korotkoff sounds as respective markers for systolic and diastolic pressures, BP readings were taken by the same observer with a standard mercury sphygmomanometer (Riester Diplomat Presameter, Germany) using the subject's left arm (any constricting clothing on the arm was removed) while sitting comfortably on a chair always between 8 a.m. and 10 a.m. Readings were taken two consecutive times with an interval of one minute and the average recorded. The MAP was calculated using the formula MAP= Diastolic BP + 1/3 Pulse Pressure.

Determination of serum electrolytes

An aliquot of 10 ml venous blood obtained from each subject by peripheral venepuncture was emptied carefully into a dry sterile plain bottle to avoid lysing of the blood. The sample was allowed 1 h to clot and retract after which it was spun using a bench centrifuge at 300 rpm at room temperature for 15 min. The serum sample was then separated from the cells and within an hour, it was used to determine serum Na^+, K^+ and Cl^- levels using ion-selective electrolyte analyzer branded Biolyte 2000 (BioCare Corporation, Hsinchu 300, Taiwan) at the Research and Diagnostic Laboratory of the College of Medicine Ambrose Alli University.

Determination of urine electrolytes

Each subject was given a 4-litre plastic container to collect a 24-h urine sample and the importance of carefully collecting all the urine passed was emphasized. The volume of urine collected was measured with a measuring cylinder and recorded. An aliquot of 10 ml urine was pipetted into a plain sterile bottle and centrifuged at 300 rpm at room temperature for 15 min and the supernatant was used to determine urine Na^+, K^+ and Cl^- using ion-selective electrolyte analyzer.

Statistical analysis of data

Data are presented as mean ± SEM or mean ± SD (for age, weight and height). The Students't-test (GraphPad Prism Software, UK) was used for the analysis. Spearman's rank correlation was used to determine correlation between two sets of variables and statistical significance was set as $p<0.05$.

RESULTS AND DISCUSSION

Table 1 shows that in hypertensive and normotensive subjects there was no statistically significant difference between the ages (58.10 ± 7.84 and 57.10 ± 11.58 years, respectively) as well as the body mass indices (26.96 ± 4.35 and 25.15 ± 2.34 kg/m^2, respectively). MAP was significantly higher ($p<0.0001$) in hypertensives (127.20 ± 4.20 mmHg) than in normotensive subjects (92.97 ± 6.25 mmHg).

Table 2 shows that serum Na^+ and Cl^- (152.8 ± 2.14 and 115.4 ± 2.62 mmol l^{-1}, respectively) in patients were significantly higher ($p<0.0001$) than the values (136.0 ± 3.23 and 102.2 ± 2.52 mmol l^{-1}, respectively) in normotensives. The serum K^+ (4.01 ± 0.08 mmol l^{-1}) in hypertensive patients was significantly lower ($p<0.0006$) than the value (4.82 ± 0.03 mmol l^{-1}) in normotensive subjects. Similarly, the urine Na^+ and Cl^- levels (300.9 ± 41.3 and 278.6 ± 4.39 mmol l^{-1}, respectively) in hypertensives were significantly higher ($p<0.0001$) than those in normotensives (147.1 ± 1.10 and 126.4 ± 1.51 mmol l^{-1}, respectively). The urine K^+ in patients (73.70 ± 0.73) was significantly higher ($p<0.0001$) than that of normotensives (55.60 ± 0.63). The 24-h urine volume in hypertensives (1410.0 ± 41.30 ml) was significantly higher ($p<0.0006$) than the value in normotensives (1253.0 ± 14.33 ml). Table 3 shows a negative correlation between MAP and serum K^+.

Our findings that serum and urinary levels of Na^+ and Cl^- were significantly higher in hypertensives than in normotensives confirm the important roles of these ions in the pathogenesis and maintenance of essential hypertension in populations who habitually consume salt. Our results corroborate the findings of studies by Morton and Abraham (1987), as well as Ukoh and Obasohan (1992); but differ from the result obtained by Adegoke et al. (1990), who found no significant differences in Na^+ excretion between normotensive and hypertensive Nigerians, most probably because they adopted any BP above 130/90 mmHg as a marker for hypertension.

Aderounmu and Salako (1979), as well as Worthington et al. (1993), who reported significantly raised plasma and intraerythrocytic Na^+ concentrations in hypertensive blacks more than the caucasians suggested that the reason may be due to differences of the cell membrane of blacks or to an increase in a Na^+ transport inhibitor, a depressed Na^+ efflux rate constant as well as a reduction in the activity of oubain-sensitive component of the Na^+-K^+-ATPase pump. Rossier et al. (2002), also support this view.

Consequently, modest dietary salt restriction employed as a definitive or adjunctive treatment of hypertension, has been shown to reduce BP or permitted drug treatment to be substantially reduced or discontinued (Alderman et al., 2001; He and MacGregor, 2002; He et al., 2005a; Melander et al., 2007). In adittion, it has been demonstrated that a BP-lowering response to reduced dietary salt intake occurs in salt-sensitive subjects (Svetkey et al., 1996; Weinberger et al., 1996; Melander et al., 2007) who constitute about half of the adult population regardless of race (Grobbee, 1991) and 73% of hypertensive and 36% of normotensive blacks (Svetkey et al., 1996). Efforts to find a genetic or physiological marker to identify salt-sensitive patients and target them for low dietary salt therapy have largely been unsuccessful, although there is clinical evidence that older, obese and black hypertensives tend to be more salt-sensitive than the general population (Blaustein and Hamlyn, 1991; He and MacGregor, 2003).

The greater urine volume in hypertensives is consistent with the higher serum Na^+ and Cl^- concentrations (Adegoke et al., 1990). This observation may explain why volume-dependent hypertension which is commonly found in blacks and the elderly, responds well to diuretic therapy or agents counteracting mineralocorticoid effects (Freis, 1995; Billinghurst, 2002).

In contrast to the findings of Ukoh and Obasohan (1992), in urban Benin City, Nigeria, that there was no significant difference in serum K^+ concentration in hypertensives and normotensives, a relative hypokalaemia significantly negatively correlated with MAP, was observed in hypertensives. This could cause compromised vascular function and may well be a vital factor in the pathogenesis of hypertension in this sub-urban population. Majority of the patients studied are poor, particularly the elderly with lower K^+ intake, and so become susceptible to hypokalaemia; and the few rich who consume more Na^+ and waste K^+ (Kaplan, 1994).

A surprise finding in this study was that the excretion of K^+ was higher in hypertensives even though they had lower serum K^+ levels. This probably reflects increased K^+ secretion in exchange for the high Na^+-Cl^- load that reaches the renal distal tubules and collecting ducts. This observation may also indicate that overall renal handling of Na^+, Cl^- and K^+ in this set of hypertensive patients was abnormal (Coleman et al., 1981). However, handling of electrolytes is modulated by a variety of substances such as aldosterone, angiotensin II, catecholamines and prostaglandins. Of these, aldosterone is the major determinant of K^+ balance (McCabe et al., 1993). The fact that serum K^+ was significantly lower in hypertensives suggests that the patients may suffer from primary aldosteronism because K^+ and Cl^- are modulated by the renin angiotensin aldosterone system (Giebisch, 1986; Vikrant and Tiwari, 2001).

Potassium supplementation, or high K^+ diet including fresh fruits (e.g. apples, bananas, oranges) and vegeta-

Table 1. Demographic characteristics of subjects with or without essential hypertension.

Characteristic	Normotensives		Hypertensives	
	Range	Mean ± SD	Range	Mean ± SD
Age (years)	33 – 80	58.10 ± 7.84	32 – 80	57.10 ± 11.58
Height (m)	1.56 – 1.72	1.63 ± 0.04	1.50 – 1.80	1.65 ± 0.07
Weight (kg)	56 – 98	71.74 ± 9.02	52 – 85	68.41 ± 6.86
BMI (kg/m ^{2})	23.01 – 33.13	26.96 ± 4.53	23.11 – 26.23	25.15± 2.34
MAP	83.30 – 106.70	92.27 ± 6.25	118.30 – 136.70	127.20 ± 4.20*

Values are comparable between both groups of subjects except for MAP. *p <0.0001 compared to normotensives.
n = 40 per group (20 males and 20 females).
BMI = Body mass index; MAP = mean arterial pressure.

Table 2. Serum and urine parameters of subjects with or without essential hypertension.

Parameter	Normotensives		Hypertensives	
	Serum	Urine	Serum	Urine
Na^+ (mmol/l)	136.0 ± 3.23	147.1 ± 1.10	152.8 ± 2.14**	300.9 ± 41.3***
K^+ (mmol/l)	4.82 ± 0.03	55.60 ± 0.63	4.01 ± 0.08**	73.70 ± 0.73***
Cl^- (mmol/l)	102.2 ± 2.52	126.4 ± 1.51	115.4 ± 2.62*	278.6 ± 4.39***
24 h Urine volume (ml)		1253.0 ± 14.33		1410.0 ± 41.30**

*p<0.01; **p<0.0006; ***p<0.0001 when hypertensives are compared with corresponding normotensive controls. n = 40 per group.

Table 3. Correlation analysis of mean arterial pressure (MAP) with serum electrolytes of subjects with or without essential hypertension.

Serum	Normotensives		Hypertensives	
	r – value	p – value	r – value	p – value
Na^+	0.1969	0.2233	0.2501	0.1196
K^+	-0.0450	0.7827	0.3481	0.0277*
Cl^-	0.2698	0.0922	0.1656	0.3070

MAP is negatively correlated with K^+.
*Statistically significant.

bles, has been demonstrated to lower BP (more in hypertensives than normotensives), potentiate the effects of diuretic therapy and lessen renal K^+ wasting (Cappucio and MacGregor, 1991; Whelton et al., 1997; Gu et al., 2001; He et al., 2005b). However, a recent report of a systematic review of available meta-analyses and randomized controlled trials found no statistically significant effect of potassium supplementation on BP excluding one trial in an African population with very high baseline BP that resulted in small overall reductions in BP (Dickinson et al., 2006). The various mechanisms reported to be responsible for the antihypertensive effect of increased K^+ intake include enhancing natriuresis, suppressing renin secretion, causing arteriolar dilation, increasing the activity of membrane-bound Na^+-K^+-ATPase and decreasing intracellular concentration of calcium, impairing responsiveness to endogenous vaso-constrictors, inhibition of superoxide dismutase activity, thereby protecting endogenously produced nitric oxide (Cappucio and MacGregor, 1991; Omogbai et al, 2005).

In conclusion, this study suggests that high serum Na^+ and Cl^+ concentrations and increased urinary K^+ excretion (which predispose to hypokalaemia) may contribute to the pathogenesis of essential hypertension in this population. Reduced dietary Na^+-Cl^- intake and K^+ supplementation may be useful as a definitive or adjunctive treatment in these patients.

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