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Alterations in Serum Magnesium and Electrocardiographic Variables of Adult Hypertensive Humans

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Abstract

As the most important risk factor for cardiovascular diseases worldwide, Hypertension has been found to be a major public health challenge with high prevalence in Africans and Nigerians especially with a rapidly growing population. It has been postulated that hypomagnesemia contributes to the development of hypertension and cardiovascular disease. This study was therefore undertaken to determine the relationship between serum magnesium levels and electrocardiographic changes in adult humans with hypertension. To achieve this, one hundred and sixty two (162) hypertensives were recruited from the University of Benin Teaching Hospital (UBTH), Benin City, Edo State, Nigeria. Participants' Blood pressure, electrocardiographic changes, antihypertensive medications and serum magnesium (Mg^{2+}) levels were investigated. Using the Pearson Product Moment Correlation Coefficient and ANOVA, Statistical measures of association (correlation) were conducted on obtained variables. A low incidence of hypomagnesaemia was observed on the average, with a high incidence of patients presenting with abnormal ECG changes; including Left Ventricular Hypertrophy. In addition, only weak correlations were observed for ECG parameter and serum Mg^{2+}levels for sampled subjects, with p-value returning a statistically significant decrease upon comparison of means (Using the One-Way Analysis of Variance (ANOVA); Other influences like antihypertensive medications, blood pressure duration and control returned an significant (weak negative) correlation with serum Mg^{2+} concentration. There is therefore a weak negative correlation between serum magnesium levels and ECG variables, including Q wave duration and QT interval duration in hypertensive adults.

Keywords: Magnesium, Electrocardiogram, Hypertension.

INTRODUCTION

One of the commonest forms of elevated blood pressure is evident in essential hypertension. Essential hypertension is a primary form of hypertension of which exact cause is actually unknown [1-2]. Though several factors have been implicated in its pathogenesis, these factors may include, but unlimited to the hyper-activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system [3]. In addition, changes in intracellular ions such as calcium, sodium, potassium, and magnesium have been implicated. Hypertension results in several changes in the cardiovascular functions which can be diagnosed with the aid of an electrocardiogram (ECG) [4].

According to the World Health Organization, prevalence of hypertension in Africa is reportedly highest in 46% of adults aged 25 years and above [5]. In Nigeria, a high prevalence of up to 28.9% and 47.2% has also been reported [6-7], forming a substantial portion of the total burden in Africa as a result of the large population of Nigeria [8]. Also, the proportion of hypertensives undergoing treatments in Nigeria is reported to be as low as 21% (23.7% men, and 17.5% women) [9]. In addition, the control of blood pressure has also been reported to be as low as 9% (5 % in men and 17.5 % in women) [9].

In most cases of hypertension, serum magnesium level is reported to affect blood pressure in humans. This is achieved by its modulating effects on vascular tone and reactivity, acting as calcium channel antagonist to stimulate production of prostacyclin and nitric oxides. These vasodilator substances then alter vascular responses to vasoactive antagonist [10]. Studies have implicated hypomagnesemia in the aetiology of hypertension. This supposes that a diet rich in magnesium, potassium and calcium is associated with a lower incidence and mortality of cardiovascular disease [11].

In Hypertensives, some resulting changes in cardiovascular functions can be diagnosed with the aid of an electrocardiogram (ECG) which ultimately records electrical currents generated by the conducting system of the heart [12].

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By implications, rhythmic contractions of the heart is maintained through orderly series of discharges patenting in the sinus node of the right atrium that progresses through the atrioventricular node and the bundle of neuromuscular fibers (the bundle of His) to the ventricles [13]. Prominent parts of the ECG are the P wave, a deflection caused by the current originating in the atrium; the QRS complex, showing the passage of the electrical activity into the ventricles; and the T wave, as the ventricles reset themselves [14].

Kisters *et al.* in an experimental study with spontaneously hypertensive rats (SHRs) reported a relationship between hypomagnesemia and increase of blood pressure [15]. In a similar vein, Tonyz and Milne (2009) in their study had reported magnesium supplementation to pose little antihypertensive effect in adult SHRs with an established hypertension; asserting that supplementation was only useful in younger animals in the per-hypertensive phase, preventing or at least attenuating the development of hypertension. This is suggestive of a far protective effect of dietary magnesium in the management of hypertension [16].

Though most epidemiological and experimental studies support a role for low magnesium in the pathophysiology of hypertension, data from clinical studies have been divergent [17]. Considering these associations, it will be useful to determine the relationship between serum magnesium levels and the progressive changes caused by hypertension which are identifiable by use of electrocardiography. This can contribute to various treatment options for the control of essential hypertension and the prevention of progressive complications that accompany it.

Aim of Study

This study determined the relationship between serum magnesium levels and electrocardiographic changes in hypertensive adult humans. Specifically, study;

i. Determined serum magnesium levels of adults with essential hypertension
ii. Ascertained ECG changes in adult hypertensive subjects
iii. Investigated the relationship between serum magnesium levels and ECG changes in hypertensive humans.

MATERIALS AND METHODS

Study Location

The study was conducted at the University of Benin Teaching Hospital (UBTH), Benin City, a tertiary healthcare facility situated in Edo state, Nigeria which provides specialized care for a large proportion of patients in Edo, Delta, and neighbouring states of Nigeria.

Study Design

This study was a descriptive, cross sectional study.

Study Population

The population of the study was drawn from adults with essential hypertension, who attend the Consultant Out-patient Clinic (COPD) unit monthly.

Sample Size and Technique

Sample size estimation

The sample size of the study was determined using the following formula below (Singh and Masuku 2004)

$$n = \frac{(Z\,\alpha/2)\,2\sigma 2}{d2}$$

Where Z α= standard normal deviate at 95 % confidence interval = 1.96

σ = standard deviation of the characteristic of interest in the target population

d = the margin of error = 0.02

Substituting the values in the above formula, the sample size (n) was calculated as

$$n = \frac{1.96\ x\ 1.96\ x\ 0.12\ x\ 0.12}{0{,}02\ x\ 0.02} = 138.29 = 139$$

To make up for attrition, 10 % of the sample size was added to make up for non-responses which was 13.83 =14 = 153.

However, a total of 162 persons were entered into this study.

Selection Criteria

Selection of subjects for participation in the study was based on;

Inclusion Criteria

Essential hypertensives of between 30 to 65 years of age, whose consent we got were selected for the study.

Exclusion Criteria

Subjects with Cerebrovascular Accident (CVA) and those on magnesium supplements were exempted from this study

Procedure

Ethical Clearance

Ethical clearance was first obtained from the Bio-research and ethics committee of the Faculty of Basic Medical Sciences, Delta State University, Abraka and, also from the Ethics and Research Committee of the University of Benin Teaching Hospital, Benin, Edo State. Participants' informed consent was sought prior to their selection for participation in the study.

Data Collection Tools

Questionnaire

By blind balloting; a structured questionnaire was used for data collection. The questionnaire had a socio demographic section for which socio demographic data was obtained and recorded for each participant. Relevant clinical information were obtained and recorded such as the period of onset of hypertension, duration of hypertension, control of blood pressure in the last three months and a record of antihypertensive medications. A blood pressure recording of ≤ 140/ 90 mmHg in the last 3 months was recorded as 'good control' while blood pressures higher than this was recorded as 'poor control'.

Weighing Scale and Standiometre

Subjects' weight was measured in kilogram with the individual barefoot, wearing his or her normal but light clothing, free of unusual weights, with the head uprightly in neutral state. Participants' heights were then obtained (in meters) with the aid of an attached standiometre while standing on a wide, firm, platform; following which their BMI was calculated using; Weight (kg) / Height (m) ^{2}.

Obtaining the Blood Pressure

The blood pressures erect and supine was measured using a mercury sphygmomanometer (manufactured by Accoson, United Kingdom in 2014). The sphygmomanometer was placed on a flat surface using an appropriately sized cuff around the patient's left upper arm placed at the level of their heart. The mean arterial blood pressures were calculated using the formula; Systolic Blood Pressure + (2 X Diastolic Blood Pressure) / 3.

Electrocardiogram (ECG) Readings

To obtain ECG readings, a 12-lead electrocardiograph machine (AK 12, 12-Channel ECG Machine; Manufactured by Carl Novel, Germany, 2012) was employed in the recording of ECG variables at about 25 mm per second rates. Obtained readings ECG recordings were then noted and recorded.

Determination of Serum Magnesium

Following venous blood collection from participants, obtained sample was placed tubes for determination of serum Mg^{2+} concentrations. Next, a standard Colorimeter (Abbott 1000 SR, manufactured by Graham Abbott, United States of America, 2007) was used to assay constituent Mg^{2+} ion, while obtaining serum Ca^{2+} and phosphate concentrations as well. Also, Na+, K+, Cl- HCO3- and urea levels were assayed and recorded

Data Analysis

Data analysis was done using IBM, SPSS (Statistical Package for Social Sciences) Version20. The categorical data (Sex, Level of Education etc.) was expressed as frequencies and percentages. The numerical data was summarized using means and standard deviation. The correlation between serum magnesium and ECG parameters (rate, segments, intervals, QRS complexes etc.) was estimated using the Pearson's correlation coefficient for the normally distributed variables. The role of chance was qualified using the p-value. The level of significance was set at $p < 0.05$ while 95 % confidence interval was constructed around estimates. The multiple linear regression analysis was modified to identify significant independent predictor ECG values and also to adjust for confounding variables. The level of significance was set at $p < 0.05$; with 95 % being the confidence interval.

RESULTS

A total of 162 hypertensive participants, consisting of 45 males (27.8 %) and 117 females (72.2 %) were recruited for the study. Subjects had an average age of between 28 to 65 years

Anthropometric Properties of Respondents

Variable	n= 162 Mean (± Std Dev)	Minimum	Maximum
Weight (kg)	78.87±15.67	49	140
Height (m)	1.65±0.08	1.35	1.85
BMI (kg/m^2)	29.26±6.37	17.17	53.35

Result is presented as Mean ± Standard Deviation

Clinical Features of Respondents

Variables	*Mean*	*SD*	*Minimum*	*Maximum*
Supine				
Pulse (BPM)	*78*	*12.0*	*54*	*110*
Diastolic Blood Pressure (mmHg)	*88.2*	*13.7*	*60*	*162*
Systolic Blood Pressure (mmHg)	*136.9*	*20.4*	*96*	*210*
Mean Arterial Blood Pressure (mmHg)	*104.4*	*14.6*	*75.3*	*177.3*
Erect				
Diastolic Blood Pressure (mmHg)	*85.3*	*14.2*	*55*	*149*
Systolic Blood Pressure (mmHg)	*134.9*	*21.3*	*93*	*200*
Mean Arterial Blood Pressure (mmHg)	*101.8*	*15.4*	*70.3*	*165*

Hypertension Characteristics of Respondents

Variable	Frequency	Percent
Duration of Hypertension (Years)		
0 to 4	83	51.2
5 to 9	35	21.6
10 to 14	24	14.8
15 to 19	7	4.3
20 to 24	6	3.7
25 to 29	5	3.1
> 30	2	1.2
Blood pressure Control in the Last 3 months		
Good Control	68	42.0
Poor Control	94	58.0
Presence of Complications of Hypertension		
Yes	27	16.7
No	135	83.3
Presence of Other Co-morbidities		
Present	76	46.9
Absent	86	53.1

Comparative Changes in Serum Magnesium in Hypertensives

Magnesium Levels	Frequency	Percent
Low	14	8.6
Normal	139	85.8
High	9	5.6
Total	**162**	**100.0**

From above table, mean serum Mg^{2+} is observed to be 1.95 mg.dL^{-1} and minimal at 1.01 mg.dL^{-1}and maximum 2.70 mg.dL^{-1} with higher respondents showing normal levels for Na^+ (83.3. %), K+ (64.2 %), Cl- (80.9 %), HCO3- (94.4 %), urea (100 %), calcium (93.8 %) and phosphate (89.5 %). Hyponatraemia was seen in 14.2 % of the respondents while only 2.5 % had hypernatraemia. Hypokalaemia was noted in 35.8 % while no patient had hyperkalaemia. Hypochloraemia was observed in 3.1 % and abnormally high levels were found in 16.0 %. 1.9 % had abnormally low serum bicarbonates and 3.7 had high bicarbonate levels. All the respondents had normal serum urea levels. Hypocalcaemia and hypercalcaemia was found in 3.7 % and 2.5 % of the respondents respectively. No patient had hypophosphataemia but 10.5 % had abnormally high serum phosphate levels.

Summary of ECG Changes in Adult Hypertensives

ECG Findings		Frequency	Percent
	Normal	20	12.3
	Abnormal	142	87.7
	Total	**162**	**100.0**

Above table shows a 12.3% respondents with normal ECG, with a 87.7% abnormal cases

ECG Characteristics of Respondents

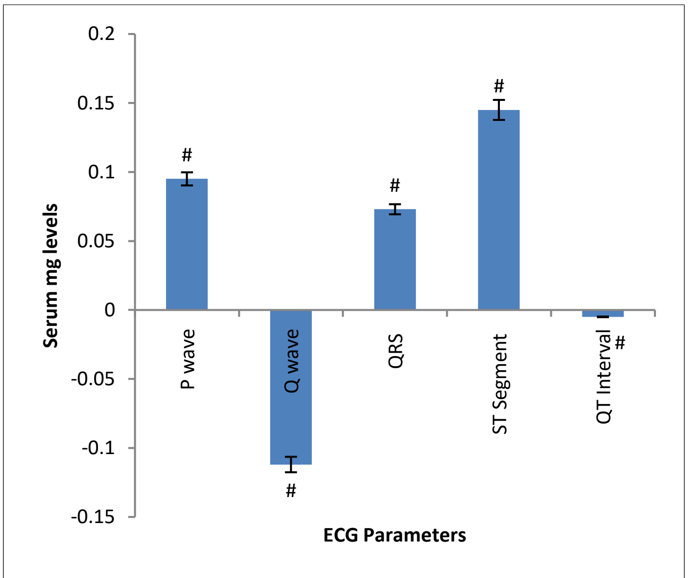
Variables	Mean	SD (±)
Heart Rate (beats per minute)	81.41	16.37
Duration of P Wave (seconds)	0.107	0.022
Duration of PR Interval (seconds)	0.170	0.037
Duration of Q Wave (seconds)	0.003	0.016
Duration of QRS complex (seconds)	0.064	0.022
Duration of ST Segment(seconds)	0.138	0.043
Duration of T Wave (seconds)	0.148	0.042
Length of Sin V1+ R in V5(seconds)	27.91	10.26
Length of S wave in V1 (seconds)	12.90	7.16
VAT in V1 (seconds)	0.008	0.013
VAT in V5 (seconds)	0.016	0.010
VAT in V6 (seconds)	0.018	0.010

Relationship between Serum Magnesium of Respondents and ECG Findings

	r	*p-value*	*Remark*
	ECG Changes		
Serum Magnesium	*-0.128*	*0.105*	*NS*

r= correlation coefficient at p < 0.05, NS = Not significant

Comparative Changes in Serum Magnesium and Selected ECG Variables



Correlation was weak and negative with statistically insignificant changes (p > 0.05) for differences in mean (student t-test) between serum magnesium levels and VAT in hypertensive subjects.

DISCUSSION

Hypertension has been found to be a major public health challenge worldwide and the most important risk factor for other cardiovascular diseases [18]. A high prevalence of hypertension has been recorded amongst persons in the African regions [18]. In Nigeria, a prevalence of up to 28.9 % and 47.2 % has been reported [19]. In this study, the number of proportion of women who came for management of essential hypertension was noted to be higher compared to the men following randomization. Akinlua *et al.* (2015) [6] carried out a systematic review of studies carried out in Nigeria among hypertensive patient and reported unfinished occurrence of hypertension ranging from 2.8% to 13.9% and 0.5% to 12.7% in men and women respectively. They also reported that in studies that used blood pressure benchmark (of 140/90mmHg), hypertension had prevalence rate of between 6.2% and 48.9% for men, and 10% to 47.3% for women, stating however that irrespective of Blood Pressure cut-offs, total prevalence rates are mostly higher in males than their female counterparts. In another study, Ekwunife *et al.* (2010) reported hypertension to be less common females than males in early adult life, with preponderant increase in women than men as they approach the fifth decade of life. Authors also observed higher prevalence of hypertension in older women (of > 60 years) than the male counterparts who reportedly had highest prevalence rates in the elderly blacks than in Caucasians [14].

Again from current study, a negatively weak correlation is observed for serum Mg^{2+} value against most assayed ECG parameters. Here, decreased serum Mg^{2+} caused statistically significant ($p < 0.05$) increase in most sampled ECG variables with an accompanying weak negative correlations in Q wave duration, as well as QT interval from ECG recordings.

From this study, hypomagnesemia prevalence in participants was as low as 8.5%. This implies huge deficiency in Mg^{2+} levels, even though recorded Hypermagnesaemia lavel was on the average, 15.2 % participants with a larger majority of 77.3 %. Muzasti and Lubis in 2015 found a similar result; where in serum Mg^{2+} level was as low as 10.7 % in hypertensive humans result of current study concurs with thos of Muzasti and Lubis. Several other reports have implicated serum Mg^{2+} in hypertensive Nigerians [19]. Odusan *et al.* had reported a prevalence rate of about 32.4% in diabetic subjects with hypomagnesaemia rate of between 36% and 93.8 % in pregnant females [19]. This may have resulted from increased basal metabolic rate due to pregnancy.

As one of the very vital cations of most cellular processes, a relatively normal Mg^{2+} levels is vital for most nerve-muscle functioning. In the cells, Mg^{2+} plays a vital role as cofactor in numerous enzymatic processes, including transportation activities that can significantly affect cellular activities during replication and metabolic processes. Available reports assert that about 20% of the 25 g (1000 mmol) of Mg^{2+} in the human body are sited in their bones, with most other extra skeletal Mg^{2+} found within cells and tissues [20]. Physiologically, though serum Mg^{2+} concentrations may not be reflections of the total volume of body Mg^{2+}, about 1% of this however is sited in the extracellular fluid spaces. Again, about 30-40% of dietary Mg^{2+} (140–360 mg/d) have been asserted to be absorbed through the jejunum and ileum, under controlled influence of 1,25$(OH)_2$ Dihydroxyl-calciferol. This is subsequently excreted (via urine). Also, about 60% cortical Mg^{2+} have been reported to be reabsorbed at the thick ascending limb of loop of the kidney, with proximal tubule and distal convoluted tubule reabsorbing 20% and 5–10% respectively [21]. All of these processes are under physiological control by special hormones; Parathyroid hormone, which increases reabsorption of Mg^{2+} at the nephron, whilst inhibiting Calcium ion reabsorption synergistically.

Physiologically, serum Mg^{2+} levels < 0.7 mmol/L, 1.4 mEq/L, or 1.7 mg/dl defines hypomagnesemia, and has a reported occurrence rate of about 15% in the general global population of hypertensive humans to about 65% prevalence amongst subjects undergoing intensive care [22]. Again, deficiency of Magnesium ion (Mg^{2+}) deficiency reportedly correlates with some of the worse clinical results of higher than normal mortality and co-morbidities, especially in hypertensive humans on critical care [23]. This has directly implicated Mg^{2+} in complicated ailments relating to tetany, hypokalemia, arrhythmias and hypocalcemia; to mention a few [24]. Reports have also shown magnesium to be a key player in cerebrovascular accident (stroke), and other cardiovascular threatening conditions like ischemic heart disease. Additionally there has been reported incidence(s) of increased urinary stone disease amongst hypertensives with magnesium deficiencies in diet supplements. From results of current study however, subjects with hypomagnesaemia were observed with no manifestation and/or symptoms as such. Albeit, hypertensive humans with hypomagnesemia who receive regular Mg^{2+} dietary supplementation may present with little or no adverse pathophysiological effects if done consistently. Also observed from current study was a low prevalence of hypermagnesemia, even though this may only be prognostic of congestive heart failure that was actually absent in all of our sampled hypertensive subjects.

Also from current study, a negatively weak correlation is returned for ECG variables and serum Mg^{2+} changes amongst sampled population of hypertensive humans. This relationship was however seen to be statistically insignificant upon comparison of mean differences ($p < 0.05$) across groups. Also observed from this study was a weak correlation between other determinants of hypertension like blood pressure (systolic and diastolic) with a statistically insignificant difference in ECG variables (P, Q, QRS and ST, QT intervals). In general, the relationship between blood pressure and serum Mg^{2+} has reportedly bore contradictory outcomes [25] with older studies asserting a strong positive correlation for blood pressure and serum Mg^{2+} concentrations in most studied hypertensive humans. Contrarily also, recent studies on the serum Mg^{2+} and blood pressure correlations have shown no correlation for serum Mg^{2+} levels and systolic blood pressure in complicated cases of cardiovascular diseases amongst hypertensive humans [28], with little or no evidence to assert any scientific link between the aforementioned parameters [29-32]. Results from study apparently concur with those of recent investigations on this subject.

CONCLUSION

This study has shown a statistically insignificant, but negatively weak relationship for serum Mg^{2+} concentration and ECG changes across sampled subjects. Therefore a it can be asserted that the relationship between serum Mg^{2+} concentrations and ECG changes in hypertensive humans is negatively weak.

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