Magnesium, calcium, sodium and potassium status in normotensive and hypertensive Johannesburg residents


Summary

Serum magnesium, calcium, sodium and potassium, and erythrocyte magnesium, sodium and potassium levels were measured in a selected group of 296 urbanised black male labourers in Johannesburg. Of these, 214 subjects were normotensive and 82 were hypertensive. The aim of the study was to examine the relationship between serum and erythrocyte electrolytes, specifically magnesium and calcium, and blood pressure in this population sample. The results showed a significant decrease in serum magnesium, calcium and potassium in the hypertensive subjects. Red blood cell magnesium was significantly lowered and red blood cell sodium was significantly raised in this group. A significant inverse correlation was found between serum magnesium and blood pressure, erythrocyte magnesium and blood pressure, serum calcium and blood pressure, and serum potassium and blood pressure. A positive correlation was observed between erythrocyte sodium and blood pressure. Of all the electrolytes assessed, magnesium (serum and erythrocyte) correlated most closely with blood pressure. The data reported here suggest that body magnesium and its interactions with calcium, sodium and potassium may, in certain groups of individuals, play an important role in the development and maintenance of high blood pressure.

The role of electrolytes in the causation of essential hypertension has been studied extensively. However, the roles of sodium and potassium have been emphasised and less attention has been paid to other electrolytes such as magnesium and calcium. Factors determining the development and maintenance of arterial hypertension include vascular tone, contractility, reactivity and transmembrane potential. These are all influenced by extracellular magnesium and calcium levels. A raised serum magnesium concentration is associated with decreased cell membrane potential, vasodilation and a consequent fall in blood pressure. Animal experiments indicate that low extracellular magnesium levels are related to hypertension, but human studies examining this association are rare. A small preliminary study on 16 white subjects hinted at a relationship between low serum magnesium and hypertension when diuretics were used to control hypertension. A negative correlation between serum magnesium levels and blood pressure has also been reported in an elderly Danish population. Some studies suggested a negative correlation between serum calcium and blood pressure, while other reports indicated a positive association. No study has been done specifically to investigate the relationship between serum and erythrocyte calcium, magnesium, sodium and potassium and blood pressure in humans. Since the prevalence of hypertension is high among urbanised blacks in Johannesburg, this population group was chosen for the study.

Subjects and methods

Two hundred and ninety-six urban black male labourers were studied (300 were originally analysed but 4 were not included in the study because of incomplete data). All had lived in Johannesburg for at least 5 years. They were chosen from a population reporting to the municipal medical centre at the local labour bureau, where all blacks starting, changing or recommencing employment in Johannesburg register and are examined medically. The purpose of this is, in part, to identify latent disease, to prevent dissemination of infectious diseases, and to screen for hypertension. All the subjects entering into the study gave signed informed consent, were healthy and were not on regular medication. There was also no history of diuretic use. Of the 296 subjects, 82 were hypertensive, with a diastolic blood pressure (DBP) greater than 95 mmHg and/or a systolic blood pressure (SBP) greater than 160 mmHg. Mean arterial pressure (MAP) was calculated from the standard formula: MAP = DBP + 1/3 (SBP - DBP). The hypertensive men were referred to the hypertension clinic at the local hospital for management.

Subjects were studied under standardised conditions in a quiet, noise-controlled room on consecutive Wednesdays between 09h00 and 14h00. A medical history was taken and a questionnaire was then completed, including enquiry about age, diet (breakfast, lunch, supper), alcohol consumption (beer, spirits, wine) and type of residence (in a hostel, with employer, in a township). The hostel is a large, all-male residential institution. Those living at their employers' homes work as domestic helpers, and have a room attached to the employer's house. Townships-dwellers live with their own, or another, family in a house. Height, mass and upper arm girth were recorded. Quetelet's index (QI) (mass (kg)/height (m)^2) was calculated. In order to eliminate additional variables, obese and very thin individuals were excluded from the study. Subjects not of normal mass to height ratio and those with arm circumference greater than 35 cm were rejected. After 15 minutes' rest, right arm blood pressure was measured with the subject sitting. Blood pressure was recorded three times in each individual by two different people (a medical doctor and a junior intern). Interoperator error was eliminated by comparing the means of every tenth reading using Student's t-test. There was no significant difference (P > 0.05).

The mean of the six measurements was taken for analysis. A standard mercury sphygmomanometer was used. SBP and phase V
DBP were measured. The radial pulse rate was measured three times and the mean recorded.

A blood sample (15 - 20 ml) was drawn from an antecubital vein without cuff compression. Serum sodium, potassium, magnesium, calcium, albumin, creatinine and γ-glutamyltransferase (GGT), and red blood cell sodium, potassium and magnesium were measured. The blood samples were analysed blind, i.e. the analysts did not know which sample belonged to which subject. Sodium and potassium levels were determined by standard flame photometry and magnesium and calcium levels were measured by atomic absorption spectrophotometry. Calcium levels were corrected according to the formula:

\[ \text{total serum calcium concentration} = [40 - (\text{albumin} \times 0.02)] \]

Serum albumin and creatinine were determined by colorimetric methods and GGT by an automated enzymatic method. Red blood cell measurements were based on the method of Meyer and Starkey. Separated erythrocytes, collected in heparinised tubes, were washed three times with iso-osmolar magnesium chloride solution. They were then lysed by the addition of saponin, and the sodium and potassium levels measured in the diluted haemolysate by flame photometry. Erythrocyte magnesium was measured in the diluted haemolysate by atomic absorption spectrophotometry after the cells had been washed with iso-osmolar sodium chloride. All other cations were measured in each sample. Wilcoxon’s signed rank test showed no significant difference in the results obtained between the two laboratories (P > 0.05).

The data were analysed with an IBM 4331 computer at the Institute for Biostatistics of the South African Medical Research Council. Where two groups were compared, and the sample sizes were large enough, the unpaired -test was applied. If the sample sizes were small and the central limit theorem was not applicable, the Mann-Whitney U-test or Wilcoxon’s signed rank test was applied for unpaired and paired data respectively. Stepwise multiple regression procedures were used to find the partial and direct correlations.

Results

Two hundred and fourteen normotensive men (mean SBP 127.7 ± 10.3 mmHg; mean DBP 74.4 ± 8.6 mmHg), and 82 hypertensive men (mean SBP 151.4 ± 17.9 mmHg; mean DBP 103.5 ± 9.0 mmHg) were studied. Pulse rate, age, height, mass and Q1 were similar in both groups (Table I). Serum magnesium, calcium and potassium and red blood cell magnesium were all significantly lower in the hypertensive group (Table II). Erythrocyte sodium was significantly higher in the hypertensive group. There was no significant difference in serum potassium and MAP between the two groups. Serum albumin, GGT, and creatinine were similar in both groups (Table I).

<table>
<thead>
<tr>
<th>TABLE I. SUBJECT DATA (MEAN ± SD) IN NORMOTENSIVE AND HYPERTENSIVE GROUPS</th>
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<tr>
<td>( N = (214) )</td>
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<tr>
<td><strong>Systolic blood pressure</strong> (mmHg)</td>
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<tr>
<td><strong>Diastolic blood pressure</strong> (mmHg)</td>
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<td><strong>Mean arterial pressure</strong> (mmHg)</td>
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<td><strong>Pulse (l/min)</strong></td>
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<td><strong>Age (yrs)</strong></td>
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<td><strong>Height (cm)</strong></td>
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<td><strong>Mass (kg)</strong></td>
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<td><strong>Quetelet's index (kg/m²)</strong></td>
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<td><strong>Arm girth (cm)</strong></td>
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</table>

**P < 0.001.**

The possible explanations for these findings include: (i) the suggestion that hypertension causes low body magnesium; (ii) the possibility that hypomagnesaemia and its effects on the other cations causes hypertension; and (iii) that perhaps a common factor exists that may result in both hypertension and normotension.

Discussion

Our major findings in this investigation were, for the group of individuals studied, significant inverse correlations between serum magnesium, serum calcium, serum potassium, erythrocyte magnesium and blood pressure (Figs 1 - 4, 6). The slopes of the regression lines of MAP, DBP and SBP were similar. A positive relationship was observed between erythrocyte sodium and blood pressure (Fig. 5). The relationships found between the cations are shown in Fig. 6.
The findings may, however, also be due to independent, unrelated causes. The finding in this study that 28% of Johannesburg urbanised black males are hypertensive is in keeping with that of Seftel. The subjects were derived from a specific group of urbanised black males, all physical labourers, and should not be regarded as a representative sample of the population as a whole.

Although there is no reported data to suggest that hypertension causes hypomagnesaemia, strong experimental evidence supports the thesis that low magnesium levels are related to raised blood pressure. Changes in erythrocyte magnesium, serum magnesium or the ratio of the intracellular magnesium to other intra- and extracellular cations, influence peripheral vascular resistance and therefore arterial blood pressure. Decreased serum magnesium is associated with increased cell membrane permeability, increased intracellular calcium and consequently increased vascular tone. Hypomagnesaemia also potentiates the constrictor action of certain neurohumoral agents. These factors may all play a role in the development and maintenance of hypertension.

A pioneer report suggested that hypertension, in the absence of renal disease, was associated with raised serum magnesium levels. Later studies, however, support our findings that there is an inverse correlation between magnesium and blood pressure.
Also, epidemiological studies have shown a negative correlation between soft drinking water (low calcium and magnesium) and hypertension. 

Magnesium is a co-factor for calcium adenosine triphosphatase (ATPase), which catalyses the active transport of calcium ions from the cytoplasm to the endoplasmic reticulum. When blood magnesium levels fall, calcium influx is enhanced, causing vasoconstriction with a raised peripheral resistance and increased blood pressure. This study shows a negative correlation between serum calcium and blood pressure. Although intracellular calcium was not measured, it is predicted that erythrocyte levels of calcium would be raised in the hypertensive subjects. High intracellular calcium levels in hypotensives were found to be significantly decreased, and intracellular sodium was found to be significantly raised in the hypertensive group. This is consistent with findings of other studies.

Fig. 6. Linear correlation coefficient for variables (Na(S) = serum sodium, K(S) = serum potassium, Mg(S) = serum magnesium, Ca(S) = serum calcium, Na(RBC) = red blood cell sodium, K(RBC) = red blood cell potassium, Mg(RBC) = red blood cell magnesium).

<table>
<thead>
<tr>
<th>SBP</th>
<th>DBP</th>
<th>MAP</th>
<th>Na(S)</th>
<th>K(S)</th>
<th>Mg(S)</th>
<th>Ca(S)</th>
<th>Na(RBC)</th>
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<th>Mg(RBC)</th>
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*Significant at 5% level.
**Significant at 1% level.
NS = not significant.

Potassium also plays a role in regulating arterial blood pressure, either directly or indirectly, by its effects on sodium. Our results show an inverse correlation between serum potassium and blood pressure which confirms previously reported studies.

Our findings could also be the result of a common factor on a sociobiological level. Many environmental and biosocial factors are common to both hypertension and hypomagnesaemia. These include alcohol consumption, the mineral content of the diet, socio-economic status and urbanisation. Malnutrition and/or alcoholism may contribute to the low-magnesium state. Dietary magnesium deficiency causes hypomagnesaemia, hypocalcaemia and hypokalaemia. The hypocalcaemia appears to be mediated by reduced parathormone secretion (or resistance to the peripheral action of parathormone), and the hypokalaemia seems to be a consequence of renal potassium wasting. Changes in plasma levels of these cations as a result of magnesium depletion, are paralleled by intracellular magnesium and potassium loss with a simultaneous gain of sodium and calcium. Although precise mechanisms for these intracellular shifts remain obscure, inhibition of membrane pumps may be implicated.

A comprehensive, detailed dietary and nutritional breakdown could not be obtained in this study, but a limited analysis relating to diet and alcohol intake was made. There were no obvious major differences between the diets of the normotensive and hypertensive men. All consumed vegetables and/or fruit, tea with milk and maize meal porridge daily, and meat and/or fish at least 3 times a week. Alcohol consumption appeared to be similar in both groups. Serum GGT concentrations were measured as another index of alcohol intake. Although the GGT levels were higher in the hypertensive group than in the normotensive group, statistical analysis showed no significant difference between the two groups. There was also no significant correlation between GGT and magnesium or between GGT and blood pressure.

Twenty-five per cent of the subjects resided in townships, 10% were live-in domestic helpers and 65% lived in hostels.
Two main residence groups were defined: hostel-dwellers and non-hostel-dwellers. The MAP for all of the subjects in the two groups was similar, 102.9 ± 17.7 mmHg and 103.7 ± 16.5 mmHg respectively. There was no significant difference in blood electrolyte levels between hostel- and non-hostel-dwellers. Dietary reasons for the hypomagnesaemic trend seem improbable because the magnesium content of the general urban diet is far in excess of that required for maintenance of balance, and Johannesburg drinking water has high magnesium levels (Cedza Laboratories, Johannesburg — personal communication). However, 65% of the subjects stayed in hostels, where the diet is often poor, and a major source of energy and fluid intake is alcohol. Although previous reports suggest that high alcohol intake is correlated with hypertension and hypomagnesaemia we did not find this. Any explanation of the apparent discrepancy between our results and the published data must include two main factors: firstly, a large proportion of the sample were hostel-dwellers; and secondly, a true and accurate assessment of alcohol and dietary intake could not be established. Alcohol consumption and diet probably do play some contributory role in developing hypomagnesaemia, but this may be minor in the incipient stages of hypertension, as observed in this group.

Serum creatinine was normal in all the subjects and there was no evidence of renal disease. Other causes for hypomagnesaemia, such as use of diuretics, diarrhoea, liver and pancreatic disease, polyauria and diabetes, were not present. The subjects were all physical labourers, and physical stress is known to be associated with a high-catecholamine state. Because of the physiological stress produced by their occupation, they probably had a higher than normal sympathetic output. Catecholamines are involved in cation transmembrane shifts. Consequently, changes in their production will result in altered cation states. The suspected high sympathetic state could explain our results. It is noteworthy that the mean age of the hypertensives was lower than that previously reported in similar studies. The biochemical results may be due to the young age of the subjects or may reflect the incipient stages of hypertension. These early blood pressure changes seem to manifest with correlating altered cation states. It is conjectured that these cation patterns in turn may vary with the stage and type of hypertension and with age.

Our results are in keeping with the hypothesis that there is an inverse relationship between magnesium levels and blood pressure. Although the exact cause-effect mechanism between cations and blood pressure remains obscure, the results here suggest that magnesium, together with its effects on calcium, sodium and potassium, may play a more important role in vascular homeostasis than was previously thought.

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REFERENCES