

# CHANGES IN BLOOD LEVELS OF TRACE ELEMENTS AND ELECTROLYTES IN HYPERTENSIVE PATIENTS

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## ABSTRACT

The involvement of elements in the pathological process of primary hypertension has been established. The serum levels of copper, iron, zinc, sodium, potassium and calcium were studied by atomic absorption spectrophotometry and flame photometry in hypertensive and normal subjects. Serum copper and zinc levels were increased in hypertensive patients (25.5% and 14.7% respectively) as compared to normal subjects. A decrease in serum sodium (21.9%), potassium (31.02%), iron (44.7%) and calcium (34.23%) was observed in hypertensive as compared to control subjects. The role of these serum element variations and their possible involvement in hypertension is discussed.

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## INTRODUCTION

The involvement of elements, especially major elements such as sodium, potassium, calcium and magnesium in the etiology, prevention and treatment of essential hypertension has received much attention in the last several years. The mechanism underlying the origin and maintenance of hypertension is still relatively obscure. The contribution to this process has been established both in man, through numerous epidemiological surveys and in experimental animals. Studies on sodium and potassium seem to show an inverse relationship between blood pressure and Na/K ratio.<sup>1</sup> Similarly, modifications in calcium and magnesium metabolism observed in certain types of hypertension in man and animals have led to the suggestion that their imbalance could contribute to the appearance of long term variations in blood pressure<sup>2</sup> due to their critical role in cardiac and vascular physiology.

The involvement of trace elements in the development of the hypertensive process is also a subject of study.<sup>3,4</sup> Zinc plays a role in the pathogenesis of essential hypertension.<sup>5</sup> The most common manifestation of

hypercupremia is hypertension and various workers suggest that high levels of copper in tissue are positively correlated with cardiovascular disease and hypertension.<sup>4,6</sup>

In order to obtain additional information concerning elemental involvement in hypertension, we decided to compare the element content of blood in normotensive and hypertensive patients.

## MATERIAL AND METHODS

### Reagents

Iron, copper, zinc, sodium, potassium and calcium standards were obtained from Fisher Scientific Company, Fairlawn, New Jersey. Ultragrade concentrated nitric acid was obtained from J.T. Baker Company, San Francisco, California. All glassware was washed with mild detergent and rinsed with distilled ionized water. Washed glassware was placed in a 20% nitric acid bath for 48 hours and then rinsed with several volumes of double deionized water. Rinsed glassware was placed in a covered polyethylene drying basket and then stored in sealed plastic bags prior to use.

### Subjects

25 hypertensive patients (10 females, 15 males) aged

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35-65 years were selected from the Outpatient Department of Liaquat National Hospital, Karachi. These subjects were considered to have essential hypertension. No known cause of high blood pressure and no associated disease could be detected after complete clinical, biological and radiological examination. None of the patients had renal impairment. All of them were on free diet and none had received anti-hypertensive therapy during the month prior to blood sampling.

25 normotensive controls (13 females, 12 males) aged 29-60 years were included in this study. In all these normotensive controls repeated examination failed to reveal a systolic blood pressure above 140 mmHg, whereas diastolic blood pressure remained below 90 mmHg. These normotensives were healthy students and staff members of the University of Karachi. There was no known history of hypertension. None of the women were pregnant or taking oral contraceptives.

### Blood sampling

Blood samples were taken by 10 mL disposable plastic syringes with low chromium steel needles. Samples of normal and hypertensive subjects were immediately transferred to acid washed glass containers. Blood samples were centrifuged, and serum was separated. Serum samples were stored at  $-20^{\circ}\text{C}$  until analysis.

### Analytical methods

Standards, samples and blanks for estimation of copper, zinc, and iron were aspirated into a Perkin Elmer 5000 atomic absorption spectrophotometer utilizing a long path air acetylene burner and cathode lamp for each metal under investigation. Each sample was read five times at a 1 second integration setting, as were appropriate standards. The concentrations of metals were found

by standard addition method. Concentrations of sodium, potassium and calcium in serum were analyzed by a flame photometer (Corning 410).

## RESULTS

Results are shown in Tables I and II. Significantly increased levels of copper (25.5%,  $p<0.01$ ) and zinc (14.7%,  $p<0.01$ ) were observed in hypertensive subjects as compared to normal subjects. Concentrations of sodium (21.9%,  $p<0.005$ ), potassium (31.02,  $p<0.01$ ), iron (44.7%,  $p<0.001$ ) and calcium (34.23%,  $p<0.001$ ) were found to be decreased in hypertensive patients.

## DISCUSSION

For most of the elements studied, our results confirmed that numerous modifications occur in the serum content of hypertensive patients as compared to normal subjects.

The level of sodium intake has been considered to be a major contributory factor in the development of essential hypertension. Sodium transport abnormalities of red blood cells, such as alterations of the sodium potassium pump, Na-K-cotransport and Na-Li counter-transport have been demonstrated in these patients.<sup>7-9</sup>

With essential hypertension, these alterations result in an accumulation of intracellular sodium, as a result of which the concentration of sodium in hypertensive patients is decreased during the present study (Table II). Our previous results also showed a decreased concentration of sodium in the serum of salt-induced hypertensive rats.<sup>10</sup> The present results also show a decreased concentration of calcium in hypertensive patients as compared to normal subjects (Table II). Decreased serum

**Table I.** Levels of trace elements in the sera of hypertensive and normotensive subjects.

Element	Normotensive	Hypertensive	% Change	<i>p</i>
Copper	79.63±16.3	99.95±19.1	25.5%	<0.01
Zinc	23.36±5.09	26.80±8.7	14.7%	<0.01
Iron	68.21±4.3	37.72±1.7	44.7%	<0.001

Values are mean ( $\mu\text{g/dL}$ )±S.D.

**Table II.** Levels of electrolytes in the sera of hypertensive and normotensive subjects.

Element	Normotensive	Hypertensive	% Change	<i>p</i>
Sodium	143.47±2.3	113.04±6.2	21.9%	<0.005
Potassium	3.61±0.4	2.49±0.3	31.02%	<0.01
Calcium	2.98±0.4	2.22±0.2	34.23%	<0.001

Values are mean (mEq/L)±S.D.

calcium levels may be the one important factor in the pathophysiology of human essential hypertension.<sup>4,11</sup>

It is suggested that most of the calcium is transported intracellularly in vascular smooth muscle cells by an altered  $\text{Na}^+$ - $\text{Ca}^{++}$  exchange mechanism. The increased intracellular calcium is involved in the contraction of vascular smooth muscle cells and is thus involved in the development of elevated blood pressure.<sup>12</sup>

The concentration of serum potassium was significantly decreased in hypertensives as compared to normotensive patients during the present study (Table II). It is difficult to give a simple interpretation of its effect because diets both deficient and enriched in potassium can lower blood pressure in hypertensive animals and humans, perhaps by modification of the  $\text{Na}/\text{K}$  ratio.<sup>1,13,14</sup> However, at the vascular level, low plasma potassium content may tend to indirectly induce vasoconstriction, whereas a high plasma content may be linked to a direct vasodilator effect.<sup>15</sup>

One of the main features of primary hypertension in which elements could be involved in both man and animals is an increased peripheral vascular resistance due to structural and functional causes.<sup>16,17</sup>

Cu was significantly higher in the serum of hypertensive patients (Table I) during the present study. Previously it was reported that intravenous injection of Cu is accompanied by a marked increase in peripheral vascular resistance in sheep,<sup>18</sup> and a Cu deficiency underlies hypotension which may partially result from a disturbance in characteristics of the structure and reactivity of the myocardium and vascular wall.<sup>4,5,19</sup> In contrast, Kleway reported that Cu deficiency induced hypertension in rats when the induction was begun after the cardiovascular system was fully developed.<sup>20</sup> Our results however showed a significantly increased serum copper level in hypertensives, which may be involved in the disturbance of the characteristics of structure and reactivity of the myocardium and vascular wall to increase blood pressure.

A significantly increased level of zinc was observed in hypertensive patients as compared to control subjects (Table I). Frithz and Ronsquist have suggested that an intracellular increase in renal Zn could favor the activity of carbonic anhydrase, a Zn metallo-enzyme, and consequently the development of hypertension via an effect opposite to that of some diuretics.<sup>21</sup> The increase in blood and tissue Zn content could be related to high sympathetic nervous activity in SHR.<sup>22</sup> The present results showed a consistent trend for the acute changes in blood iron, copper, zinc, sodium, calcium and potassium levels in hypertension. The variations in the concentration of trace elements in blood and different tissues could also be related in some ways to variations in the metabolism of hormones whose essential role in element homeostasis is well established. Further investigations are needed to study the implications of hormones in the variation of

element concentration during hypertension.

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