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SERUM TOTAL AND IONIZED CALCIUM LEVELS IN HYPERTENSION PATIENTS

General Medicine

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ABSTRACT

Essential Hypertension is associated with disturbed calcium metabolism. Calcium is the fifth most abundant element in the human body. 172 patients (84 Male and 88 Female) and 242 healthy controls (136 Male and 106 Females) were included in the study and 3 ml of fasting blood sample was collected from both patients and controls. A p-value less than 0.05 was considered statistically significant. The present study shows significantly reduced serum total calcium and albumin levels in hypertensives. However the serum ionized calcium levels are comparable in both groups as there was no significant difference. To conclude lowered serum ionized calcium can accelerate the hypertension and aging process which may be improved by calcium supplementation.

KEYWORDS

Hypertension, Calcium, Albumin, Parathyroid hormone, Magnesium.

INTRODUCTION:

Hypertension (HTN) is a cardiac chronic medical condition in which the systemic arterial blood pressure is elevated 1. Essential hypertension is associated with disturbed calcium metabolism. Calcium is the fifth most abundant element in the human body. It is an essential element that is only available to the body through dietary sources**.** The calcium ions play a major role as a second messenger in excitation contraction coupling in cardiac and smooth muscle cells. [1]

Three hormones, PTH, vitamin D, and calcitonin, are known to regulate serum Ca 2+ by altering their secretion rate in response to changes in ionized Ca 2+. PTH secretion in blood is stimulated by a decrease ionized Ca 2+ and, conversely, PTH secretion is stopped by an increase in ionized Ca 2+. PTH exerts three major effects on both bone and kidney. In the bone, PTH activates a process known as bone resorption, in which activated osteoclasts break down bone and subsequently release Ca 2+ into the ECF. In the kidneys PTH conserves Ca 2+. Active form of vitamin D increase Ca 2+ absorption in the intestine and enhances the effect of PTH on bone re-absorption. Calcitonin, which originates in the medullary cells of the thyroid gland, is secreted when the concentration of Ca 2+ in blood increases. Calcitonin exerts its $^{2+}$ Ca -lowering effect by inhibiting the actions of both PTH and vitamin D. Although calcitonin is apparently not secreted during normal regulation of the ionized Ca 2+ concentration in blood, it is secreted in response to a hypercalcemic stimulus.

As the results reported by various authors on serum total calcium [2],[3],[4] and serum albumin [5] were found to be varying, it was planned to study serum total calcium, serum ionized calcium and serum albumin levels in patients with essential hypertension, their first degree relatives and in normal controls. Three extracellular calcium fractions: ionized, protein-bound, and complexed calcium are in equilibrium with one another in the serum. Ionized calcium (Ca 2+) is the physiologically active form whereas protein-bound calcium is apparently inactive. The function of complexed calcium, which is bound to small anions such as bicarbonate, citrate, phosphate, and lactate, is uncertain. [4] HTN is a multi-factorial disorder in which various physiological mechanisms participate to elevate BP. [6] Many hypotheses were proposed about the possible mechanisms underlying essential HTN including. So our aim is to study Serum Total and Ionized Calcium levels in Hypertension Patients.

MATERIAL AND METHODS:

172 Patients (84 Male and 88 Female) and 242 healthy controls (136 Male and 106 Females) were included in the study and 3 ml of fasting blood sample was collected from patients and controls. Patients were informed to refrain from smoking or drinking tea or coffee for at least thirty minutes before measuring blood pressure. Blood pressure was recorded in sitting position after resting for 10 minutes and 2 readings were recorded and mean of these readings was noted as a final blood pressure.

Inclusion criteria: Subjects between the age group of 40 -60 years were selected. Samples from cases were collected before institution of any hypertensive treatment. The criteria for diagnosis of hypertension were systolic pressure of >140 mm of Hg and diastolic pressure of >90 mm of Hg.

Exclusion criteria: Hypertensive patients who were already on anti-hypertensive treatment were excluded from the study. Study subjects were examined systematically to exclude any disease (Secondary hypertension) or factors known to cause or associated with hypertension. Subjects on drugs like steroids, oral contraceptive pills, and thyroxin were excluded from the study. Similarly, subjects with any underlying condition or taking any drug known to alter serum calcium levels or calcium supplementations have been excluded from the study.

Statistical Analysis: All values were expressed as mean ± standard deviation (SD). Statistical analysis was done by using Microsoft Excel and SPSS for windows version 11.5 (SPSS, Inc., Chicago). A P-value less than 0.05 were considered statistically significant.

RESULTS:

Total number of subjects included in this study was 414.Among these 172 were cases (Hypertensive) and 242 were controls (Normotensives). Results showed that there is a significant increase in mean diastolic and systolic blood pressure in hypertensive case group than control. Results of our study have shown that the mean serum total calcium level is decreased in hypertension patients than controls. Analysis of cases and controls with respect to age: The age of the subjects in the study group ranged from forty to sixty years. The mean and standard deviation for the age of the cases and controls were 44.29± 7.71years and 45.46± 7.41

years respectively. The study group and the control group did not differ from each other statistically with reference to age. Serum total and ionized calcium are decreased in hypertensive group than normotensive control group. Table –1.

DISCUSSION:

Results of our study have shown that the mean serum total calcium level is decreased in hypertension patients than controls but decrease is not significant. The present study shows significantly reduced serum total calcium and albumin levels in hypertensives. However the serum ionized calcium levels are comparable in both groups as there was no significant difference. This is in agreements with studies of [2], [3] Serum calcium levels were also found to be significantly lower [3] also reported reduced calcium level in males with elevated diastolic blood pressure. [4] did not find any change in serum calcium levels in hypertensives when compared to controls. Alterations in intracellular calcium are thought to be involved in the common pathway mediating the secretion and action of many hormones including the pressor action of catecholamines and Angiotensin II. Intracellular calcium may be involved in regulation of blood pressure. Calcium regulating hormones like 1, 25- Dihydroxy vitamin D levels of plasma, renin activity, and circulating ionized calcium contribute to the pathophysiology of the essential hypertension. [9], [10]

Decreased levels of serum ionized calcium are associated with essential hypertension. [11] But in our study, the serum ionized calcium levels in normotensives and hypertensives were not significantly different. However, this author [11] has notstudied on serum albumin levels. These results are not matching with our study. The serum total calcium levels are found to be lower in hypertensive males and females in comparison to the corresponding controls. The serum total calcium levels are also found to be lower in the first degree relatives of the hypertensives when compared with the corresponding controls. The data correlates well with the other previous studies. [12] The study shows that there is no significant difference in serum ionized calcium levels of hypertensives when compared to the corresponding controls. The levels are also comparable in the first degree relatives of hypertensives and corresponding controls. [13] Our study shows that there is significant decrease in serum albumin levels in hypertensives and their first degree relatives when compared with the corresponding controls. [14] The present study shows there may be a role of serum total calcium in the pathophysiology of hypertension, although, further studies are required to confirm these observations. [15] Serum total calcium and serum albumin estimation may be used to predict the risk of hypertension in normotensives with familial history of hypertension. Serum free (ionized) calcium reflects true calcium status of the body in health and disease. It is biologically active and tightly regulated by calcium binding hormones. Serum total calcium is the sum of 3 forms, ionized or free (50%), protein-bound (40%) and soluble form, complexes with anions such as bicarbonate and phosphate. Total calcium is thus greatly influenced by protein concentration, especially albumin [14]. Some of the previous studies have shown conflicting results. Some have reported that serum total calcium was not different between hypertensive and normotensive groups, but serum ionized calcium levels were low [3], [15] A recent study in U.S. showed increased serum total and free calcium levels in hypertensive adults [4] The present study measures both serum total and free calcium in hypertension in an attempt to further resolve the controversy and extend our understanding of the pathophysiology of hypertension. The present study revealed decrease in both serum total and free calcium. This is in agreement with researchers who have studied only ionized calcium which was found to be decreased [6], [16].Some have studied only serum total calcium levels and found it to be lowered in hypertensive subjects [17], [18]. An association between serum total calcium and hypertension is plausible, including a direct effect on vasculature by enhanced vascular resistance, alteration in extracellular binding of calcium, interaction between serum calcium, and other cations such as sodium, potassium and magnesium, renal vasoconstriction causing kidney dysfunction and hyperactivity of renin-angiotensin system from hyperparathyroidism [4]

Low serum ionized calcium levels in hypertensives reflect increased levels of intracellular ionized calcium. Increased intracellular calcium may be due to reduced calcium extrusion via an ATP-dependent pump, and decreased vascular smooth muscle membrane stability. Also, intracellular calcium serves as a second messenger in excitation-contraction coupling for vascular smooth muscle cells; causing contraction. This explains why abnormal cellular metabolism and subsequent elevated intracellular concentration of calcium could contribute to hypertension [8]. Serum free (ionized) calcium is biologically active and tightly regulated by calcium binding hormones whereas serum total calcium is the sum of 3 forms, ionized or free (50%), protein-bound (40%) and soluble form, complexes with anions such as bicarbonate & phosphate. . Studies also found that the blood pressure levels are directly associated to ionized calcium concentrations in those patients [17], [18]. Variations were also observed in extracellular calcium contents of hypertensive patients than controls (7, 19). Some studies hypothesized that, due to abnormal membrane transport of calcium in hypertensives, the serum ionized calcium level is observed low, but the same is increased intracellularly resulting arteriolar vasoconstriction in [19], hypertension [20], [21], [22], [23], [24], [25]

This disequilibrium in ionized calcium concentration may be the consequences of altered sodium calcium membrane transport.in smooth muscles, observed by Blaustein [26]. Actually these observations are partly influenced by some other factors, the effect of calcium on blood pressure is influenced by sodium,potassium, magnesium, parathyroid hormone and renin concentrations. Increasing the extracellular ionized calcium concentration can cause the membrane stabilization, resulting in the relaxation of vascular smooth muscles, found by some authors [27], [28] Some authors have shown that persons with low calcium diet are more prone to develop hypertension [5]. Calcium supplementation was also found to stabilize the blood pressure in hypertensives [29]

CONCLUSION:

Abnormal cellular ion transport resulting in altered membrane control over intracellular calcium may be related to hypertension. In our study, we have found the significant decrease of serum ionized calcium in hypertensives when compared to control subjects, whereas serum total calcium did not follow the same trend. Our study suggests to conclude that lowered serum ionized calcium can accelerate the hypertension and aging process which may be improved by calcium supplementation.

Table 1: ***Estimation of Biochemical Parameters (M±SD) of Hypertension and Normotenisve patients***

Total Number 414 (Hypertension Patients and Normotensive Controls)				
S. No	Parameters	Hypertension (172 No.s)	Normotensive – Controls (242 No.s)	P Value
1	Age (40-60 Yrs)	44.29 ± 7.71	45.46 ± 7.41	< 0.001
2	Systolic Blood Pressure	159.18 ± 7.99	119.23 ± 7.20	< 0.001
3	Diastolic Blood Pressure	109.32 ± 9.01	76.89 ± 3.28	< 0.001
4	Total Calcium	9.82 ± 1.36	10.36 ± 1.67	Not Significant
5	Ionised or Free Calcium	7.6 ± 1.02	10.23 ± 1.63	< 0.001
6	Albumin	3.1 ± 0.42	4.92 ± 0.66	< 0.001

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