Serum Calcium in Essential Hypertension and its Co-relation with Severity of the Disease

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Abstract

Calcium plays an important role in the pathophysiology of essential hypertension. Alterations in the intracellular free Calcium regulation as well as disturbances of extracellular calcium homeostasis have been observed in patients with essential hypertension. Present study centers on estimating serum calcium level in patients with essential hypertension and establishing relationship between serum calcium level and severity of hypertension. In this study serum calcium levels were measured in 80 cases of essential hypertension which included 37 cases of grade I and 43 cases of grade II hypertension. The result showed that serum Calcium levels were significantly decreased in grade I (P<.0001) as well as grade II (P<.0001) hypertension cases when compared to age matched normotensive control. Furthermore, Grade II hypertension cases were having significantly lower serum Calcium level (P<.0001) than grade I hypertension cases. As an extension to this study it can be proposed safely that diet high in calcium could possibly alter the course and progression of hypertension as evidenced by so many other studies.
INTRODUCTION

Hypertension is one of the most prevalent cardiovascular disorders posing a major public health challenge to the population in socio-economic and epidemiological transition. According to an estimate overall 26.4% of the adult population in year 2000 had hypertension and 29.2% were projected to have this condition by year 2025\(^{(1)}\). Approximately 54% of all strokes and 47% of all ischemic heart disease were attributed to high blood pressure \(^{(1)}\). Although our understanding of the pathophysiology of elevated arterial pressure has increased significantly, in 90-95% of hypertensive cases etiology is still largely unknown.

Abnormalities of calcium metabolism in cases of essential hypertension have been described by many researchers in recent past \(^{(2,3)}\). Although some other researchers \(^{(4)}\) disagree with the above presumption. The calcium ion plays a major role as an intracellular second messenger in excitation contraction coupling in cardiac and smooth muscle cells. The free intracellular calcium concentration thus, determines the tension in vascular smooth muscle cells thereby resulting in peripheral vascular resistance. Abnormal Calcium metabolism has been projected as one of the important causative factor for essential hypertension by many workers. It has been hypothesized that a generalized defect of calcium regulation might be of importance in the pathogenesis of essential hypertension. In one hypothesis a primary calcium-deficiency in essential hypertension has been linked to subsequent membrane instability and altered intracellular free calcium concentrations \(^{(5)}\). Many workers have come to a conclusion that highly positive co-relation exists between serum calcium level and essential hypertension. Serum calcium level was found to be higher in hypertensive patients than in controls\(^{(6)}\). In one study lower arterial blood pressure have been observed in people living in sunny areas and decrease of arterial blood pressure values after exposure to UVB radiation indicating some role of calcium and vitamin D in pathophysiology of hypertension and its treatment\(^{(7)}\). Some people hold contrary views in co-relating calcium with hypertension. An increase in dietary calcium was found to reduce blood pressure in some patients\(^{(8)}\). This work is an attempt to find out a possible co-relation between serum total calcium and hypertension (and its severity).
MATERIAL AND METHODS

The study was carried out on eighty newly diagnosed or untreated essential hypertension patients (i.e. patients with no known cause of hypertension) randomly selected from those admitted in various wards or attending various outdoors of RIMS, Ranchi. Blood pressure of the subjects were measured and classified strictly in adherence to JNC 7 recommendations (9). Ethical clearance had been taken from the appropriate institutional authority. Twenty five persons with normal blood pressure selected from the attendants of the patients, medical / nursing students and hospital staffs were taken as normotensive age and sex matched controls. Both the groups i.e. case and control groups were examined thoroughly and systematically including routine investigations to exclude any diseases or factors known to cause hypertension. Subjects having any condition or taking any drug known to alter serum calcium have been excluded from the study. Written informed consent has been taken from every subject taking part in the study and the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975.

ESTIMATION OF SERUM CALCIUM

Serum total calcium was estimated by using Arsenazo III method (10). The calcium present in the serum reacts with Arsenazo III under neutral conditions to form a purple colored complex which has maximum absorbance at 650 nm. The serum calcium concentration has been calculated with the help of Photometric Colorimeter. PROCEDURE: -

For estimation serum total calcium 1ml of Arsenazo III reagent had been mixed with 10 μl of serum sample and incubated at 37 ºc for 5 minutes. The colored complex formed is compared for optical density against standard by the photometric colorimeter (Environmental scientific co.; model no. 313) at the wavelength of 650nm with a fixed optical path of 1cm. CALCULATION: -

Calculation of the serum calcium concentration in the sample was done using the optical density data by following formula –

\[
\text{Ca (mg/dl) = } \frac{\text{OD}_T - \text{OD}_B}{\text{OD}_S - \text{OD}_B} \times \text{C}_{\text{Std}}
\]

\(\text{OD}_T\) - Optical density of test sample.
ODB – Optical density of blank  
ODS – Optical density of standard  
C\textsubscript{a\textsubscript{std}} – Calcium concentration of standard (mg/dl)

CONVERSION FACTOR: -

Calcium (mmol/l) = Calcium (mg/dl) × 0.2495

STATISTICS:-
Statistical analysis had been done by applying Student’s ‘t’ test using statistical software Medcalc (version 11.6.1.0)

RESULTS:
The serum calcium levels of control group grade I hypertension and grade II hypertension and pre-hypertension groups are shown in table I.

In the present study the mean serum calcium concentration of control subjects was found to be 2.53 ± 0.08 mmol/l with a range of 2.37 to 2.70 mmol/l. The females were found to have lower mean serum calcium level (2.55 mmol/l ± 0.08) than males (2.55 mmol/l ± 0.07) but the difference was not significant (p= 0.1). The mean calcium values were found to be in agreement with recommended normal range of serum calcium concentration in both sexes. The mean serum calcium concentration of grade I hypertension cases was found to be 2.30 ± 0.072 mmol/l ranging between 2.16 to 2.58 mmol/l which was significantly lower (p<.0001) than that of control group but, was significantly higher (p=.009) than grade II hypertensive individuals (mean serum calcium level 2.25 ± 0.09 mmol/l). Both grade I and Grade II hypertensive subjects of male and female sub-group showed significantly lower values of serum calcium than their respective control counterparts (p<0.0001 in all sub-groups).

DISCUSSION

The present study shows significantly reduced serum calcium level in hypertensive individuals as compared to control group. Grade II hypertensive subjects were found to have lowest value compared to grade I hypertensive and control group subjects. This shows a direct inverse relationship between serum calcium level and grade of hypertension. The results were in close agreement with that of others (11, 12). The NAHNES I study was probably the 1st and one of the largest epidemiological surveys linking the inverse relationship between calcium level (and its dietary intake) and blood pressure (13). Toyuz et al. (12) also reported reduced serum calcium level in hypertensive individuals. However, Koschet al. (14) did not find any change in serum calcium levels in hypertensive individuals. In approximately two third of the studies based on this subject done by 1994, increase in calcium intake produced a mild antihypertensive response, with an average decrease of 4-7 mm Hg systolic and 2-4 mm Hg diastolic blood pressure (15).
These changes in the blood pressure with low serum calcium level could possibly be attributed to some poorly known alterations in cell membrane transport mechanisms. Abnormal cellular ion transport resulting in altered membrane control over intracellular calcium may be related to essential hypertension. The free intracellular calcium concentration determines the tension in vascular smooth muscle cells, thereby resulting in peripheral vascular resistance. Calcium has a direct effect on peripheral vascular tone. Alternations 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. Ionized serum Ca is reported to be lower in low-renin hypertensive patients and higher in high-renin hypertensive patients than in normal-renin hypertensives or in normotensives. Plasma renin activity in essential hypertension has a continuous negative correlation with serum Mg and a positive correlation with serum ionized Ca. Hence, plasma renin in hypertension may reflect (or contribute to) Ca and Mg flux changes across cell membranes.

Besides these, there are many other factors which are, directly or indirectly, implicated in the pathogenesis of essential hypertension and are influenced by serum calcium level. Endothelial cell dysfunction is one of them which is accompanied by a decrease in the production and/or the release of nitric oxide and the increase of contracting factors with resultant increase in peripheral vascular resistance. Another notable factor which is indirectly involved in the pathogenesis of essential hypertension is altered lipid metabolism in the situation of low serum calcium level or decreased dietary calcium intake. Low calcium diet or low serum calcium stimulates increased production of 1,25-dihydroxyvitamin D which in turn, stimulates adipocyte Ca2+ influx and, as a consequence, stimulates lipogenesis, suppresses lipolysis, and increases lipid accumulation; whereas increasing dietary calcium inhibits these effects and markedly accelerates fat loss. Many researchers even recommend a regular consumption of the recommended daily levels of dietary calcium to combat with hypertensive disorders. Pasi Jolma et al. found that calcium supplementation reduced blood pressure in hypertensive individuals during chronic nitric oxide synthase inhibition and abrogated the associated impairments in endothelium-dependent and endothelium-independent arterial relaxation. High-calcium diet had been found to enhance the vasorelaxation in nitric oxide-deficient hypertension.

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**Serum calcium in essential hypertension**


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**Table I**

Table showing serum calcium concentration in control group, Grade I and Grade II hypertensive subjects (both male as well females); n= no. of subjects; SD= standard deviation; p value < 0.05 had been taken as level of significance.

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