Original Research Article

Estimation of serum calcium and serum phosphorus levels in newly detected essential hypertensive patients

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Abstract

Introduction: Hypertension remains the leading cause of death worldwide and one of the world's great public health problems (WHO). Affecting 1 billion people worldwide, systemic hypertension remains the most common, readily identifiable and reversible risk factor for myocardial infarction, stroke, heart failure, atrial fibrillation, aortic dissection and peripheral arterial disease. In this study, total serum calcium levels and corrected serum calcium levels of essential hypertension patients are compared and correlated with matched normotensive controls.

Aim of the study: To compare the total and corrected serum calcium levels among patients with newly detected essential hypertension and normotensive controls.

Materials and methods: This study was a cross sectional study, with cases and controls enrolling 100 newly detected essential hypertension patients as cases and 50 suitable healthy individuals with normal blood pressure as controls, as per JNC-8 guidelines. Cases were selected from those who visited hypertension clinic and those who were admitted in wards during the study period. Controls were selected from those who attended medical outpatient department for minor ailments and healthy volunteers. Serum calcium and phosphorus levels were estimated using standard levels and the interpretation was done with blood pressure values.

Results: Group A was the study group which included 100 newly detected essential hypertensive patients. Group B was the control group which included 50 normotensive individuals. In Group A, 52 (52%) were males and 48 (48%) were females and in Group B, 26 (52%) were males and 24 (48%) were females. There was a negative correlation noted between the total and corrected serum calcium levels as against the systolic blood pressure. There was no correlation noted between the total and corrected serum calcium levels as against the diastolic blood pressure.

Conclusion: The total and corrected serum calcium levels were found to be significantly lowered in cases when compared to controls. Also, a significant negative correlation between the calcium levels and systolic blood pressure was noted while there was no correlation noted with the diastolic blood pressure in the cases. This study also noted that there is no significant difference in both the calcium levels with age, sex, BMI, lifestyle, smoking, alcohol, family H/o hypertension in newly detected essential hypertensive patients.

Key words

Smoking, Alcohol, Hypertension, Serum calcium, Serum phosphorus.

Introduction

Hypertension currently is defined as a usual BP of 140/90 mmHg or higher, BP levels for which the benefits of pharmacological treatment have been definitively established in randomized placebo-controlled trials [1]. Clinically, hypertension might be defined as that level of blood pressure at which the institution of therapy reduces blood pressure related morbidity and mortality. From an epidemiologic perspective, there is no obvious level of blood pressure that defines hypertension. In adults, there is a continuous, incremental risk of cardiovascular disease, stroke, and renal disease with increasing levels of both systolic and diastolic blood pressure [2]. The overall prevalence of hypertension varies from 6 – 32%, thus affecting 1 billion population worldwide. In India, the prevalence of hypertension is 59.9 and 69.9 per 1000 in males and females in urban population while it is 35.5 and 35.9 per 1000 in males and females in rural population respectively [3]. Primary hypertension, which accounts for 95 percent of all cases of hypertension, has been traditionally defined as high blood pressure for which an obvious secondary cause (e.g. renovascular disease, aldosteronism, pheochromocytoma, or gene mutations) cannot be determined although primary hypertension is a heterogeneous disorder, some of the main causes of high blood pressure in primary hypertension are known. For example, overweight and obesity may account for as much as 65 to 75% of the risk for primary hypertension [4]. Other factors, such as sedentary lifestyle, excess intake of alcohol or salt, and low potassium intake, are also known to increase blood pressure in many patients who are classified as having primary hypertension. There are several hypothesis those abnormalities of calcium homeostasis at both an organ and cellular level as a primary factor in the pathogenesis of human and experimental hypertension. Also, a low calcium intake has been associated with an increase in blood pressure in several epidemiological studies [5]. An increase in leucocyte cytosolic calcium levels have been reported in some hypertensives, similarly, an increase in RBC and platelet cytosolic calcium levels have also been reported in some hypertensives. In one-third of patients with hyperparathyroidism, hypertension is noted and can be attributed to renal parenchymal damage due to nephrolithiasis and nephrocalcinosis. However increased calcium levels also have a direct vasoconstrictive effect. In some cases, hypertension can be treated by correcting hypercalcemia [6, 7].

Materials and methods

This study was carried out in Department of General Medicine Government Dharmapuri Medical College Hospital, Dharmapuri during the period between April 2017 and July 2017. This study was ethically approved by the Ethical committee of Government Dharmapuri Medical College Hospital, Dharmapuri.

Inclusion criteria

- Newly detected essential hypertension patients.

Exclusion criteria

- Essential hypertension.
- Known cases of hypertension.

- Patients on antihypertensive agents.
- Chronic renal failure.
- Diabetes mellitus.
- Ischemic heart disease.
- Patients with hypertension inducing drugs.
- Other causes of secondary hypertension.

Applying these criteria, 100 essential hypertensive patients were selected and included in the study after informed consent (Group A). Similarly, 50 normotensive controls were selected and involved in the study after informed consent (Group B).

Measurement of BP [8]

BP was measured as per JNC – 7 guidelines. Subjects were instructed not to take caffeine or smoking within 30 min preceding the reading and were seated quietly for 5 min in a quiet room after emptying the bladder, with the arm bared and supported at the level of the heart and the back resting against a chair. A mercury manometer with appropriate cuff size was used to measure the blood pressure. Korotkoff sounds phase I (appearance) was taken as systolic BP while phase V (disappearance) was taken as a measure of diastolic blood pressure. Two sets of BP readings were taken 30 min apart in both arms in sitting posture; if the pressures differ the arm with the higher pressure was taken. Lower limb BP was also taken in patients less than 40 years of age while BP recordings for postural hypotension were measured for those who aged more than 60 years.

Estimation of serum calcium [9, 10]

Arsenazo III Method

The principle of this method is that calcium bind specifically with arse Nazo III at an acidic pH to form a blue – purple colored compound. The intensity of the color of the compound is directly proportional to the amount of calcium present in the sample.

Estimation of serum phosphorus [11]

Unreduced phosphomolybdate Method

The principle of this method is that phosphate ions in acidic medium react with ammonium molybdate to form a phosphomolybdate complex. This complex has an absorbance in the ultraviolet range (340 nm). The intensity of the color of the complex formed is directly proportional to the amount of inorganic phosphorus present in the sample. In the phosphorus estimation kit, there will be a standard sample with measured phosphorus of 5 mg/dl with which a standard stock solution(S) has to be prepared.

Statistical analysis

Data was entered in Microsoft excel spread sheet and analyzed statistically using SPSS software version 11.5. Results were considered significant if the 'p' value was below 0.05.

Results

A total of 150 individuals were selected. They were divided into two groups, group A and group B. Group A was the study group which included 100 newly detected essential hypertensive patients. Group B was the control group which included 50 normotensive individuals. In Group A, 52 (52%) were males and 48 (48%) were females and in Group B, 26 (52%) were males and 24 (48%) were females. The mean age in group A was 55.52± 10.782 years and the mean age in group B was 52.06 ± 10.88 years. The majority of hypertensives in the study group were asymptomatic (46%), and among the symptomatic individuals, the commonest symptom was giddiness (24%) followed by a headache (10%).

Distribution of family history of hypertension between Group A and Group B was as per **Table – 1**. There was a statistically significant difference noted in the distribution of blood pressure (systolic and diastolic) between the groups A and B. ($P < 0.05$) as per **Table - 2**. There was a statistically significant difference noted in the total serum calcium levels between the groups A and B. ($P < 0.05$) as per **Table - 3**. There was no statistically significant difference

noted in the total serum phosphorus levels between the groups A and B ($P < 0.05$) as per **Table - 4**.

Table – 1: Distribution of family history of hypertension between Group A and Group B.

Family history of hypertension	Group		Total
	A	B	
NO	63 (63.0%)	34 (68.0%)	97 (64.7%)
YES	37 (37.0%)	16 (32.0%)	53 (35.3%)
TOTAL	100 (100.0%)	50 (100.0%)	150 (100.0%)
P value between groups is 0.590 statistically not significant.			

Table – 2: Systolic and diastolic blood pressure distribution between Groups A and B.

Blood pressure (mmHg)	Group	N	Mean	Std. Deviation	Std. Error Mean
SYSTOLIC	A	100	169.2800	15.81847	1.58185
	B	50	111.7200	6.88103	.97312
DIASTOLIC	A	100	101.4000	8.61054	.86105
	B	50	71.1600	6.31280	.89276

P value between groups is 0.000 < 0.001 statistically significant.

Table – 3: Distribution of total serum calcium levels between group A and Group B.

TOTAL SERUM CALCIUM (mg/dl)	GROUP	N	Mean	Std.	Std. Error
	A	100	8.9160	.62529	.06253
	B	50	9.7042	.79350	.11222

P value between groups is 0.000 < 0.001 statistically significant.

Table – 4: Distribution of serum phosphorus levels between Group A and Group B.

SERUM PHOSPHORUS (mg/dl)	GROUP	N	Mean	Std.	Std. Error
	A	100	3.6829	.39549	.03955
	B	50	3.7866	.37802	.05346

P value between groups is 0.127 not significant.

Discussion

Systemic hypertension remains the most common, readily identifiable and reversible risk factor for myocardial infarction, stroke, heart failure, atrial fibrillation, aortic dissection and peripheral arterial disease [12]. The evidence is growing that calcium physiology is altered in essential hypertension, but whether this is a secondary association or a causal relationship is unresolved. Intracellular calcium ions are known to have direct effects on peripheral vascular tone and it has been reported in various trials that hypertensive persons have increased concentrations of intracellular free calcium that decrease to normal levels with antihypertensive treatment [13]. Various epidemiological studies stated that the calcium status of humans with essential hypertension and genetic animal models of hypertension is characterized by low serum total and ionized calcium concentration, increased intracellular calcium, increased urinary

calcium excretion, and increased parathyroid hormone (PTH) concentration [14]. This study used total serum calcium and corrected serum calcium, the latter is an alternative but not a substitute to serum ionized calcium [15]. In this study, the mean total serum calcium and corrected serum calcium levels in group A(cases) were 8.9160 ± 0.62529 mg/dl and 8.8263 ±.6525 mg/dl while the mean total serum calcium and corrected serum calcium levels in group B (controls) were 9.7042± 0.79350mg/dl and 9.6550± 0.80053 mg/dl respectively. Statistical analysis revealed that the total and corrected serum calcium levels were significantly lowered in essential hypertensives when compared to their matched normotensive controls ($P < 0.001$ and $P < 0.001$ respectively) [16]. This observation is supported by some of the following studies. The mean total serum calcium levels were significantly ($p<0.01$) decreased in males and females in the hypertensive group when compared with normotensive controls. In the first-degree relatives also the total serum calcium levels were significantly decreased ($p <0.01$) when compared with the controls [17]. In their study he observed hypertensive subjects had lower mean serum levels of ultra-filterable calcium ($p = 0.01$), ionized calcium ($p = 0.09$), and complexed calcium ($p= 0.04$) and higher levels of protein-bound calcium ($p = 0.07$) [18]. Calculated serum concentrations of complexed calcium were significantly lower in hypertensive subjects ($p = 0.04$), while protein-bound calcium concentrations were higher ($p = 0.07$). Serum phosphorus and albumin concentrations, as well as estimated dietary calcium intake, were not different between the two groups [19]. Fu Y, Wang S., et al. in their study suggested that that the hypertensive group consistently demonstrated a significantly decreased activity of ATPase studied, with significantly lower plasma calcium and higher cytosolic calcium levels when compared with those in normotensive group ($P < 0.01$ or $P < 0.05$, respectively). No significant differences were found in either plasma Mg^{2+} or intracellular Mg^{2+} level between the two groups. [20]In this present study a correlation between calcium levels and systolic blood pressure was attempted and found that the total and corrected serum calcium levels had a significant negative correlation with systolic blood pressure ($P < 0.01$and $P < 0.01$ respectively) [21]. In our study we also attempted a correlation between the calcium levels and diastolic blood pressure and found that there was no correlation between the total and corrected serum calcium levels and diastolic blood pressure ($P >0.05$and $P > 0.05$ respectively).In his study on 'the serum calcium fractions in essential hypertensive and matched normotensive subjects' AR Folsom et al., also noticed that there were no significant correlations between the serum calcium fractions and diastolic blood pressure levels [22].

Conclusion

The total and corrected serum calcium levels are significantly lowered in newly detected essential hypertensive patients when compared to normotensive controls [23]. The total and corrected serum calcium levels have a significant negative correlation with the level of systolic blood pressure in newly detected essential hypertensive patients [24]. The total and corrected serum calcium levels have no significant correlation with the diastolic blood pressure in newly detected essential hypertensive patients [25].

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