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Original Research Article

Serum calcium levels in newly detected essential hypertensive patients

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ABSTRACT

Background: Systemic hypertension is global disease responsible for significant mortality and morbidity. Essential or primary hypertension accounts for the majority of people with hypertension. Although our understanding of the pathophysiology of essential hypertension has grown a lot, its aetiology still remains hypothetical. Few studies in literature have found some correlation with serum calcium levels and blood pressure of the individuals.
Methods: A total 200 patients, 100 newly diagnosed essential hypertensive and 100 normotensive patients were included in the study. A detailed history and clinical profile was taken. Blood sample was collected, serum calcium and serum albumin were determined and corrected calcium was calculated and the results were tabulated and appropriate statistical analysis was done.
Results: The mean total serum calcium and corrected calcium levels were significantly lowered in essential hypertensive compared to the normotensive individuals. There was no correlation between total serum and corrected calcium levels against systolic and diastolic blood pressure. There was also no difference in serum total and corrected calcium levels among different subsets in essential hypertensive group.
Conclusions: Essential hypertension still remains the most common form of hypertension present worldwide causing significant mortality and morbidity. Despite increased advances in medicine and large number of studies done in context with the cause of essential hypertension, its aetiology still remains hypothetical. Even though studies have shown some correlation of calcium fractions with hypertension, the aetiology is still unclear.

Keywords: Essential hypertension, Calcium, Corrected calcium

INTRODUCTION

In 2008, globally, nearly 40% of adults of age 25 and above were diagnosed with hypertension. People who had hypertension increased from 600 million in 1980 to nearly 1 billion in 2008. Its prevalence is highest in Africa and lowest in Americas. It is responsible for nearly 45% of mortality due to heart disease and 51% of mortality due to cerebrovascular accidents.[1] Affecting 1 billion people worldwide, systemic hypertension is considered to be the most common, easily diagnosable risk factor for many of the cardiovascular and cerebrovascular diseases. Because of increasing and aging of population in developed and developing countries, the burden of hypertension is rising globally and is estimated to affect 1/3rd of the world's population by 2025 that is around 1.5 billion people.[2] Although our understanding of the pathophysiology of essential hypertension has increased, the aetiology still remains hypothetical. Various studies have shown that essential hypertension is associated with disturbed calcium metabolism like increased cytosolic calcium and decreased serum calcium levels and also increased urinary excretion of calcium in patients with primary hypertension.[3-5]

In this study total serum calcium levels and corrected serum calcium levels of essential hypertension patients were compared and correlated with matched normotensive controls. Also the calcium levels were compared and correlated within the various subsets of hypertensive population viz., age, sex, alcohol, smoking, lifestyle, BMI.

METHODS

This study was carried out in the department of general medicine and in collaboration with department of biochemistry in Mahatma Gandhi medical college and research institute during the period of March 2013 to March 2014. This study was ethically approved by the ethical committee of Mahatma Gandhi medical college & research institute. This was a cross sectional study with 100 cases of newly detected essential hypertensive and 100 controls of normotensive individuals. Cases and controls were selected randomly from those who attended the outpatient department of general medicine. Patients with newly detected essential hypertension above the age of 18 years of both sexes were included. Those chronic renal failure, diabetes mellitus, heart disease and liver disease were excluded.

Procedure

The person must be seated comfortably, with the legs uncrossed, and the back and arm supported, in a way that the upper arm is at the level of the heart (the mid-point of the sternum). The person should relax and instructed not to talk during the procedure and readings should be taken after 5 minutes of posturing. For patients who are over 65, diabetic or receiving anti-hypertensive therapy, check for postural changes by taking readings immediately and 2 minutes after the patient stands. The prerequisite for BP recoding is no caffeine in the preceding hour, no smoking for preceding 15 minutes, no exogenous adrenergic stimulants like phenylephrine in nasal decongestants or eye drops for papillary dilation, aquiet and warm setting.

Blood pressure was measured using mercury sphygmomanometer. The cuff should encircle and cover 2/3rds of the arm length. The "ideal" cuff should have a bladder length that is 80% and a width that is at least 40% of arm circumference. Blood pressure was measured in both arms during first examination. Minimum of 2 readings taken at an interval of at least 1 minute apart and the average of those 2 readings were taken as the final value. Patient who fulfilled the criteria were enrolled into the study and hypertensive and normotensives were marked as cases and controls respectively and grouped as group A and group B respectively. A detailed history and examination were done for the all the subjects. A blood sample and ultrasound abdomen were done after their consent. Serum calcium and albumin were estimated by Arsenazo III method and albumin BCG method.[22,23] Corrected serum calcium level was calculated by serum calcium (mg/dl) + {0.8 [4.0–serum albumin (g/dl)]}

Statistical analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance. The following assumptions on data is made, Assumptions: dependent variables should be normally distributed, 2. Samples drawn from the population should be random, cases of the samples should be independent. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (inter group analysis) on metric parameters. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Pearson correlation between calcium and corrected calcium levels with various clinical parameters was computed. Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc, $p \leq 0.001$ was considered as strongly significant.

RESULTS

A total of 200 individuals were randomly 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.

Table 1: Serum calcium levels in two groups studied.

Serum calcium	Group A		Group B	
	N	%	N	%
<8.5	36	36.0	9	9.0
8.5-9.5	54	54.0	78	78.0
>9.5	10	10.0	13	13.0
Total	100	100.0	100	100.0

Table 2: Corrected calcium levels in two groups studied.

Serum calcium	Group A		Group B	
	N	%	N	%
<8.5	48	48.0	12	12.0
8.5-9.5	47	47.0	81	81.0
>9.5	5	5.0	7	7.0
Total	100	100.0	100	100.0

Group B was the control group which included 100 normotensive individuals. In group A, 45 (45%) were males and 55(55%) were females and in Group B, 26(55%) were males and 24(45%) were females. The mean age in group A was 53.47±10.04 years and the mean age in group B was 48.28±6.45 years. In group A, 73 (73%) were non-

smokers and 27 (27%) were smokers and in group B, 33(73%) were non-smokers and 17 (27%) were smokers.

Table 3: Comparison of serum calcium and corrected calcium levels in two groups studied.

Parameters	Group A	Group B	P value
Serum calcium	8.75±0.53	9.00±0.45	<0.001
Corrected calcium	8.62±0.61	8.87±0.40	0.001

Table 4: Comparison of serum calcium levels and corrected calcium levels according different clinical in group A.

Variables	Serum calcium levels (mg/dl)	Corrected calcium levels (mg/dl)
Gender		
Male	8.73±0.54	8.62±0.62
Female	8.75±0.53	8.63±0.59
P value	0.955	0.938
Smoking		
No	8.70±0.53	8.58±0.60
Yes	8.88±0.52	8.75±0.61
P value	0.145	0.225
Alcohol		
No	8.76±0.55	8.62±0.62
Yes	8.73±0.47	8.66±0.59
P value	0.852	0.793
Life style		
Non-sedentary	8.69±0.54	8.58±0.59
Sedentary	8.81±0.52	8.66±0.62
P value	0.246	0.502
Family history		
No	8.78±0.53	8.65±0.63
Yes	8.58±0.53	8.46±0.47
P value	0.158	0.250

Table 5: Pearson correlation between study variables with Serum calcium levels in two groups studied.

Pair	Group A		Group B	
	R value	**P value**	**R value**	**P value**
SBP vs. serum calcium levels	-0.149	0.139	-0.116	0.252
SBP vs. corrected calcium levels	-0.173	0.085+	-0.156	0.122
DBP vs. serum calcium levels	-0.115	0.253	-0.034	0.738
DBP vs. corrected calcium levels	-0.135	0.181	-0.024	0.815

In group A, 80 (80%) were non alcoholics and 20 (20%) were alcoholics and in Group B, 85 (85%) were non alcoholics and 15 (15%) were alcoholics. 72% (72) patients in group A had a sedentary lifestyle. The prevalence of family history of hypertension among hypertensive individuals was 16% (16). The mean systolic blood pressure of group A and group B were 166.06±14.02mmHg and 125.62±6.49 mmHg while the mean diastolic blood pressures were 97.62±5.38 mmHg and 80.70±5.21 mmHg respectively. The mean total serum calcium and corrected serum calcium levels in group A were 8.75±0.53 mg/dl and 8.62±0.61 mg/dl while the mean total serum calcium and corrected serum calcium levels in group B were 9.00±0.45mg/dl 8.87±0.40 mg/dl respectively.

The calcium levels were significantly lowered in group A when compared with group B. There was no 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. There was no significant difference in the total and corrected serum calcium levels with age, sex, BMI, life style, smoking, alcohol, family history of hypertension in newly detected essential hypertensive patients

Study design

A comparative two group study; lower serum calcium is significantly more associated with group A with p<0.001. Lower corrected calcium levels is significantly more associated with group A with p<0.001. There was no significant difference in the total and corrected serum calcium levels with sex, life style, smoking, alcohol, family history of hypertension in newly detected essential hypertensive patients. There was no correlation noted between the total and corrected serum calcium levels as against the systolic and diastolic blood pressure.

DISCUSSION

Hypertension still seems to be one among the top risk factors, reversible risk factors which are is easily detectable for most of the common diseases (cerebrovascular accident, myocardial infarction arrhythmias like atrial fibrillation etc.,) responsible for mortality and morbidity.[2] There is enough evidence now to say that there is some relationship between calcium physiology and hypertension but whether it is secondary association or whether altered calcium metabolism is the reason behind or is it the cause for essential hypertension is still unclear. There are various trials which show that that the increased levels of intracellular calcium decrease to normal levels due to treatment with antihypertensive drugs, so it is known that there is some direct effect of calcium ions on vascular tone in the peripheral vessels.

Total serum calcium and corrected serum calcium levels

In our study the mean serum calcium level and mean corrected calcium level in group (essential hypertensive)

were 8.75±0.53 and 8.62±0.61 and in group B (normotensives) were 9.00±0.45 and 8.87±0.40. The mean total and corrected calcium levels were significantly decreased in essential hypertensive when compared to normotensives which was statistically revealed by a p<0.001 and 0.001 respectively. Our study was supported by Sudhakar et al in which the total and corrected calcium levels were decreased in males and females in hypertensive group compared to normotensive group.[5]

Study done by Folsom et al also observed that mean serum levels of ultra filterable calcium (p=0.01), ionized calcium (p=0.09), and complex calcium (p=0.04) and levels of protein-bound calcium (p=0.07) were lower in hypertensive group.[32] Bolli et al and Touyz et al also reported a decrease in total serum calcium levels in hypertensive subjects. Study by Strazzullo et al.[3,8,10] also showed that total serum calcium levels were lowered in hypertensive group. Wang et al in their study demonstrated that in the hypertensive group there was lower plasma calcium levels and higher cytosolic calcium levels when compared to the normotensive subjects.[11] Study conducted by McCarron et al showed that ionized calcium levels were lower in essential hypertensive group compared to similar total calcium levels in hypertensive and normotensive groups. Studies by Harlan et al, Rolf et al and Kesteloot et al, showed that direct and positive correlation between serum total calcium levels and arterial pressure which is in contrast with our study.[13-15] This paradoxical correlation is probably due to the failure of them to correct for hemoconcentration that attends hypertension which is because of an increase in serum albumin concentration to which most of the calcium is bound.

Correlation of total and corrected serum calcium levels with systolic blood pressure

In our study we found no correlation between calcium levels and systolic blood pressure of the people in the hypertensive population. Folsom et al had conducted a study in which he also found that no correlation between the different calcium fractions and the systolic blood pressure of the individuals.[9] This supports our study. In contrast to the study done by us, reports by Staessen, Sartor, Jorde and Kesteloot resulted in a favourable correlation between blood pressure and the serum calcium levels.[13,14,16]

Study by Phillips et al done identified a positive correlation between the blood pressure both systolic and diastolic and calcium levels this was identified after making adjustment for age.[18] This correlation which was elicited remained significant but was reduced after adjusting for other fractions like albumin. Furthermore this completely disappeared after making adjustments with other fractions like globulin and haematocrit values. Henceforth these different fractions could possibly be the reason for the association between blood pressure and calcium levels of the individuals. Study done by Morris et al and Martinez also demonstrated a negative relationship between calcium level and pressure.[19]

Correlation of total and corrected serum calcium levels with diastolic blood pressure

We also found that there was also no correlation between the calcium levels and corrected calcium levels total and corrected calcium levels when compared with the diastolic blood pressure of the hypertensive individuals (p=0.253 and p=0.181 respectively). This negative correlation between calcium fractions and diastolic blood pressure was also supported by Folsom et al, in contrast to this Jorde et al and Kesteloot, Geboers found a positive correlation between calcium levels and the blood pressure especially the diastolic blood pressure of the study people.[13-17] But studies by Kesteloot found there was positive correlation between the calcium levels and both the systolic and diastolic blood pressure in men but in females they found the correlation with diastolic pressure alone.[15]

Correlation of total and corrected serum calcium levels with various subsets of study group (essential hypertensive group)

In this study we also correlated serum total and corrected calcium levels with various subsets of essential hypertensive like age, sex, smoking, alcohol, family history, BMI, and lifestyle. There was no significant difference found between the various subsets and calcium levels in our study. Folsom et al and Staessen, Sartor et al found that there was no significant difference between total calcium levels and both the sexes.[9,16] Jorde et al observed that there was decrease in serum total calcium level with increasing age in men while there was a increasing trend in women.[14] Brot et al observed no difference among smokers and non-smokers with serum ionized calcium levels. According to Sudhakar et al serum total calcium levels were significantly lowered among first degree relatives of essential hypertensive when compared to normotensives.[14,20] In a observational study by Sundsfjord, Jorde et al there was a positive correlation between BMI and serum calcium level in both the sexes.

Limitations

Limitations of current study were; follow up could not be done as it was a cross sectional study, various fractions of calcium couldn't be done due to constraints and calcium supplementation was not attempted in the patients due to ethical reasons.

CONCLUSION

The total and corrected serum calcium levels are significantly lowered in newly detected essential hypertensive patients when compared to normotensive controls. The total and corrected serum calcium levels have no correlation with the level of systolic blood pressure in newly detected essential hypertensive patients.

The total and corrected serum calcium levels have no significant correlation with the diastolic blood pressure in newly detected essential hypertensive patients. The total and corrected serum calcium levels showed no significant difference with age, sex, BMI, life style, smoking, alcohol, family history of hypertension in newly detected essential hypertensive patients.

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