A Study on Serum Calcium Level in Resistant Hypertension

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ABSTRACT

Introduction: Hypertension is one of the common public health problem in the world and gradually increasing in Nepal. Serum calcium level has shown to be associated with cardiovascular disease. Disturbed calcium metabolism plays important role in pathogenesis of essential hypertension.

Methods: Four hundred people including 200 normotensives and 200 hypertensives were enrolled in the study, their blood pressure and total serum calcium were measured. Hypertensive group was divided into two: Hypertensives on Calcium channel blockers (CCBs) and hypertensive other than CCBs. Serum Calcium level was measured with calcium-O- Cresopthalein complex(OCPC) reaction. All other baseline investigations including blood sugar, renal function tests, complete blood counts, thyroid function tests were done to exclude secondary causes in hypertensive group. Statistical analysis was done using SPSS version 21. Differences between the groups were analyzed with independent "t" test.

Results: Significant difference in serum calcium level was found in between normotensive and hypertensive. Difference in serum calcium level between hypertensive on CCBs and hypertensive other than CCBs were insignificant.

Conclusion: Significantly reduced serum calcium level is found in hypertensive individuals as compared to normotensive group. Lower level of serum calcium level affects the blood pressure. Essential Hypertension is associated with significant familial predisposition.

Key words: Essential Hypertension, JNC VII, OCPC complex, Serum calcium

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INTRODUCTION

Hypertension is one of the leading causes of death and disability among adults all over the world. It remains the major risk factor for coronary, cerebral and peripheral vascular disease. Essential hypertension comprises more than 90% of hypertension. Hypertension is an emerging health problem in Nepal. The burden of hypertension is 6% to 32% worldwide.[1] According to an estimate overall 26.4% of the adult population in year 2000 had hypertension and 29.2% will be projected to have this condition by year 2025.[2] Approximately 54% of all strokes and 47% of all ischemic heart disease were attributed to high blood pressure.

Disturbed calcium metabolism plays important role in pathophysiology of essential hypertension. Calcium acts as an intracellular second messenger in excitation-contraction coupling in vascular smooth muscle cells(VSM). The free intracellular calcium concentration determines the tension in VSM cells, thereby contributing to peripheral vascular resistance (PVR). Increased PVR is found in HTN.[3]In one hypothesis a primary calcium deficiency in essential hypertension has been linked to subsequent membrane instability and altered intracellular free calcium concentrations.[4]In a country like Nepal, people tend to have a diet rich in Sodium and poor in Potassium, and Calcium .[5] JNC 7[6] classification is used for grading of hypertension

METHODS

This is cross sectional study on the total serum calcium level on essential hypertensive patients which was conducted in Cardiology department of Manhamohan Cardiothoracic Vascular and Transplant Centre (MCTVS), Tribhuvan University Teaching hospital for a period of 6 months (Sept 2012 to Feb 2013). Total of 400 Patients were enrolled in the study visiting cardiology department of MCTVS, divided into experimental group is divided into 2 main groups: Normotensive group (control)-comprising 200 subjects visiting for nonspecific chest pain and non-hypertensive between 20 to 70 years. Hypertensive group(Case)-comprising 200 patients, between 20 to 70 years, who were recently diagnosed to have essential hypertension or who were already diagnosed or newly diagnosed to have essential hypertension and or under medications. Two patients were excluded from the study as they were found to have hyperthyroidism. Blood pressure of the subjects were measured and classified strictly in adherence to JNC 7 recommendations. INCLUSION CRITERIA being Patients with essential hypertension, the criteria for the diagnosis of essential hypertension was systolic BP (SBP) of ≥ 140 mm Hg and diastolic BP (DBP) of ≥ 90 mm Hg. The criteria for the controls were patients visiting for non-specific chest pain with normotensive individuals without any family history of hypertension. Patient on any antihypertensive therapy, age more than 14 years were included. EXCLUSION CRITERIA being patient below 14 years and with secondary hypertension. In every case, a careful history was taken and a thorough examination was done. Routine investigation like estimation of blood sugars, serum creatinine, blood urea , cholesterol complete blood counts(CBC) , Thyroid function Tests(TFTs) were done in every hypertensive case including total serum calcium level to exclude any disease or factors known to cause hypertension. Only total serum calcium level was measured in normotensive controls. Total serum calcium level was measured by the calcium method which is a modification of calcium-O- Cresopthalein complex (OCPC) reaction originally reported by Schwartzonbach et al, Stern and Lewis later adapted this reaction to colorimetric calcium assay. Statistical analysis was performed using SPSS version 21. Differences between the groups were analyzed using independent "t" test. Statistical significance was set at $P<0.05$.

RESULTS

Among 198 patients enrolled in hypertensive cases, male population of 59.4% were affected. 82 patients of age group 40-50 years had highest incidence of Hypertension. Most common risk factor was familial found in 55 patients.

Table 1: Demographic and test parameters of the participants in both groups. All are noted to be mean values taken from the statistical analysis

Parameters	Normotensive	Treatment with CCB	Treatment without CCB
Age(years)	37.9 ± 9.16	49.8 ±9.83	50.7 ± 9.959
BMI(Kg/m2)	23.14 ± 2.12	24.66 ±1.81	24.48 ± 1.78
Serum calicum level(mmol/L)	2.39 ± 0.08	2.12 ± 0.16	2.13 ± 0.11
SBP(mmHg)	121.29 ± 7.62	133.52 ± 11.41	140.42 ± 16.72
DBP(mmHg)	76.59 ± 6.76	85.07 ± 10.64	89.32 ± 13.98
MAP(mmHg)	91.49 ± 5.82	101.22 ±9.08	106.35 ± 13.30
Duration of treatment(Years)	-	2.95 ± 2.66	1.35 ± 1.87

Table2: Differences in serum calcium level between normotensives and hypertensive

Parameter	Normotensive (N= 200)	Hypertensive (N= 198)	P value
Serum Calcium level(mmol/L)	2.39±0.08	2.13±0.14	<0.001

There was significant difference in serum calcium level noted in 2 groups.

Table 3: Serum calcium level in grade I and grade II hypertensive subjects.

Parameter	Grade I Hypertension N= 37	Grade II Gypertension N= 15	P Value
Serum Calcium Level(mmol/L)	2.13±0.10	2.11±0.11	0.702

Grade II hypertension was associated with lower level of serum calcium level as compare to grade I hypertension, but was not statistically significant.

DISCUSSION

This study shows significant decrease in total serum calcium level in hypertensive patients than normotensive controls and the results are in close agreement with that of others who also found a significant decrease in serum calcium in patients with essential hypertension .[7,8] Though there are not enough study describing the relation of serum calcium and hypertension, but the findings of the present study are in agreement with that of Sudhakar, Sujhata, Babu, Padmanathi and Reddy.[28] Toyuz et al also reported reduced serum calcium level in hypertensive individuals.[9] However, Kosch et aldid not find any changes in serum calcium levels in hypertensive individuals.[10] 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 .[11]

Serum total calcium is the total sum of 3 forms, ionized or free, protein-bound and soluble form complexed with anions such as bicarbonate and phosphate. Around 50% of total serum calcium is in the ionized form, 40% in the bound form mainly to albumin, and 10% bound to anions.[12] Ionized calcium, the physiologically active form in the blood, is an accurate indicator of calcium homeostasis.[13] However, ionized calcium measurement is more expensive and is affected by a number of factors including method of collection, choice of anticoagulant, pH changes, and variability of reference range used by different laboratories using different analyzers.[14] Total calcium measurement is least affected by these changes, correlates well with ionized calcium measurement, and is routinely used in clinical practice to assess calcium status in health and disease.

CONCLUSION

Decreased level of serum calcium level is associated with essential hypertension. There is no significant variation in serum calcium level in hypertensive treated with Calcium Channel blockers and without CCBs. Essential hypertension has significant genetic predisposition. It also can be concluded that serum calcium may be used as a diagnostic and prognostic marker for essential hypertension. Further, the study also reveals a state of hypocalcemia in hypertensives, so the study therefore opens avenues for prevention and treatment of hypertension and fatal complications like stroke, myocardial infarction and renal failure by serum calcium estimation and their therapeutic supplementation.

REFERENCES

1. Leonard D, McDermott R, Odea K, Rowley KG, Pensio P, Sambo E, et al. Measuring prevalence : Obesity, diabetes and associated cardiovascular risk factors among Torres Strait Islander People. Aust N Z J public health 2002;26:144-9
2. Touyz RM, Milne FJ, Alterations in intracellular cations and cell membrane ATPase activity in patients with malignant hypertension. J Hypertens 1995;13:867-74.
3. KhashayarSakhaee and NaimM.Maalouf; Dietary Calcium, Obesity and Hypertension—The End of the Road?-*The Journal of Clinical Endocrinology and Metabolism*2005 Vol 90,NO 7 4411-4413.
4. A R Folsom,CL Smith, RJ Prineas and RH Grimm Jr ; Serum calcium fractions in essential hypertensive and matched normotensive subjects- *American Heart Association*,1986 Vol 8, 11-15
5. Michael B.Zemel; Calcium Modulation and Obesity; Mechanism and Implications *Journal of the American College of Nutrition*, Vol. 20, No. 90005 (2001), 428S-435S.
6. Seventh Report of the Joint National Committee on Prevention,. Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)December 2003 in Hypertension 2003;42:1206
7. Y. Fu, S. Wang, Z. Lu, H. Li, and S. Li, —Erythrocyte and plasma Ca2+, Mg2+ and cell membrane adenosine triphosphatase activity in patients with essential hypertension, Clin. Med. J. (Engl), 1998, pp. 147-149.
8. R. M. Touyz, F. J. Milne, H. C. Seftel and S. G. Reinach, —Magnesium, calcium, sodium and potassium status in normotensive and hypertensive Johannesburg residents. S. Afr, Med. J., 1987, pp. 377-381.
9. Touyz, R.M., Milne, F.J. and Reinach S.G. (1992). Intracellular Mg2+, Ca2+,Na2+ and K+ in platelets and erythrocytes of essential hypertension patients: relationto blood pressure. J. Hypertens., 14, 1189-1209.
10. The Journal of Endocrinology & Metabolism vol. 90; 2005
11. Symposium notes: Non-pharmacologic Management of Hypertension; National Kidney Foundation; 1994.
12. Moore EW. Ionized calcium in normal serum, ultrafiltrates, and whole blood determined by ion-exchange electrodes. J Clin Invest. 1970;49:318–334.
13. Calvi LM, Bushinsky DA. When is it appropriate to order an ionized calcium? J Am SocNephrol. 2008;19:1257–1260.
14. Forman DT, Lorenzo L. Ionized calcium: its significance and clinical usefulness. Ann Clin Lab Sci. 1991;21:297–304.