

Serum and Erythrocyte Magnesium levels in Offsprings of Essential Hypertensive Parents

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ABSTRACT

Hypertension is an important public health challenge worldwide, 95% of which are primary or essential hypertension, where the exact causes are not known. It has been thought that magnesium level has an association with hypertension and plays role in the pathogenesis of essential hypertension. Several evidences suggested that decreased magnesium level may be a significant modifiable risk factor for developing essential hypertension. To explore the relationship between serum and erythrocyte magnesium level with blood pressure, this case control study was carried out in the Department of Biochemistry, Bangabandhu Sheikh Mujib Medical University (BSMMU), during the year 2006. Thirty offsprings of essential hypertensive parents were taken as cases and 30 age and sex-matched offsprings of normotensive parents were taken as controls. Serum & erythrocyte magnesium were measured by colorimetric Calmagite method. Significantly lower serum magnesium level (mg/dl) was found in cases than that of controls (1.90 ± 0.210 vs 2.13 ± 0.366 , $p < 0.01$) and erythrocyte magnesium (mg/dl) was also found to be lower in cases when compared with that of controls (4.46 ± 0.699 vs 5.43 ± 0.775 , $p < 0.001$). Mean systolic and diastolic blood pressure were found to be significantly higher ($p < 0.01$) in cases as compared to controls. Though it is difficult to draw any definite conclusion, it may be assumed that, a hereditary predisposition to hypertension may be related to magnesium metabolism and magnesium deficiency might have a role in the future development of hypertension in the offsprings of essential hypertensive parents.

Key words: Essential Hypertension, Serum Magnesium, Erythrocyte Magnesium.

Introduction

Blood pressure is affected by many genetic and environmental factors and their complex interactions. The elucidation of the pathophysiological mechanism of essential hypertension (EHT) remains one of the most formidable challenges in medicine till today.

A large number of abnormalities have been described as causative factors for EHT such as defect in Na, K, and Ca metabolism, increased sympathetic activity, vascular hypersensitivity to endogenous neurohormonal constricting agents and decreased sensitivity to endogenous

vasodilators¹. The role of electrolytes in the causation of EHT has been studied extensively but physiological role of magnesium was ignored. A number of experimental as well as clinical evidences suggest that magnesium may play an important role in pathogenesis, prevention and control of essential hypertension²⁻⁶. Mg^{2+} activates $Na^+ - K^+$ ATPase pump which, in turn, plays a major role in regulating $Na^+ - K^+$ transport. Again Mg^{2+} plays an important role in the control of arterial tone and blood pressure, primarily via the regulation of vascular membrane sites for

Mg²⁺-Ca²⁺ exchange. A reduction in extracellular Mg²⁺ can produce hypertension, vasospasm and potentiation of vasoconstrictor agents by allowing excess entry of Ca²⁺ concomitantly reducing the potency of vasodilators⁷⁻⁹.

In animal experiments, an elevation of blood pressure in Mg deficient rats¹⁰ and the delayed onset of hypertension in spontaneously hypertensive rats given Mg have been reported¹¹. Although conflicting results have been obtained in clinical studies concerning dietary magnesium¹²⁻¹⁴, it has been reported that oral Mg supplementation causes a further reduction of blood pressure in hypertensive patients on diuretic therapy¹⁵ and uncomplicated hypertensive patients⁴. Many studies showed that serum and erythrocytes Mg levels are decreased in hypertensive patients as compared with normotensive subjects and an inverse correlation has been reported between blood magnesium level and blood pressure¹⁶⁻¹⁹. However, only a few reports have dealt with the relationship of magnesium and blood pressure in children. Shear et al.²⁰ made 8 years follow up in the Bogalusa Heart Study and pointed out that, there is a high probability that, subjects with positive family history belongs to the high blood pressure group. They also indicated that family history can be a predictor of hypertension. Shudhakar et al¹⁸ reported that children with family history of hypertension have high blood pressure and decreased serum & erythrocyte magnesium level.

In the present study, we measured serum and erythrocyte magnesium concentration (S-Mg, E-Mg) in offsprings of essential hypertensive parents.

Materials and methods

This case-control study was conducted in the Department of Biochemistry, Bangabandhu Sheikh Mujib Medical University (BSMMU), during the year 2006, to observe the serum and erythrocyte magnesium level of the normotensive offsprings of essential hypertensive parents. For this study 30 offsprings (15 boys and 15 girls)

with age range of 12-30 years of essential hypertensive parents (secondary causes of hypertension of the parents were excluded) were taken as cases and age-and sex-matched 30 offsprings (19 boys and 11 girls) of normotensive parents were taken as controls from the Cardiology Outpatient Department of BSMMU. The dietary history was more or less similar in both groups. The systolic and diastolic blood pressure were measured twice at 5 minutes interval in the right arm using a mercury sphygmomanometer following a standard procedure. The average of two successive readings of blood pressure was taken as the blood pressure of the participants. With all aseptic precautions, about 5ml of venous blood was drawn using disposable syringes. Then 2.5 ml of blood was immediately transferred into a heparinised tube (Lithium heparin) and rest into metal free test tube. Serum was separated after centrifugation. For erythrocyte, heparinated tube was also centrifuged at 4000 rpm for 10 minutes. After removing buffy coat layer, erythrocytes were washed three times by resuspending in normal saline, each time centrifuging at 4000 rpm for 10 minutes. Serum and erythrocyte magnesium were measured by Colorimetric Calmagite Method.

Data were expressed as mean±SD and were analyzed by using the software SPSS version 12.0 for windows. 95% confidence limit was considered as level of significance.

Result

For this study, 30 offspring (15 males and 15 females) of essential hypertensive parents and 30 (19 males and 11 females) from normotensive parents were included as cases and controls respectively.

Table-1 : Age & sex distribution of study subjects

| Groups | Total number n | Male | Female | Age (Mean ± SD) |
|----------|----------------|------|--------|-----------------|
| | | | | in years |
| Cases | 30 | 15 | 15 | 18.93±2.23 |
| Controls | 30 | 19 | 11 | 19.33±2.86 |

2 test for sex and unpaired't' test for mean age, between case and control found statistically insignificant (p > 0.05).

Table-II shows the blood pressure status of cases and controls. The mean \pm SD of systolic blood pressure in cases were 122.33 \pm 9.17 mmHg and diastolic pressure were 72.89 \pm 5.97 mmHg. In controls, mean \pm SD of the systolic pressure were 106.50 \pm 7.21 mmHg and diastolic pressure were 68.33 \pm 5.62 mmHg. The mean difference of blood systolic and diastolic blood pressure was statistically significant ($p < 0.01$).

Table -II: Comparison of blood pressure in study group

| Blood pressure (mmof Hg) | Cases n=30 | Controls n=30 | 'p' value |
|------------------------------|-------------------|-------------------|-----------|
| Systolic BP (Mean \pm SD) | 122.33 \pm 9.17 | 106.50 \pm 7.21 | <0.01 |
| Diastolic BP (Mean \pm SD) | 72.83 \pm 5.7 | 68.33 \pm 5.62 | <0.01 |

Unpaired 't' test was done as test of significance; level of significance was 0.05.

Table-III shows the comparison of mean serum magnesium and erythrocyte magnesium concentration between two groups. The concentration of serum and erythrocyte magnesium in different groups were expressed as mean \pm SD in mg/dl.

Serum magnesium level (mg/dl) in cases and controls were 1.90 \pm 0.210 and 2.13 \pm 0.366 respectively. Erythrocyte magnesium level (mg/dl) in cases and controls were 4.46 \pm 0.699 and 5.43 \pm 0.775 respectively. Both serum magnesium and erythrocyte magnesium levels were found significantly low in cases compared to that of controls ($p < 0.01$)

Table III: Comparison of serum & erythrocyte magnesium level in study group

| Parameter | Cases n=30 | controls n=30 | 'p' value |
|---|------------------|------------------|-----------|
| Serum Magnesium (mg/dl) Mean \pm SD | 1.90 \pm 0.210 | 2.13 \pm 0.366 | <0.01 |
| Erythrocyte Magnesium (mg/dl) Mean \pm SD | 4.46 \pm 0.699 | 5.43 \pm 0.775 | <0.001 |

Unpaired 't' test was done as test of significance; level of significance was 0.05.

Discussion

In this study, we measured serum and erythrocyte Mg²⁺ concentration in 30 (normotensive) offsprings of essential hypertensive parents and 30 offsprings of normotensive parents to explore the relation between magnesium level and blood pressure.

The mean systolic (SBP) and diastolic (DBP) pressures (mm of Hg) in cases were (122 \pm 9.17) and (72 \pm 5.9) respectively and in the controls were 106 \pm 7.21 and 68 \pm 5.62 respectively. Both SBP and DBP were significantly higher in cases than that of controls which are in agreement with many other such studies^{18,19}. The serum magnesium and erythrocyte magnesium (mg/dl) levels in cases were found to be significantly lower when compared with controls ($p < 0.01$ and $p < 0.001$ respectively). The result is consistent with the study done by Shudhakar et al. in India¹⁸. But in a follow up study in Japanese children, Shibutani et al. found only decreased level of erythrocyte magnesium¹⁹. However, Nelson and Henningsen²¹ reported no changes in E-Mg level in the offsprings of established hypertensive parents.

Na⁺ and K⁺ transport across the cell membrane has been found to play an important part in the development of hypertension, with Na⁺-K⁺ ATPase playing a central role in this mechanism. It is well known that Mg⁺⁺ acts as a cofactor of many enzymes, including Na⁺-K⁺ ATPase in cell membrane²². Decreased Na⁺-K⁺ ATPase activity is considered to cause an elevation of intracellular Na⁺ and Ca⁺⁺ levels via the Na⁺-Ca⁺⁺ exchange system, thus being involved in the onset of hypertension²³. In a follow-up study in Japanese children, Shibutani et al¹⁹ found that family history positive children who had low erythrocyte magnesium levels showed significantly higher blood pressure after two years than their family history negative counterparts. They also inferred that, children with a hereditary predisposition to hypertension, a decreased in intracellular magnesium levels reduces Na⁺-K⁺ ATPase activity and also increases intracellular sodium levels, thus causing a rise of blood pressure.

The present study supports the hypothesis proposed in other studies that children who have hereditary predisposition to hypertension,

decreased magnesium level may cause an elevation of blood pressure.

The serum and erythrocyte magnesium levels were found significantly lower in offsprings of essential hypertensive parents as compared to those of normotensive parents. Further larger scale study is needed for assessment of association and risk relationship between hypomagnesemia and hypertension. Magnesium levels would be a good screening tool for individuals at risk of developing hypertension, if these findings are confirmed by large scale studies.

References

1. Ryan MP and Brady HR. The role of magnesium in the prevention and control of hypertension. *Ann Clin Res* 1984; Suppl 43: 81-8.
2. Karppanen H. Minerals and blood pressure. *Ann Med* 1991; 23: 299-305.
3. Weinsier RL and Norris D. Recent developments in the etiology and treatment of hypertension: dietary calcium, fat and magnesium. *Am J Clin Nutr* 1985; 42:1331-8.
4. Haga H. Effect of dietary magnesium supplementation on diurnal variations of blood pressure and plasma Na⁺- K⁺ ATPase activity in essential hypertension. *Jpn Heart J* 1992; 33: 785-800.
5. Laurant P and Touyz RM. Physiological and pathological role of magnesium in the cardiovascular system: Implications in hypertension. *J Hypertens* 2000; 18: 1177-91.
6. Touyz RM. Magnesium in clinical medicine. *Front Bio sci* 2004; (9): 1278-93.
7. Altura BM and Altura BT. Interactions of Mg and K on blood vessels- aspects in view of hypertension. Review of present status and new findings. *Magnesium* 1984; 3: 175-94.
8. Iseri LT and French JH. Magnesium: nature's physiologic calcium blocker. *Am Heart J* 1984; 108: 188-93.
9. Gomez MD and Mark N. Magnesium and cardiovascular disease. *Anaesthesiology* 1998; 98: 222-240.
10. Altura BM, Altura BT, Gebrewold A, Lising H, Gunther T. Magnesium deficiency and hypertension: Correlation between magnesium deficient diet and microcirculatory changes in situ. *Science* 1984; 223: 1315-17.
11. Berthelot A and Esposito J. Effect of dietary magnesium on development of hypertension in spontaneously hypertensive rat. *J Am Coll Nutr* 1983; 4: 343-53.
12. Motoyama.T, Sano H, Fukuzaki H. 'Mg supplementation in patients with essential hypertension'. *Hypertension* 1989; 13: 227-232.
13. Duralach J, Duralach V, Rayssinguier Y, Bara M, Bara AG. 'Magnesium and blood pressure. II Clinical studies'. *Magn Res* 1992; 5: 147-53.
14. Kawano Y, Matsuoka H, Takishita, Omae Y. 'Effect of magnesium supplementation in hypertensive patients: assessment by office, home and ambulatory blood pressure'. *Hypertension* 1998; 32: 260-265.
15. Dyckne T and Wester PO. Effect of magnesium on blood pressure. *BMJ* 1983; 286:1847-49
16. Lawrence M, Resnick, Raj K Gupta, John HL. Intracellular free magnesium in erythrocytes of essential hypertension: Relation to blood pressure and serum divalent cations. *Proc Natl Acad Sci USA* 1984; 6511-6515.
17. Touyz RM, Milne FJ, Seftel HC, Reinach SG. Magnesium, calcium, sodium and potassium status in normotensive and hypertensive Johannesburg residents. *SAMT* 1987; 72: 377-381.
18. Shudhakar K, Sujatha M, Rao VB, Jyothy A, Reddy PP. 'Serum and erythrocyte magnesium levels in hypertensives and their first degree relatives. *J Ind Med Assoc* 1999; 97: 211-213.
19. Shibutani Y, Sakamoto K, Katsuno S, Yoshimoto S, Matsura T. Relation of serum and erythrocyte magnesium levels to blood pressure and family history of hypertension. *Acta Paediatr Scand* 1990; 79: 316-321.
20. Sher CI, Burke GI, Freedman DS, Berenson GS. 'Value of childhood blood pressure measurements and family history in predicting future blood pressure status: results from 8 yrs. of follow- up in the Bogalusa Heart Study. *Pediatrics* 1986; 77(6): 862-869.
21. Nelson D and Henningsen NC. Erythrocyte contents of electrolytes (Na, K, Mg, Zn) in healthy male controls and offspring to established hypertensive patients: a follow-up study. *Scan J Clin Lab Inves* 1983; 43: 317-322.
22. Waker WEC and Parisi AF. Magnesium metabolism. *N Engl J Med* 1968; 278: 658-63.
23. Blaustein MP. Sodium ions, calcium ions, blood pressure regulation and hypertension: a reassessment and a hypothesis. *Am J Physiol* 1977; 232: 165-73.