ORIGINAL ARTICLE

Correlations of Serum Magnesium and Potassium in Acute Myocardial Infarction, Chronic Ischemic Heart Disease and Normal Healthy Volunteers of Bangladesh

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ABSTRACT

Magnesium (Mg) and potassium (K) are the major intracellular cations whose presence in the serum are low, but minor changes of those may show a remarkable change in the various body functions specially in the heart. The study was designed to find out the correlation between serum Mg and K in acute myocardial infarction (AMI), chronic ischemic heart disease (CIHD) and normal healthy volunteers. It was carried out over a period of 18 months in the Department of Biochemistry, Bangabandhu Sheikh Mujib Medical University (BSMMU) in collaboration with Department of Cardiology, Sir Salimullah Medical College & Mitford Hospital (SSMC & MH) and Atomic Energy Center, Dhaka. A total of 101 subjects were included in which 32 subjects were AMI, 34 CIHD and 35 normal healthy volunteers. Serum glucose and serum creatinine were estimated to exclude diabetes and renal dystrophies. Estimation of serum CK-MB and ECG tracing were done as diagnostic tools of AMI and to categories the subjects into various groups. Serum Mg was estimated by Atomic absorption spectrophotometer and serum K by Ion sensitive electrode. The present study shows that there is a strong positive correlation of serum Mg and K in AMI, CIHD and healthy control subjects ($r = 0.566$, $p < 0.01$ level). So it is suggested to estimate and supplement both Mg and K in IHD patients for their better management.

Key Words: AMI, IHD, CIHD, Mg, K

Introduction

Magnesium (Mg) is one of the most abundant intracellular cations in the body. Approximately 40% of the Mg contained in the adult human body resides in the muscles and soft tissue, about 1% in the extracellular fluid (ECF), and rest in the skeleton[1]. The plasma Mg level is maintained remarkably constant in healthy individuals[2].

Mg is an essential co-factor for sodium-potassium adenosine triphosphatase (Na-K-ATPase), an enzyme that influences cardiac irritability by regulating the concentration gradient of Na (sodium) and K (potassium) across myocardial cell membranes. Mg has an essential role on the electron transport system for transmembrane ion flux, excitation-contraction coupling, energy metabolism and prevention of early atherosclerotic changes[3].

Deficiency of Mg causes a great variety of manifestations including growth failure and death of young plants and animals. Mg deficiency is associated with initiation and propagation of free radical myocardial tissue damage through oxidation of myoglobin, which is essential for intracellular transport and storage of oxygen (O_2)[4]. Mg deficiency increases

cardiac irritability and facilitates cardiac arrhythmias[5], causes coronary artery vasospasm, leading to myocardial ischemia and sudden death[6]. Deficiency of Mg has been associated with hypocalcemia and hypokalemia[7]. It is required for secretion of parathyroid hormone (PTH) as well as for PTH action[8].

K is the principal cation in intracellular fluid (ICF), nerve and muscle function and Na-K-ATPase[9]. It also regulates the PH and maintains the osmolarity of both the ICF and ECF (extracellular fluids)[10]. Total body K content in adult is about 3000-3500 mmol, among this 89.6% in ICF, 2.4% in ECF, 8% in bone, dense connective tissue & cartilage. Plasma contains only 0.4% of total body K. So very small change of K can cause remarkable change in the heart[11].

Various studies in different parts of the world suggest that Mg and K play an important role in cardiovascular system (CVS) especially on heart and blood vessels. Deficiency of both of them can cause serious cardiac disease[12, 13]. Studies also found specific correlation between serum Mg and K axis[14]. Often Mg and K deficiency occurs simultaneously in the heart[15].

Experimental observations with data support the view that, Mg and K metabolism are closely linked[14]. Whong, Oie, Aikawa et al. in 1984[16] investigated the frequency with which hypomagnesemia is found in hypokalemic patients. Among 106 hypokalemic patients, 45 patients or 42% were hypomagnesemic. In the year of 1983 Brown, Brown & Murphy[17] stated that immediately following an AMI there is a reduction in serum K, probably due to increased plasma catecholamine levels. There is also a decrease in serum Mg[18] due to catecholamine induced lipolysis[19] and similar decrease has been demonstrated in other stressful situations[20]. In a study Choudhury *et al*. (2009a)[21] found a significant lower serum Mg and K level in AMI. Also in another study Choudhury *et al*. (2009b)[22] observed a significant lower serum Mg and K persists in CIHD in comparison to normal healthy volunteers and they assumed that there may be a positive correlation between them. These observations point to a high incidence of hypomagnesemia among hypokalemic IHD patients.

A considerable number of people are suffering from IHD which includes AMI and CIHD in Bangladesh. Morbidity and mortality from these diseases are also very high. Effort should therefore be directed at prevention of these diseases as well as their complications. The relationship between Mg, K and IHD is becoming clear day by day from the different studies done around the world. But very little study is reported so far in Bangladesh. Thus, the study was designed to find out the correlation between serum Mg and K in patients of AMI, CIHD and normal healthy volunteers of Bangladesh.

Materials and Methods

This prospective study was carried out in the Biochemistry Department of Bangabandhu Sheikh Mujib Medical University (BSMMU) in collaboration with coronary care unit (CCU) of Sir Salimullah Medical College & Mitford Hospital and Atomic Energy Center, Dhaka.

Both male and female suspected AMI, angina pectoris & old MI were included in the study who gave their written consent and who have no recent history of treatment with laxatives containing Mg.

Patients suffering from diabetes mellitus, chronic renal disease and who have taken any diuretics prior to collection of sample were excluded from the study.

A total of 101 subjects were included in this study and were grouped as follows:

Group-1 (n = 32): Patients with acute myocardial infarction: The diagnosis was based on World Health Organization (WHO) criteria, including history, ECG changes, and elevated levels of serum CK-MB isoenzyme. Sample was collected within 24 hours from the onset of AMI.

Group-2 (n = 34): Chronic ischaemic heart disease: This group consists of angina pectoris or old MI. The diagnosis was based on history, clinical examination, resting and/or exercises ECG.

Group-3 (n = 35): Control subjects: Age matched healthy volunteers without any symptoms and signs of IHD were taken as controls. They were selected on the basis of history taking, clinical examination and ECG.

Data were collected through a preformed data collection sheet (questionnaire). The subjects were informed about the nature and purpose of the study and consent were taken from the patients themselves or from family members in case of unconscious patients. Blood sample was collected and questionnaire was filled up. Finally the subjects of this study were included on the basis of exclusion criteria.

Blood samples were collected from the subjects with all aseptic precautions 10 ml of venous blood were collected from the median cubital vein by a disposable plastic syringe. The needle was detached from the nozzle and blood was transferred immediately into a dry, clean, de-ionized, graduated, screw-capped plastic test tube with a gentle push to avoid hemolysis. The test tubes were kept in slanting position till formation of clot. Centrifuging the blood at 3000 rpm for 5 minutes, serum was separated and supernatant was taken into three small plastic test tubes (eppendorf), containing 1 ml in each. All the tests were carried out as early as possible. Whenever there was a delay, the serum samples were stored in the Ultra freeze at-20^{0}C.

The proper cleaning of plastic and glassware was very important for the indices of this study. Plastic ware, glassware, and pipettes were cleaned with detergent and then thoroughly with tap-water. All the instruments were kept immersed for 24 hours in 20% nitric acid (HNO_3) in deionized water. Then they were washed thoroughly with tap-water. Finally they were washed three times with deionized water and dried open in the air.

Following biochemical tests were carried out for each of the subjects:

Serum Mg levels were estimated by Atomic absorption spectrophotometer.

Serum K was estimated by Ion sensitive electrode (ISE).

Serum glucose was estimated enzymaticlly with the help of Glucose Oxidase (GOD).

Serum creatinine was estimated by Alkaline Picrate method.

Serum CK-MB was estimated by Kinetic Immunoinhibition method using spectrophotometer.

Twelve lead ECG was performed to detect myocardial infarction or normal healthy subjects.

Data were expressed in various forms as presentation and statistical analysis required. Appropriate statistical analysis i.e. one way analysis of variance (ANOVA) test and Pearson correlation test were done using computer based SPSS software programme. Mean values of the different parameters were compared for difference between groups and 95% confidence limit was taken as level of significance.

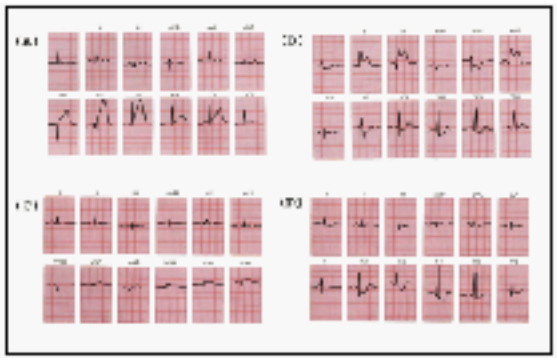

Fig 1: ECG of different types of acute myocardial infarction (A) acute anteroseptal MI (B) acute inferior MI (C) right ventricular infarction (D) posterior MI.

Results

The laboratory investigations of blood glucose, serum creatinine, serum CK-MB, serum Mg and K were expressed as mean ± SD and the results were expressed in SI units (e.g. mmol/L, µmol/L etc.)

The mean level of serum glucose (mmol/L) of group-1 (AMI), group-2 (CIHD) and group-3 (control) were 6.49 ± 1.80, 6.40 ± 2.07 and 6.01 ± 2.93 respectively. The total mean serum glucose level was 6.29 ± 2.32 mmol/L. No statistically significant mean difference of serum glucose level ($p > 0.05$) between the groups was found (Table-I).

A total mean serum creatinine level (µmol/L) was 86.89 ± 48.58, ranging from 35-125.3. In group-1 (AMI), the mean serum creatinine level was 92.41 ± 65.85, in group-2 (CIHD) it was 90.70 ± 49.99 and in group-3 (control) it was 78.15 ± 20.99 ranging from 44-125.3, 35-122.7 and 45-115 µmol/L respectively. No statistically significant mean difference of serum creatinine level (p > 0.05) between the groups was found (Table-I).

The mean level of serum CK-MB was 215.25 ± 69.35 U/L in group-1 (AMI), 18.67 ± 7.97 U/L in group-2 (CIHD) and in group-3 (control) it was 15.92 ± 4.76 U/L. A highly significant mean difference was found statistically between the groups (p < 0.001) indicating group-1 (AMI group) had too much higher level of serum CK-MB than other groups (Table-I).

The total mean serum Mg level (mmol/L) was 0.70 ± 0.13, ranging from 0.27-1.04. The mean level of serum Mg was 0.58 ± 0.10 in group-1 (AMI), 0.68 ± 0.06 in group-2 (CIHD) and 0.83 ± 0.09 in group- (control), ranging from 0.27-0.82, 0.51-0.84 and 0.68-1.04 respectively. A highly significant mean difference (p < 0.001) was found in serum Mg level among the three groups of study population through the analysis of variance (ANOVA) test of significance of difference (Table-II).

Table I: Comparison of Serum glucose, creatinine and CK-MB status between group-1 (AMI), Group-2 (CIHD) and Group-3 (healthy control) subjects

Parameters	Group-1 (AMI) n=32		Group-2 (CIHD) n=34		Group-3 (Control) n=35		T otal n=101	
	Mean	±sd Range	Mean	±sd Range	Mean	±sd Range	Mean	±sd Range
Glucose (mmol/L)	6.49	±1.80 4.1	±7.7 6.40	±2.07 3.9	±7.6 6.01	±2.93 3.6	±7.5 6.29	±2.32 3.6 ±7.7
Creatinine (umol/L)	92.41	±65.85 44-125	90.70	±49.99 35-122	78.15	±20.99 45-115	86.89	±48.58 35-125
CK-MB (U/L)	215.25	±69.35*** 98-322	18.67	±7.97 7.60-37.30	15.92	±4.76 7.80-25.70	80	±100.44 7.6-322

Results are mesn ± SD, data were subjected to one way Analysis of Variance (ANOVA) Mean were significantly different at p < 0.05 at 95% confidence limit. *** Significant at 0.001 level.

Total mean serum K level (mmol/L) was 3.81 ± 0.66, ranging from 2.20-5.50. The mean level of serum K in the individual groups were 3.28 ± 0.50, 3.69 ± 0.44 and 4.43 ± 0.46, ranging from 2.20-4.20, 2.60-4.40 and 3.20-5.50 in group-1 (AMI), group-2 (CIHD) and group-3 (control) respectively. A highly significant mean difference (p < 0.001) was found in serum K level among the three groups of study population through the analysis of variance (ANOVA) test of significance of difference (Table-II).

Table II: Comparison of Serum Mg, and K status between group-1 (AMI), Group-2 (CIHD) and Group-3 (healthy control) subjects

Parameters	Group-1 (AMI) n=32		Group-2 (CIHD) n=34		Group-3 (Control) n=35		T otal n=101	
	Mean	±sd Range	Mean	±sd Range	Mean	±sd Range	Mean	±sd Range
Magnesium (mmol/L)	0.58	±0.10*** 0.27	±0.82 0.68	±0.06*** 0.51	±0.84 0.83	±0.09 0.68	±1.04 0.70	±0.13 0.27 ±1.07
Potassium (mmol/L)	3.28	±0.50*** 2.20	±4.20 3.69	±0.44*** 2.60	±4.4 4.42	±0.46 3.20	±5.50 3.81	±0.66 2.20±5.50

Results are mesn ± SD, data were subjected to one way Analysis of Variance (ANOVA) Mean were significantly different at p < 0.05 at 95% confidence limit. *** Significant at 0.001 level among the study groups.

The incidence of hypomagnesemia in the patients with AMI was 86.66% and in CIHD it was 58.06%. The incidence of hypokalemia in AMI patients was 60% and in CIHD patients it was 22.58%. Hypomagnesemia was reported in 76.92% of hypokalemic subjects.

The correlation of serum Mg and K was done by Pearson correlation text. The results of the tests shows a strong positive correlation (r = 0.566 where correlation is significant at the 0.01 level) of serum Mg and of AMI, CIHD and normal healthy control subjects (Fig-2).

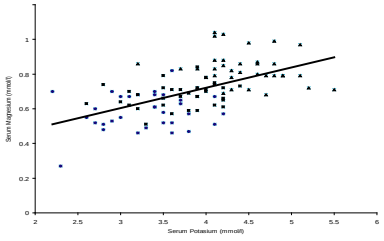

Fig. 2: Regression line showing correlation of serum Mg and K level between group-1 (AMI), group-2 (CIHD) and group-3 (Healthy Control). Correlation is significant at the 0.01 level.

Discussion

Serum glucose and serum creatinine were estimated to exclude diabetes and renal ailment. Serum CK-MB was estimated to diagnose the AMI. ECG monitoring was done to categorize the different subjects into groups. All the subjects in the study were non-diabetic with the mean (± SD) serum glucose level 6.29 ± 2.3 mmol/L. The mean (± SD) serum creatinine level of the subjects was 86.89 ± 48.58 µmol/L. All the subjects of AMI (group-1) showed a very high level of serum CK-MB and the mean (± SD) value was 215.25 ± 69.35 U/L. The subjects of CIHD and normal healthy control subjects showed a very close picture within normal reference range and their mean (± SD) value were 18.67 ± 7.97 U/L and 15.92 ± 4.76 U/L respectively.

In the present study a significant mean difference was found in serum Mg and K level between the three groups of study subjects and Pearson correlation test shows a strong positive correlation of serum Mg and K level between AMI, CIHD and normal healthy control groups indicating there might be a close relationship of Mg and K homeostasis in the body

The present study has shown that serum Mg level in control subjects ranges from 0.68-1.04 mmol/L (mean 0.83 ± 0.09 mmol/L). The normal average values of serum Mg reported in literature have varied from 0.7 to 1.45 mmol/L[15, 23, 24]. Figures of this study are very much similar to those of Wacker & Parisi (1968)[25] and Walser (1967)[26] who found the normal serum Mg level between 0.7 to 1.0 mmol/L. The reason for this variation may be due to difference in Mg content of drinking water in different geographic area. It also may depend on variation in sample size and measurement technique of Mg.

The mean serum Mg level in AMI group of this study was significantly lower than that of control group. The fundamental cause of AMI-related hypomagnesemia is unknown. But Flink et al. (1981)[15] demonstrated that the rise in catecholamines in AMI activates the enzyme adenyl cyclase, which brings about an increased synthesis of cyclic AMP. Cyclic AMP could then induce lipolysis, thus increasing FFA could chelate Mg and give a lower serum Mg level.

Significantly lower serum Mg level in CIHD group than control group was observed in this study. Dyckner (1980)[27] also showed a similar type of significantly lower serum Mg level in both AMI and non AMI (ischemic) groups than a reference group. Findings of this study fully agree with Dyckner's study. Rasmussen et al. (1988)[28] demonstrated that patients with both acute and chronic IHD retained greater amounts of Mg compared with healthy controls after undergoing an intravenous Mg loading test. This result was believed to represent the presence of underlying Mg deficiency in both AMI and CIHD patients.

The Present study reveled 76.92% hypomagnesemia in hypokalemic subjects. This finding supports the study of Boyd et al. (1983)29, and Whang et al. (1984)[16], who reported a 38% and 42% incidence of coexisting hypomagnesemia in hypokalemic patients respectively. Furthermore they proposed that in hypokalemic patients, serum Mg level should be routinely determined. In studying experimental depletion of Mg in humans, Shils (1969)[30] described the subsequent development of hypokalemia and hypocalcemia and stated that Mg is essential for the normal metabolism of both K and Ca. Kafka et al. (1987)[24] concluded in a study that hypokalemia and hypomagnesemia may occur in AMI in the absence of prior diuretic use. All of these studies make agreement with the findings of this study.

It is evident from the findings of present study that there is a significant lower serum Mg and K level in AMI & CIHD and there is a positive correlation between them. Evaluating the total findings from home and abroad it can be stated that low serum level of Mg and K may be the risk factor for IHD. Thus it is suggest from the above discussion that estimation and supplementation of both Mg and K is essential in case of IHD and AMI patients.

In can be concluded that statistically there is a

strong positive correlation of serum Mg and K in AMI, CIHD and normal healthy control subjects indicating close metabolic relationship between Mg and K both in different state of IHD patients as well as in normal healthy controls. So it is strongly recommended supplementation of both Mg and K in hypokalemic subjects to get the optimum benefit of treatment.

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References

1. Aikawa JK. Magnesium: Its biologic significance. Boca Raton, FL: CRC Press: 1981.
2. Elin RJ. Assessment of magnesium status. Clin Chem 1987; 33: 1965-1970.
3. Seelig MS, Heggtveit HA. Magnesium interrelationships in ischemic heart disease: a review. Am J Clin Nutr 1974; 27: 59-79.
4. Kramer JH, Misik V, Weglicki WB. Magnesium deficiency potentates free radical production associated with post ischemic injury to rat hearts: vitamin E affords protection. Free Radic Biol Med 1994; 16: 713-723.
5. Eisenberg MJ. Magnesium deficiency and cardiac arrhythmias. NY State J Med 1986; 86: 133-136.
6. Turlapaty DMV, Altura BM. Magnesium deficiency produces spasms of coronary arteries: Relationship to etiology of sudden death ischemic heart disease. Science 1980; 208: 198-200.
7. Anast CS, Mohs JM, Kaplan SL, Burns TW. Evidence for parathyroid failure in magnesium deficiency. Science 1972; 177: 606-608.
8. Wong ET, Rude RK, Singer FR, Shaw ST. A high prevalence of hypomagnesemia and hypermagnesemia in hospitalized patients. Am J Clin Pathol 1983; 79: 348-352.
9. Mayes PA. Nutrition. In: Murray RK, Granner DK, Mayes PA, Rodwell VW, eds, Harper's Biochemistry, 25th edn, Lange Medical Publication, Prentice-Hall International, USA 2000: pp 648-660.
10. Champe PC, Harvey RA. Nutrition. In: Champe PC, Harvey RA, eds, Lippincott's Illustrated Reviews: Biochemistry, 2nd edn, Lippincott-Raven Publishers, JB Lippincott Company, Philadelphia 1994: pp 303-318.
11. Ganong WF. The general and cellular basis of medical physiology. In: Review of Medical Physiology, 19th edn, Lange Medical Publication, Simon & Schuster Company, US 1999: pp 1-46.
12. Nordrehaug JE. Malignant arrhythmias in relation to serum potassium values in patients with an acute myocardial infarction. Acta Med sand Suppl 1981; 647: 101-107.
13. Sasaki S, Oshima T, Teragawa H, Matsuura H, Kajiyama G, Kambe M. Magnesium status in patients with cardiovascular diseases. Rinsho Buori 1999; 47: 396-401.
14. Whang R, Flink EB, Dyckner T, Wester PO, Aikawa JK, Ryan MP. Magnesium depletion as a cause of refractory potassium repletion. Arch Intern Med 1985; 145: 1688-1689.
15. Flink EB, Brick JE, Shane SR. Alterations of long-chain free fatty acid and magnesium concentrations in acute myocardial infarction. Arch Intern Med 1981; 141: 441-443.
16. Whang R, Oei TO, Aikawa JK, Watanabe A, Vannatta J, Fryer A, Markanich M. Predictors of Clinical Hypomagnesemia, Hypokalemia, Hypophosphatemia, Hyponatremia and Hypocalcemia. Arch Intern Med 1984; 144: 1794-1796.
17. Brown MJ, Brown DC, Murphy MB. Hypokalemia from beta2-receptor stimulation by circulating epinephrine. N Engl J Med 1983; 309: 1414-1419.
18. Abraham AS, Eylath U, Weinstein M, Czaczkes E. Serum magnesium levels in patients with acute myocardial infarction. N Engl J Med 1977; 296: 862-863.
19. Rayssiguier Y. Hypomagnesemia resulting from adrenaline infusions in ewes: Its relation to lypolysis. Horm Metabol Res 1977; 9: 309-318.
20. Abraham AS, Shaoul R, Shimonovitz S, Eylath U, Weinstein M. Serum magnesium levels in acute myocardial and surgical conditions. Biochem Med 1980; 24: 21-26.
21. Choudhury MBK, Arslan I, Mohibullah AKM, Mollah FH, Akhter MS, Quarashi SB, Rahman S, Hoque N, Akhtaruzzaman M. Reduced Serum Level of Magnesium and Potassium: a Consequence of Acute Myocardial Infarction. Bangladesh J Med Biochem, 2009; 2(1): 12-17.

22. Choudhury MBK, Akhtaruzzaman M, Hoque N, Rahman MS, Hassan MM, Begum R, Khan MR. Reduced Serum Level of Magnesium and Potassium persists in Chronic Ischemic Heart Disease. Bangladesh J Med Biochem, 2009; 2(1): 49-53

23. Dyckner T, Wester PO. Magnesium deficiency - guidelines for diagnosis and substitution therapy. Acta Med Scand 1982; 661(suppl): 37- 41.

24. Kafka H, Langevin L, Armstrong PW. Serum magnesium and potassium in acute myocardial Infarction. Arch Intern Med 1987; 147: 465-469.

25. Wacker WEC, Parisi AF. Magnesium metabolism (concluded). N Engl J Med 1968; 278: 772-776.

26. Walser M. Magnesium metabolism. Rev Physiol Biochem Exp Pharmacol 1967; 59: 185-341.

27. Dyckner T. Serum magnesium in acute myocardial Infarction: Relation to arrhythmias. Acta Med scand 1980; 207: 59-66.

28. Rasmussen HS, McNair P, Goransson L, Balslov S, Larsen OG, Aurup P. Magnesium deficiency in patients with ischemic heart disease with and without acute myocardial infarction uncovered by an intravenous loading test. Arch Intern Med 1988; 148: 329-332.

29. Boyd JC, Bruns DE, Wills MR. Frequency of hypomagnesemia in hypokalemic states. Clin Chem 1983; 29: 178-179.

30. Shils ME. Experimental human magnesium depletion. Medicine (Baltimore) 1969; 48: 61-85.