Medical Journal of the
Islamic Republic of Iran

Volume 3
Number 3,4
Payiz & Zemestan 1368
Fall & Winter 1989

Basic Science In Medicine

ESTIMATION OF POTASSIUM, CALCIUM, AND MAGNESIUM IN BLOOD AND MYOCARDIAL TISSUE, AND DIAGNOSTIC IMPORTANCE OF URINARY MAGNESIUM EXCRETION IN EXPERIMENTALLY-INDUCED MYOCARDIAL INJURY

KASHAV ANAND,* M.B., B.S., M.D., ABRAR ALI KHAN,** M.B., B.S., M.S., AND RAJENDRA KUMAR GUPTA,*** M.B., B.S., M.D.

*From the *Department of Physiology,**Department of Anatomy, and ***Department of Pathology, School of Medicine, Kerman University of Medical Sciences, Kerman, Islamic Republic of Iran.*

ABSTRACT

The results obtained in the present investigations point to a definite correlation between the onset of myocardial injury, electrocardiographic changes and biochemical changes. Changes in the electrocardiogram and elevated serum levels were paralleled by an increased excretion of magnesium in urine as early as one hour. Serum calcium and serum potassium levels did not show any significant result, but in coming days these ions including serum magnesium might help clinicians diagnose myocardial infarction. In this study, increased urinary magnesium excretion was found to coincide with elevated serum transaminases, and it is suggested that in addition to the other estabilised diagnostic criteria, estimation of serum as well as urinary magnesium may be used as an additional index of myocardial infarction.

MJIRI, Vol.3, No.3 & 4, 151-155, 1989

INTRODUCTION

Tension and worries in the developing societies have lead to a steady increase in the incidence of myocardial infarction, which has reached epidemic proportion. Experimental and clinical studies on myocardial infarction are engaging the attention of medical scientists. Simple techniques such as careful history coupled with certain routine laboratory tests along with electrocardiography are sufficient for diagnosing myocardial infarction. The profound environment of electrolytes especially potassium, calcium, magnesium, sodium and phosphorus in the pathophysiology of cardiovascular structure and function has become more and more appreciated during recent years. Cardiac necrosis was first recognized in conjunction with potassium deficiency by Schrader, et.al.[1] Lehr, et. al.[2] and Jenings, et. al.[3] showed a marked increase in tissue calcium, sodium and water and a decrease in tissue magnesium and potassium contents in myocardial necrosis. They also showed that administration of magnesium offers considerable protection against the development of myocardial infarction. Various workers have produced diffuse myocardial injury in experimental animals after infusions of sympathetic catecholamines (isoprenaline,

Table I. Serial Estimation of Serum Potassium* in Isoprenaline Induced Myocardial Injury in Mongrel Dogs

Group		1 Hr	2 Hr	3 Hr	4 Hr	5 Hr	6 Hr
Control (10)	Mean	4.38	4.30	4.26	4.22	4.22	4.18
	S.D.	±0.51	±0.42	±0.46	±0.46	±0.54	±0.48
Experimental A(5)	Mean	4.18	3.92	3.84	3.88	3.88	4.12
	S.D.	±0.39	±0.41	±0.38	±0.46	±0.46	±0.48
Experimental B(20)	Mean	4.07	3.48	3.65	3.68	3.80	3.86
	S.D.	±0.56	±0.40	±0.39	±0.43	±0.46	±0.48
Groups Compared:							
	t	0.73	0.81	1.63	1.26	1.12	0.20
Control vs Experimental A							
	p	-	-	-			
	t	1.43	5.03	3.66	3.06	2.16	1.60
Control vs Experimental B							
	p	-	<0.001	<0.01	<0.01	<0.05	-

* Milliequivalent per litre (mEq/L)

epinephrine and norepinephrine) in high doses offering this as an experimental model for infarct studies.[4-7]

The aim of this work has been to investigate the importance of the trace elements in the pathogenesis as well as diagnosis of myocardial infarction.

MATERIAL AND METHODS

Myocardial injury was produced in mongrel dogs by infusing isoprenaline 2-4 microgram per kilogram per minute for six hours. The animals were divided into two groups randomly. The control group comprised of ten and the experimental group of 25 animals. The control group received infusion of physiological saline at a rate of 2 microgram per kilogram per minute for six hours. Out of the experimental group of 25 dogs, five were given 2 micrograms isoprenaline in physiological saline per kilogram per minute and labelled as experimental group A, while experimental group B (20 animals) received isoprenaline at 4 micrograms per kilogram per minute dissolved in physiological saline (low dose and high dose, respectively). Serial recording of ECG was done and blood samples were taken every hour for estimation of serum electrolytes. After six hours of infusion, the animals were sacrificed and their hearts removed and injected with 10% sucrose solution through the aorta. Tissue samples of the left ventricle were taken consistently from areas showing signs of massive hemorrhage and infarct. The tissues were dried at 125 °C and were digested by the method adopted by Yunice, et. al.[8] Suitable aliquots of the

Table II. Serial Estimation of Serum Calcium* in Isoprenaline- Induced Myocardial Injury in Mongrel Dogs

Group		1 Hr	2 Hr	3 Hr	4 Hr	5 Hr	6 Hr
Control (10)	Mean	9.86	9.79	9.46	9.76	9.75	9.72
	S.D.	±0.56	±0.57	±0.53	±0.54	±0.54	±0.52
Experimental A(5)	Mean	9.68	9.64	9.50	9.42	9.28	9.16
	S.D.	±0.41	±0.40	±0.37	±0.43	±0.47	±0.59
Experimental B(20)	Mean	9.92	9.80	9.71	9.50	9.33	9.09
	S.D.	±0.53	±0.53	±0.55	±0.47	±0.47	±0.51
Groups Compared:							
	t	0.59	0.49	0.93	1.14	1.53	1.76
Control vs Experimental A							
	p	-	-	-	-	-	-
	t	0.28	2.05	0.23	1.31	2.12	3.06
Control vs Experimental B							
	p	-	-	-	-	<0.05	<0.01

* Milligrams per decilitre (mg/DL)

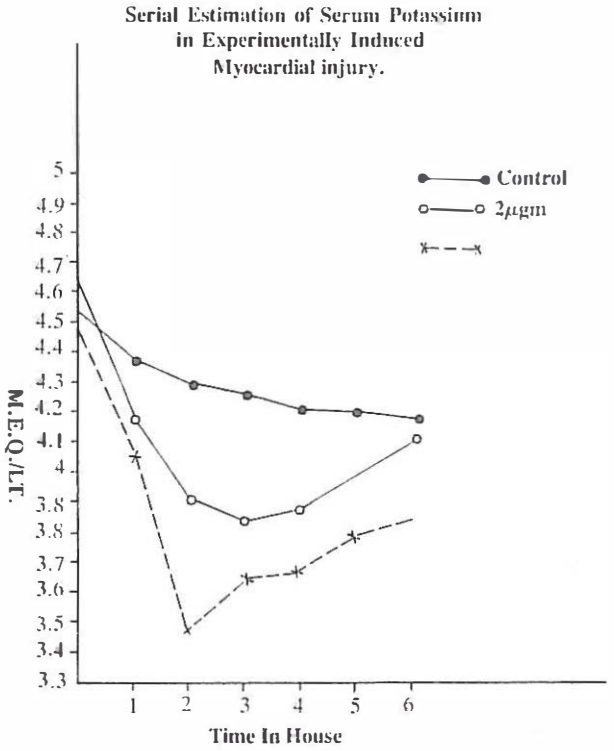

Fig. 1. The animals given 2 mcg belong to experimental group A and those given 4 mcg belong to group B.

samples were taken for analysis of calcium and magnesium. Determination of magnesium in serum as well as myocardium was done by colorimetric method using titan yellow.[9] The same procedure as described above was adopted for urine, except that a correction was made for urine colour by running a "blank" and "test" through the entire procedure with water substituted for titan yellow. Determination of serum as well as myocardial tissue calcium was done by EDTA titration method.[10] Serum potassium was estimated in C-120 AIMIL flame photometer.

RESULTS

The present investigation was planned to assess the relationship of the various diagnostic criteria used in acute myocardial infarction and mainly focused on changes in serum as well as myocardial electrolytes with relation to changes in ECG. Table I and Fig. 1 show the results of serial serum potassium analysis. Animals receiving 2 μg dose of isoprenaline did not deviate significantly from control.

Animals receiving 4 μg (high dose group) did not differ significantly from control at one hour, but the serum potassium values fell drastically ($P < 0.001$) at two hours, the fall being sustained very significantly ($P < 0.001$) up to four hours. By the end of the fifth hour a

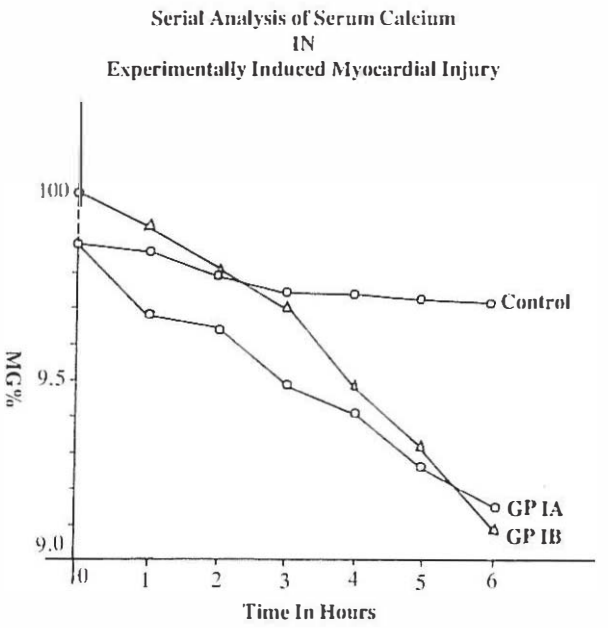

Fig.2. The Groups II and II B represent the experimental Animals in Groups A and B respectively.

slight rise in serum potassium had occurred in this group, though values were still significantly low ($P < 0.05$), while an increase in serum potassium was recorded at the end of the sixth hour.

There was no significant difference between control animals and experimental animals infused with low dose isoprenaline. However a significant decrease ($P < 0.05$) in serum calcium occurred at the fifth hour and this decrease became more significant ($P < 0.01$) by the end of the sixth hour of infusion (Fig. 2).

A very highly significant ($P < 0.001$) accumulation of calcium was observed in the experimental animals in

Table III. Myocardial Concentration* of Magnesium & Calcium in Animals Receiving Isoprenaline Infusion Compared To Saline Control Infusion

		Control	Experimental	
			A	B
Magnesium	Mean	120.40	90.18	63.13
	S.D.	±6.80	±4.43	±10.25
Calcium	Mean	5.18	-	10.30
	S.D.	±0.55	-	±1.10
Magnesium Control vs Experimental	t		7.44	10.55
	p		<0.001	<0.001
Calcium Control vs Experimental	t			9.19
	p			<0.001

* Milligram per 100 gram fat free dry weight.

Table IV. Serial Estimation of Urinary Magnesium* in Isoprenaline-Induced Myocarial injury in the Mongrel Dogs.

	Experimental group B					
	Mean Base Line Value: 6.72 ± 1.12					
	1 Hr	2 Hr	3 Hr	4 Hr	5 Hr	6 Hr
Mean	6.94	15.06	14.66	15.52	13.47	12.45
S.D.	±1.13	±6.49	±6.97	±8.52	±2.83	±5.16

* Milligrams per 100 ml.

the high dose group (4 μg of isoprenaline/kg/min) in comparison to control animals (Table III).

Myocardial magnesium content was estimated in both groups of experimental animals. These animals showed a very highly significant ($P<0.001$) decrease in relation to control animals in their content of myocardial magnesium. Drastic decrease in myocardial magnesium content was observed in serial urinary magnesium levels (Table IV). The rise in urinary magnesium started at one hour and was maintained until the end of the sixth hour of the infusion, with maximal excretion observed at four hours. This increase in urinary magnesium, decrease in serum potassium, decrease in serum calcium and accumulation of calcium in myocardium showed significant relation with changes in serum enzymes and ECG changes observed in the experimental groups (Table V).

DISCUSSION

The role of magnesium in the structural integrity and function of heart tissue has come to attention within recent years. Cardiac mitochondria are very sensitive to loss of magnesium. According to Seeling,[11] efflux of magnesium from and influx of calcium into mitochondria are associated with impaired mitochondrial structure and function. The results obtained in the present study point to such ionic translocations as a consequence of myocardial ischemia. Serum magnesium was observed to be significantly increased in dogs infused with isoprenaline. These findings corroborate with the findings of Clarke, et. al.,[12] and Cummings.[13] Decrease in serum magnesium levels were recorded in patients with myocardial infarction admitted to the hospital by Holtmeier,[14] Hughes and Tonks[15] and Nath, et. al.[16] However, Brown, et. al.[17] and Hyattet et.al.[18] observed no such decrease in patients suffering from MI as compared to normal persons. This difference in results was attributed to irregularly obtained samples for estimation after the onset of myocardial infarction.

The hearts of patients who died of myocardial infarction were reported to have significanlty decreased magnesium content (Heggtveit, et.al.[19] and Iseri, et.al).[20] The present study confirms the findings of the aforementioned workers.

The hypermagnesemia observed in the present study was found to correlate with increased urinary excretion of magnesium (Table IV). Kraikit, Panitch, et. al.[6] observed marked influx of calcium into myocardium in dogs injected with epinephrine, but no significant changes in serum calcium levels were noted. Iseri,[20] Yunice, et. al.,[8] and Jennings, et. al.[21] reported a decrease in magnesium and potassium concentrations and an increase in calcium and sodium concentrations in infarcted myocardium. Our results obtained in this study are in conformity with the above cited investigators. Fleckenstein[22] reported increased trans-

Table V. Serial Estimation of Serum Magnesium* in Isoprenaline-Induced Myocardial Injury in Mongrel Dogs

Group			1 Hr	2 Hr	3 Hr	4 Hr	5 Hr	6 Hr
Control (10)	Mean		1.32	1.27	1.18	1.07	1.14	1.10
	S.D.		±0.37	±0.39	±0.08	±0.11	±0.34	±0.33
Experimental A(5)	Mean		1.44	1.23	1.54	1.72	2.02	2.38
	S.D.		±0.19	±0.15	±0.05	±0.11	±0.28	±0.16
Experimental B(20)	Mean		1.51	1.36	1.62	1.83	2.04	2.18
	S.D.		±0.26	±0.23	±0.21	±0.24	±0.29	±0.35
GroupsCompared:								
Control vs Experimental	A	t	0.64	0.05	1.94	9.85	4.71	7.77
		p	-	-	-	<0.001	<0.001	<0.001
Control vs Experimental	B	t	1.58	0.77	3.77	9.20	7.30	7.69
		p	-	-	<0.001	<0.001	<0.001	<0.001

* Milligrams per decilitre.
Figures within parentheses indicate the number of animals in that group.

membrane influx of calcium in rats administered isoprenaline. Nicherson et. al.[23] and Mauret et. al.[24] showed that myocardial lesions induced by exogenous potassium dficiency appeared analogous to those elicited by various locally-necrotizing agents, especially catecholamines. Concentration of these ions around the anoxic cells (Harriss, et. al.,[25] Salmanovich,[26] and Printzmetal, et. al)[27] contributes to the temporary marked increase in electric potential gradient between the structurally deteriorating center of the infarcted area and the surrounding tissue. The study of serum magnesium, potassium, sodium and estimation of excretion of urinary magnesium shall be a great tool for diagnosing a case of myocardial infarction in the near future, although this still requires elaborate study.

REFERENCES

1. Schrader GA, Prickett CO, Salmon WD: Sympatomatology and pathology of potassium and magnesium deficiencies in rats. J Nutrition 14: 85-109, 1937.
2. Lehr D, Chau R, Kaplan J: Presentation of experimental myocardial necrosis by electrolyte solutions. In: Bajusz E, Rona G (eds): Myocardiology. vol 1, Baltimore: University Park Press, 684, 1972.
3. Jennings RB, Shen AC: Calcium in experimental myocardial ischaemia. In: Bajusz E, Rona W (eds): Myocardiology: recent advances in studies in cardiac structure and metabolism. Baltimore: University Park Press, 639, 1972.
4. Chappel CI, Rona G, Gaudry R: The influence of adrenal cortical steroids on cardiac necrosis produced by isoproterenol. Acta Endocrinol 31:419-24, 1959.
5. Bloom S, Davis DL: Calcium as mediator of isoproterenol-induced myocardial necrosis. Am J Pathol 69: 459-70, 1972.
6. Kraikitpanitch S, Haygood CC, Baxter DJ, et al: Effects of acetylsalicylic acid, dipyridamol and hydrocortisone on epinephrine-induced myocardial injury in dogs. Am Heart J 92(5),615-22,1976.
7. Mahajan V, Kumar M, Chakravarty RN, Wahi PL: Studies of cardiovascular effects of noradrenaline in monkeys. Bull PGI. 10:2, 1976.
8. Yunice AA, Baxter DJ, Kraikitpanitch S: Myocardial calcium in experimental myocardial infarction. Cardiology 59:367-75, 1974.
9. Neill DW, Neely RA: Estimation of magnesium in serum using Titan Yellow. J Clin Pathol 9:162-3, 1956.
10. Richard HJ: Clinical Chemistry: Principles and Techniques. Harper and Row, 491, 1964.
11. Seelig MS: Myocardial loss of functional magnesium. Part.I.Effect on mitochondrial integrity and pottassium retention. In: Bajusz E, Rona G (eds): Myocardiology. Baltimore: University Park Press, vol I, 615, 1972.
12. Clark BB, Cummings JR: Arrhythmias following experimental coronary occlusion and their response to drugs. Ann NY Acad Sci 64,543-5,
13. Cummings JR: Electrolyte changes in heart tissue and coronary arterial and venous plasma following coronary occlusion. Circul Res 8:865, 1962.
14. Holtmeier HJ: Magnesium-Soffwechselsstörung und Herzinfarct. In: Hilmeyer L, Holtmeier HJ (eds): Herzinfarct und schoch. Stuttgart
15. Hughes A, Tonks RS: Platelets, magnesium, and myocardial infarction. Lencet 1:1044-6, 1965.
16. Nath K, Sikka KK, Sur BK, Saxena CP, et al: Serum magnesium in clinical and experimental myocardial infarction. Ind J Med Res 57:317, 1969.
17. Brown DF, McGandy RB, Gillie E, et al: Magnesium-lipid relation in health and patients with myocardial infarction. Lancet 2:933-5, 1958.
18. Hyatt KH, Levy L, Nichaman M, et al: Relationship of serum magnesium levels to serum cholesterol and triglyseride levels and to myocardial infarction. Applied Spectroscopy 20: 142, 1966.
19. Heggveit HA, Tauser P, Hunt B: Magnesium content of normal and ischaemic human heart. Proceedings of the Seventh International Congress of Clinical Pathology, Montreal, p. 53, July 13-19, 1969.
20. Iseri LT, Alexander RLC, MacCaughey RS, et al: Water and electrolyte contents of cardiac and skeletal muscles in heart failure and myocardial infarction. Am Heart J 43: 215, 1952.
21. Jenning RS, Kelterbach JP, Sommers HM: Cell death: Electrolyte alteration in injured and dying myocardiac cells. In: Bajusz E(Ed), Electrolyte and cardiovascular Diseases. Basel, S Karger, 142, 1965.
22. Fleckenstein A: specific inhibitor and promotors of calcium action in the excitation-contraction coupling of heart muscle and their role in the prevention and production of myocardial lesions. In: Harris P, Opie LH (eds). Calcium and the Heart. New York: Academic Press, 135, 1971.
23. Nickerson M, Karr GW, Dresel PE: Pathogenesis of electrolyte steroid-cardiopathy. Circ Res 9:209, 1961.
24. Maurat JP, Mercier JN, Ledoux CH, et al: The myocardial infarction of rat during experimental potassium depletion. Am Electron microscopic study. Arch Mal Coeur 58:1004, 1965.
25. Harris AS, Bisteni RA, Russel RA, et al: Excitator factors in ventricular tachycardia resulting from myocardial ischaemia. Potassium a major excitement. Science, 119:200, 1954.
26. Salmanovich VS: Electrolyte shift in the heart in experimental myocardial infarction. In: Aterosklerozy infarkt Miokarda, Medhiz, Moscow.
27. Prinzmetal M, Ekmekci A, Kwoczynski J: Angina pectoris. III. Demonstration of a clinical origin of ST deviation in classic angina pectors, its variants from early myocardial infarction and some non cardiac conditions. Am Cardiol 3:276, 1959.