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REDUCTION OF EXPERIMENTAL MYOCARDIAL INFARCT SIZE BY PRE-TREATMENT WITH MAGNESIUM SULFATE IN RATS

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Abstract : Experimental myocardial infarction was induced in albino rats by administration of isoprenaline hydrochloride, 85 mg/kg, sc, daily for two consecutive days. Such rats were pretreated with either saline or magnesium sulfate (60 mg/kg) po, daily for three weeks, to serve as control or treated groups respectively. Heart specimens were taken for gross and histological examination at 24 hr, on 5th day, 12th day and 21st day. Infarct size was significantly reduced in the magnesium-treated group ($P < 0.05$). We conclude that magnesium sulfate exerted a potent prophylactic effect in limiting infarct size in rats.

Key words : myocardial infarction isoprenaline magnesium sulfate

INTRODUCTION

Magnesium has been implicated in different cardiac diseases (1-4). *In vitro* experimental studies have revealed that magnesium depletion in superfusate medium potentiated contractile responses of coronary arteries to various stimuli (5). Magnesium may be a physiological calcium antagonist and this prevents contraction of vascular smooth muscle (4-6). Myocardial tissue magnesium levels in subjects who died of ischemic heart diseases was found to be lower than in subjects who died from other causes (7). Magnesium also exerted a potent prophylactic effect in limiting the infarct size in the dogs with permanent coronary artery occlusion (8).

However, prophylactic use of magnesium in myocardial infarction as a result of catecholamine stress has never been investigated. And in view of (i) difficulty in procuring healthy dogs, (ii) the high intra and post-operative mortality rates and (iii) specialized skill required for coronary ligation procedure, we planned the present study to investigate the prophylactic role of magnesium in catecholamine-stress induced myocardial infarction in rats.

METHODS

Thirty two albino rats of either sex, weighing 200±25 g were divided into two groups of 16 rats each. In one group, magnesium sulfate 60 mg/kg in 1 ml of saline po was administered daily for three weeks. The control group was fed with an equal volume of saline. During this period both groups were given standard rat feed (Hindustan Lever) and water *ad libitum*. At the end of three weeks, myocardial infarction was produced by the method of Rona et al (9). Rats of both the groups were given isoprenaline hydrochloride 85 mg/kg, sc daily on two consecutive days. The animals were then divided into four sub-groups of four animals each. The animals were sacrificed by quick decapitation and hearts removed (a) at 24 hr (b) on 5th day (c) 12th day and (d) on 21st day following the catecholamine stress.

The macroscopic lesions and microscopic findings were graded according to Rona et al (9) as follows:

Macroscopic lesion: Grade 0: no lession; Grade 1: mottling of apex and distal part of left ventricle; Grade 2: well demarcated necrotic area limited to

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TABLE I : Macroscopic and microscopic finding in control and magnesium pre-treatment at 24 hr, on 5th day, 12th day and 21st day. (Data are grades, $\bar{x} \pm$ SEM** from 4 animals in each sub-group).

	24 hr		*5th day*		*12th day*		*21st day*	
	Control	*Magnesium*	*Control*	*Magnesium*	*Control*	*Magnesium*	*Control*	*Magnesium*
Macroscopic findings	1	1NS	3	1*	3	1*	3	1*
Microscopic findings	2	1.25 ± 0.25^{NS}	3	1*	3	1*	3	1*

$P < 0.05$ as compared to respective control values.
NS = Not significant.
**SEM = O for all groups wherever not limited.

the apex; Grade 3: necrosis involving one-third of left ventricle and extending to interventricular septum and right ventricle; Grade 4: large necrosis involving more than half of the left ventricle interventricular septum and right ventricle.

Microscopic lesion: After hematoxylin-eosin staining of the sections of the heart, the grading was done. Grade 0: no lesion; Grade 1: focal lesion of subendocardial portion of the apex and papillary muscle; Grade 2: focal lesion on left ventricle with right ventricle involvement; Grade 3: confluent lesion of the apex, papillary muscle, with focal lesion of ventricles and auricles; Grade 4: confluent lesion throughout the heart, massive necrosis and aneurysm formation.

The statistical comparison were done by the Wilcoxon rank test.

RESULTS

Macroscopic findings: There was no significant difference in the infarct size between the two groups at 24 hr. However, infarct size was significantly reduced in the magnesium-treated group was compared to control on 5th, 12th and 21st post-infarction days ($P < 0.05$ for each) (Table I).

Microscopic findings: At 24 hr there was no significant difference in the two groups, though the infarct size was less in the magnesium-treated group. Infarct was significantly reduced in the magnesium group on 5th, 12th and 21st post-infarction days ($P < 0.05$ for each) (Table 1).

DISCUSSION

The results indicated that magnesium pre-treatment caused a statistically significant reduction in myocardial infarct size as compared to control. Our findings are in accordance with those of Lal and Sharma (8) who found a potent prophylactic effect of magnesium sulfate in limiting the infarct size in dogs in coronary ligation model.

When the extracellular magnesium concentration is low, the basal tension of the isolated coronary artery is increased and its contractile response to vaso-constrictive agents is potentiated, whereas when the magnesium concentration is high, the basal tension of the artery is depressed and its response to vasoconstrictive agents in depressed causing vasodilation (5). As all the vasoactive agents utilize Ca^{++}ions for eliciting contractile responses, there are evidence to support that magnesium may be the naturally occuring calcium antagonist in the vascular system (4-6). Magnesium produces improvement in collateral circulation and also diminish muscle damage (10-12). However, the exact mechanism of prophylactic role of magnesium in limiting myocardial infarct size remains to be elucidated.

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