

SHORT COMMUNICATION

LIMITATION OF EXPERIMENTAL MYOCARDIAL INFARCT SIZE BY MAGNESIUM SULFATE PRE-TREATMENT IN DOGS

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**Abstract :** The present study was designed to evaluate the ability of magnesium sulfate (30 mg/kg, iv, 24 hr and 2 hr prior) to limit myocardial infarct size following permanent left coronary artery occlusion in adult mongrel dogs. Non-perfused myocardium which is the area at risk was visualised by injecting methylene blue intraatrially, 24 hr after coronary artery occlusion. The infarcted myocardium was visualised by triphenyl tetrazolium chloride staining. Infarct size (expressed as % of the risk zone) was significantly reduced in the treatment group ( $P < 0.001$ ). We conclude that magnesium sulfate exerted a potent prophylactic effect in limiting the infarct size in the dogs with permanent coronary artery occlusion.

**Key words :** infarct size mangesium sulfate coronary artery occlusion

INTRODUCTION

The role of magnesium in cardiac diseases has been recently reviewed (1,2). Experimental studies, in-vitro have shown that depletion of magnesium from superfusate medium potentiates contractile responses of small and large coronary arteries to various stimuli (3). Magnesium may be a physiologic calcium antagonist and thus may prevent the contraction of vascular smooth muscle (2,3,4). It has also been reported that magnesium level in myocardium in subjects who died of ischemic heart diseases is lower than subjects who died from other causes (5). However, it appears that to date no study concerning the effect of magnesium on myocardial infarct size has been reported. In the present study, we have examined the effect of magnesium sulfate in experimental myocardial infarction in dogs.

METHODS

Eighteen adult mongrel dogs of either sex in weight range of 12-18 kg were used for this study. They were anaesthetised with sodium thiopentone (30 mg/kg, iv). Endotracheal intubation was done

and respiration was maintained with Harvard Respirator. The lead II of the ECG was recorded. Under aseptic conditions chest was opened through left side thoracotomy in 4th intercostal space. The pericardium was incised, the anterior descending branch of left coronary artery identified and separated, a double silk ligature passed under it and an intermittent myocardial ischemia was produced to stabilize the myocardium (6,7). Then the artery was ligated permanently after 10 min. of intermittent ischemia (7). The thorax was closed after reducing pneumothorax and ECG lead II was recorded again.

After 24 hr of coronary artery occlusion animals were again anaesthetised, ECG recorded and methylene blue injected intraatrially. The animals were killed with an overdose of sodium thiopentone. The hearts were excised and its right ventricle, right atrium, left atrium, fatty tissue and valve tissue were separated from the left ventricle. The left ventricle tissues were frozen and sliced into transverse sections of 5 mm thickness and were allowed to thaw. The epicardial and endocardial, methylene blue-perfused and non-perfused areas were traced.

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To visualize the infarcted myocardium, the slices were incubated in triphenyl tetrazolium chloride (T.T.C) 1% solution for 20 min at 37°C. The infarct areas remained unstained whereas remaining areas were stained pink by T.T.C. These areas were traced and the planimetry was done. The methylene blue nonperfused area is the area at risk, which is defined as the perfusion field of an occluded coronary artery. The myocardial infarction will develop within this field (8). The percentage risk zone was calculated as the methylene blue non-perfused area with respect to % of left ventricular mass. The T.T.C. unstained area is the infarct area. The percentage infarct area was calculated as T.T.C. unstained area with respect to % of risk zone (9).

**Treatment Protocol:** The dogs were randomly assigned to either group. The treatment group comprised of 8 dogs and were given magnesium sulfate (30 mg/kg, iv) 24 hr and 2 hr prior to coronary occlusion. The control group comprised of 10 dogs and were given normal saline (1 ml/kg, iv) 24 hr and 2 hr prior to coronary occlusion. All the results were expressed as Mean±SEM. The statistical comparisons were performed using unpaired 't' test.

## RESULTS

Two dogs out of 8 in the drug treatment group and 4 out of 10 dogs in control died postoperatively, probably of a lethal arrhythmia. They were excluded from the study leaving 6 dogs in the control group and 6 in the magnesium pretreatment group.

There was no statistically significant difference in the % risk zone between the control and the magnesium pretreatment group (Table I). However, there was a statistically significant reduction in the infarct size (expressed as % of risk zone) in the magnesium group as compared to the control (Table I).

There was no statistically significant difference between the two groups, with respect of preocclusion heart rate, postocclusion heart rate and the heart rate 24 hr after coronary occlusion. After coronary occlusion, heart rate increased slightly in the two groups; however, after 24 hr of coronary occlusion heart rate decreased to a similar extent in each group (Table I).

## DISCUSSION

The results indicated that magnesium pretreatment caused a statistically significant reduction in myocardial infarct size as compared to the control group. The infarct size in the drug treatment group was only 46% of the control group which is suggestive of some protective effects of magnesium.

When the extracellular magnesium concentration is low, the basal tension of the isolated canine coronary artery is increased and its contractile response to vaso-constrictive agents such as catecholamines is potentiated, whereas when the magnesium concentration is high, the basal tension of artery is decreased and its response to vasoconstrictive agents is depressed causing vasodilation (3). As all the vasoactive agents utilize

TABLE I : Heart rate, percentage risk zone and percentage infarct with respect to risk zone in control and magnesium pretreatment.\* (Data are Mean ± SEM from 6 animals in each group)

GROUPS	Weight (kg) KG.	Heart rate (Beats/min)			Percentage risk zone	Percentage infarct with respect to risk zone
		Preocclusion	Postocclusion	24 hr after occlusion		
CONTROL	14.17 ±0.54	155.5 ±2.60	163.5 ±1.54	143.67 ±4.94	27.83 ±2.63	76.54 ±3.01
MAGNESIUM PRETREATMENT	16 ±0.63	157.83 <sup>NS</sup> ±9.88	168.33 <sup>NS</sup> ±10.77	143.30 <sup>NS</sup> ±8.43	25.68 <sup>NS</sup> ±1.65	35.33* ±1.50

\*P < 0.001 vs Control; NS — Not statistically significant.

\*(Magnesium sulfate 30 mg/kg iv, 24 hr and 2 hr prior to left coronary artery occlusion)

Ca<sup>++</sup> ions for eliciting contractile responses, there are evidences to support that magnesium may be the naturally occurring calcium antagonist in the vascular system (2,3,4). Magnesium also produces improvement in collateral circulation thereby relieving pain in myocardial infarction and diminishing muscle damage (10,11).

However, the exact mechanism of prophylactic

role of magnesium in limiting myocardial infarct size, as documented in the present study, remains to be elucidated.

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