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THE ROLE OF INTRAVENOUS MAGNESIUM IN REDUCING SHORT TERM MORTALITY OF ACUTE MYOCARDIAL INFARCTION AS COMPARED TOSTREPTOKINASE AND PLACEBO.

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ABSTRACT *In a randomized control trial of 84 patients of acute myocardial infarction who were divided into 3 therapeutic groups randomly i.e. magnesium treated group, streptokinase treated group and placebo group. The number of patients were 28 in each group. Each group compared in reference of mortality, complications and serum magnesium levels of post myocardial infarction period of 28 days. Significant hypomagnecemia was present in all cases of acute myocardial infarction on the day of admission in CCU. During the 28 days, mortality was 2(7.14%) in magnesium and streptokinase treated group and 3(10.71%) in placebo group. In magnesium treated group least number of arrhythmiaSwere observed 10(17.8%), while in other two study groups number of arrhythmia were observed 11 (39.28%) in each group. We also observed that, least number of pump failure in magnesium treated group. No adverse effect of intravenous magnesium were observed. This study conclude that all the cases of acute myocardial infarction should be given IV magnesium soon after admission in CCU, as this is cheap and safe drug which can reduce short term complications and mortality after acute myocardial infarction.*

KEYWORDS :

INTRODUCTION

In cardiovascular diseases, acute myocardial infarction is one of the most common life tlireateningdisease all over the world. The infarction may be uncomplicated or complicated. Magnesium the major intracellular cation, is associated with cardiac rhythm disturbances and size of infarct in acute myocardial infarction. Magnesium infusion can reduce peripheral resistance and increased cardiac output without any corresponding increase in cardiac work, thus magnesium infusion if started early after onset of myocardial infarction, may limit infract size and prevent serious arrhythmias and reduces mortality . Hence we conducted a randomized case control study among intravenous magnesium, streptokinase and placebo therapy in patients of acute myocardial infarction

MATERIAL AND METHODS

The study was done in 84 patients of acute myocardial infarction, who were admitted in CCU. Department of Medicine, S.P. Medical College, Bikaner. Acute myocardial infarction was diagnosed by clinical sympatomatology and electrocardiogram. Exclusion criteria's for magnesium therapy were serum creatinine > 2mg%, atrioventricular blocks of II and HI degree, diabetes mellitus and shock.

Methods

All patients of acute myocardial infarction who had symptoms of acute myocardial infarction less than 12 hours were included in the study. Immediately after admission samples of blood and urine were taken with special precautions. Serum magnesium is determined photometrically in tungstic acid and filtrate of serum by forming a red lake with titen yellow in alkaline solution. Colour formation is potentiated by polyvinyl alcohol.

After collection of samples standard dose of streptokinase were given to those patients who can afford it and if there is no contraindication for streptokinase, these patient were designated, Group I. Other patients were randomly divided into two therapeutic groups, Group IIand Group III**.** In group II, intravenous magnesium sulphate8 mmolstatthen 65 mmol infusion m 24 hours as maintenance dose were given. Group HI patients were given placebo therapy of isotonic saline 500cc for 24 hours. These patients were monitored clinically and by cardiac monitoring during first week and again reviewed up to 4 weeks regularly. Urinary magnesium estimation was done on the same day and 7th day. Serum magnesium was done on same day, 7th day and 15th day of admission.

Statistical Analysis

Serum and urinary magnesium were expressed as mean ± SD. Course and complication as morbidity and mortality of acute MI was compared with serum and urinary magnesium level and with mode of treatment i.e. TV magnesium therapy, streptokinase therapy and placebo by chi square test.

RESULTS

All the three groups were age and sex matched, mean age was 54.81±0.201, 54.18±0.220 and 55.27±0.192 years in magnesium, streptokinase and placebo treated groups respectively (Table 1).

The mean serum magnesium level was low in all study groups. At the time of admission serum magnesium was 1.89 ± 0.036 mg%, gradually it rose, at 7th day 2.11 ±0.055 mg% and day 15th 2.13 ± 0.066 mg% (mean ± SD) [11]. Likewise mean urinary magnesium levels were also low on day 1st and 7th which was 5.94 ± 0.34 mg% and 6.47 ± 0.34 mg% respectively in all three groups (Table 2).

When the serum magnesium and urinary magnesium level were compared among complicated myocardial infarction and uncomplicated myocardial infarction. The mean serum magnesium was 2.05 ± 0.026 in uncomplicated myocardial infarction while it was significantly low in complicated myocardial infarction i.e. 1.79 ± 0.028 ($p < 0.001$). In uncomplicated myocardial infarction the mean urinary magnesium level was 6.40 ± 0.124 while in complicated myocardial infarction it was 6.05 ± 0.031 that 15 again significantly low in complicated myocardial infarction ($p < 0.001$) (Table 3).

Similarly life threatening complications like cardiac arrhythmias were less in magnesium treated group i.e. 5 (17.8%), out of which 2 ventricular premature beats, 1 atrial premature beats and 2 I° atrioventricular block. In streptokinase group total II (39.28%) cardiac arrhythmias were present out of which 3 ventricular premature beats, 1 atrial premature beats, 1 ventricular fibrillation and 3 1° atrioventricular blocks, 2 III° anterioventricular blocks and 1 bifasicular block was present. In placebo group 11 (39.28%) cardiac arrhythmias were present out of which 5 ventricular premature beats, 1 atrial premature beats, 1 ventricular fibrillation, 3 1° atrioventricular block, 1 11° atreoventricular blocks were present (Fig. 1).

In our study we compared the each study group* in view of severity of pump failure according to Killip's classification. In magnesium treated group only 10 patients (35.7%) had clinical pump failure, whereas in streptokinase and placebo group, 16 and 15 patients (57% and 53.5%) were having pump failure. When we compared the severity of pump failure, in magnesium treated 18,8,1and 1 patient of Killip class I, n, EH,IV pump failure respectively while in streptokinase group 12,11,3and 2patient bf Killip class I, II, III, IV pump failure respectively, in placebo group 13,13and 2patient of Killip class I, II, IV pump failure respectively (Table 4,Fig. 2).

We also searched for the mortality in 4 weeks duration, it was in 2 patients (7.14%)in magnesium treated group and same number in streptokinase group while in placebo group it was 3 (10.71%)(Table 5).

DISCUSSION

The short term mortality is quite high in acute myocardial infarction. Various therapeutic options were tried to reduce the short term mortality and use of IV magnesium therapy may be a good option.

Magnesium and other electrolytes play a major role in genesis of acute complications e.g. post Acute Myocardial Infarction cardiac arrhythmias. Magnesium deficiency interferes with function of membranes ATPase of the cells and these cells cannot attract the potassium against transmembrane concentration gradient[12]. The number of arrhythmias were less in magnesium treated group (17.8%) than other two study groups (each had 39.28%).It could be because of higher Mg^{++} or correction of hypomagnesemia. As magnesium ions enter in cells, it decreases the calcium ions current 13 in cells, this turn decreases the sinus rate and prolong A.V. nodal refiactornness , or when IV. magnesium therapy given in patients of Acute Myocardial Infarction probably it inhibits post infarction hypomagnesemia[14] or caused balance of magnesium ions between inside and outside of cells.

In view of severity of pump failure, according to killip's classification magnesium treated group were having less number of pump failure i.e. 10 patient of Killip's class II to IV and 18 patients were not having any signs of pump failure that belongs to class I. In streptokinase treated group, 17 patients were having pumb failure (11,3 and 2 belongs to class II, IIIand IV respectively). 12 patients belongs to class I i.e. without any signs of pump failure. In placebo group total 15 patients were having pump failure, out of which 13 in class II and 2 in class IV, 13 patients were not having any signs of pump failure i.e. class I

Mortality rate was equal in magnesium and streptokinase treated group i.e. 2 in each group. Considering the cost of magnesium therapy. It can be a cost effective alternative to streptokinase therapy. It is very surprising that no death has been caused by arrhythmia in magnesium treated group. It further supports antiarrhythmic action of magnesium.

Killip's classes gives a clinical idea about size of infarction, so magnesium by reducing the infarct size, causes least number of heart failure in post infarction period. Possibly the magnesium reduces an infarct size by inhibiting calcium influx into ischemic myocardial cells and by increasing coronary perfusion, by the reducing the coronary artery tone, likewise magnesium also reduce the peripheral vascular resistance thus by reducing after load that reduce the cardiac work and decrease the oxygen demand of myocardium[1].

Killip's classification also have some correlation with expected mortality. Class IV patient have maximum mortality in early post infarctional period[15]

SUMMARY

Hypomagnesemia is a constant feature in myocardial infarction and it has been documented and supported by other studies as well. Intravenous magnesium therapy is definitely a cost effective alternative to streptokinase and in view of reducing mortality, as mortality was equal in streptokinase and magnesium treated group and it proves beyond doubt that magnesium having antiarrhythmic action, it supported by the facts that incidence of arrhytlimias were significantly less ($p < 0.001$).

Table 1 Age and Sex distribution of various groups

S.N.	Groups	Mean age in years	% of female	% of males
1.	Magnesium treated	54.81 ±0.201	10.7%	89.3%
2.	Streptokinase	54.18 ±0.220	7.1%	92.9%
3.	Placebo group	55.27 ±0.192	10.7%	89.3%

Table 2 Comparison of mean serum magnesium level among studied group

S. No.	Groups	Mean serum Mg level in (mg%)			Mean urinary Mg. level (mg%)	
		1st day	7th day	15th day	1st day	7th day
1.	Magnesium	1.93±0.20	2.15±0.166	2.18±0.181	6.29±1.37	6.80±1.12
2.	Streptokinase	1.86±0.20	2.14±0.20	2.17±0.182	5.61±0.756	6.50±0.763
3.	Placebo	1.88±0.14	2.05±0.12	2.06±0.09	5.94±0.964	6.12±0.86

Table 3 Comparison of Serum and Urinary Magnesium Level in Complicated and uncomplicated MI of three study groups

S. No.		Streptokinase Group			Magnesium treated group			Placebo Group		
		1st day	7th day	15th day	1st day	7th day	15th day	1st day	7th day	15th day
1.	Mean Serum magnesium level complicated AMI inmg%	1.80±0.175	2.05±0.184	2.11±0.214	1.89±0.079	2.15±0.048	2.22±0.30	1.80±0.161	2.02±0.112	2.04±0.028
2.	Mean serum magnesium level of uncomplicated MI in mg%	1.84±0.267	2.11±0.25	2.16±0.09	1.96±0.26	2.15±0.15	2.16±0.16	1.98±0.095	2.08±0.128	2.08±0.106
3.	Mean urinary magnesium level in complicated MI inmg%	5.531±0.2I	6.36±0.32		6.48±0.36	6.97±0.43		5.54±0.162	5.47±0.12	
4.	Mean urinary magnesium level in uncomplicated MI in mg%	5.63±0.83	6.71±0.97		6.30*1.55	6.89±1.19		6.65±0.848	6.70±0.795	

Table - 4 Comparison of number of patients of pump failure (Killipclases) amoung 3 groups

SN	Pump failure	Number of Patients in Magnesium treated group (%)	Number of Patients in Streptokinase group (%)	Number of Patients in Placebo Group (%)
1.	Killip Class I	18(64.28)	12(42.85)	13(46.42)
2.	Killip Class II	08(28.57)	11(42.85)	13(46.42)
3.	Killip class HI	01(3.57)	3(10.71)	-
4.	Killip class IV	01(3.57)	2(7.14)	2(7.14)
Total		28	28	28

Table 5 Comparison of number of morbidity and mortality among three groups

S. N.	Groups	Total No. of Cases	No. of Cases of uncomplicated AMI	No. of Cases of complicated AMI	No. of Mortality	Percentage mortality	Caused of Mortality
1.	Magnesium	28	15	13	2	7.14	I. Pump Failure II.Cardiogenic shock due to Acute M.R
2.	Streptokinase	28	09	19	2	7.14	I.Ventricular fibrillation II. Pump failure
3.	Placebo group	28	10	18	3	10.71	I.Pump failure II. Cardiogenic shock due to Acute M.R. III. Ventricular fibrillation
	Total	84	35	49	7	8.33	

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