A Study on Effects of Magnesium Sulphate Infusion in Preventing Cardiac Arrhythmia During Off Pump Beating Heart Coronary Artery Bypass Grafting (CABG) Surgery

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ABSTRACT

Objective: The objective of the present study was to see the effect of magnesium in preventing cardiac arrhythmias in patients undergoing coronary artery bypass grafting (CABG) surgery.

Methods: This study was carried out in the Department of Anesthesia, Analgesia and Intensive Care Medicine (Cardiac Anesthesia Wing) of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka who underwent CABG surgery under general anaesthesia. A total of 60 patients scheduled for CABG were consecutively selected and were randomly divided into study group and control group. Patients aged 35-70 years irrespective of sex, ASA grade I & II, NYHA functional class I & II and ejection fraction 35-65% were included in the study. The study group was treated by vecuronium, fentanyl and magnesium sulphate infusion, while the control group was treated by vecuronium and fentanyl infusion. The demographic variables, preoperative clinical characteristics, peroperative variables and haemodynamic findings were observed at different time intervals.

Results: The mean ages of the study and control groups were 51.0 ± 6.9 years and 53.8 ± 6.2 years respectively. Males demonstrated their predominance in both magnesium (83.3%) and control (76.7%) groups. The distribution of preoperative confounding factors like diabetes, previous MI, hypertension and ejection fraction were not statistically different between the study groups. Two-thirds (67.7%) of the patients in magnesium group and 53.3% in the control group required 3 grafts. Number of 4 grafts in magnesium and control groups was 20% and 30% respectively and that of 2 grafts was 13.3% and 16.7% respectively. In the study group, out of 30 patients, 3(10%) developed arrhythmia, while in the control group out of 30 patients, 5(16.7%) developed arrhythmia (p = 0.353). The haemodynamic parameters in patients receiving magnesium were more stable during the whole period of observation.

Conclusion: The findings of the study suggest that magnesium could reduce the development of arrhythmia to an acceptable level in patients undergoing beating heart CABG surgery. However, further study with large sample is recommended to achieve a conclusive remark.

Key words: Magnesium sulphate, off-pump, beating heart, coronary artery bypass grafting, cardiac arrythmia etc.

INTRODUCTION:

Among cardiac surgical diseases coronary artery disease is one of the leading causes of death in both developed and developing countries. Despite significant progress in nonsurgical management of coronary artery disease like stent technology and anticoagulant therapy (e.g. Clopidogrel, which has

improved the long-term patency after angioplasty), the usefulness of coronary artery bypass graft surgery has not reduced; rather it is gaining popularity day by day. Cardiac dysrhythmia is commonly seen after CABG surgery. The incidence of postoperative supraventricular arrhythmia has been reported to be 11-54% and the incidence of

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ventricular arrhythmia to be 2-13% in open heart bypass surgery. 1 Knowledge of aetiology & progression of arrhythmia may allow us to reduce the use of pharmacological and electrical procedures aimed at assuring normal sinus rhythm. Most antiarrhythmic medications currently used (beta-blockers and amiodarone) have some side effects. The decrease in the concentrations of ions such as potassium and magnesium is an important factor in most of the cases of arrhythmia that do not have organic causes.1 Identifying and detecting these ionic imbalances may protect the heart from side-effects of anti-arrhythmic drugs. Cardiac dysrhythmia potentially leads to complications, thromboembolic events, hemodynamic disorders, prolonged hospital stay and increased costs.2 It is not only a rhythm disturbance, but also quite a serious morbidity factor because of its complications and therefore, prophylaxis is very important.

Magnesium sulphate prevent the development of arrhythmia both intraoperatively & postoperatively.³ Magnesium is a cation, the serum level which is tightly regulated in a narrow range of approximately 0.7-1.0 mmol/L, for only 1% of the total body content of magnesium is extra cellular.⁴ When serum ionized magnesium level falls below 0.7 mmol/L, it is, although controversial, indicative of arrhythmia. As only 1% of the total body magnesium is extracellular, the value of measuring the serum levels has been questioned.⁵

The mechanism of action by which magnesium sulphate prevents arrhythmia is unclear. The oretically prolongation of the cardiac action potential by lengthening the refractory period at the atrioventricular mode could be achieved.1 Magnesium is a natural calcium blocker. 5 Alteration of intra and extra cellular magnesium concentration may affect cell function through their effect on calcium handling.4 Magnesium is essential for the replication and transcription of DNA, as well as cellular energy metabolism, membrane stabilization, nerve conduction and calcium channel function.5 This study was therefore, intended to find the efficacy of magnesium sulphate in preventing arrhythmia in patients undergoing beating heart CABG surgery.

METHODS:

The present cross-sectional study was carried out in Department of Anesthesia, Analgesia and Intensive Care Medicine (Cardiac Anesthesia Wing) of Bangabandhu Sheikh Mujib Medical University, Dhaka. over a period of 1 year from January 2009 to December 2009. Patients undergoing CABG surgery under general anaesthesia were the study population. Patients with age ranging between 35-70 years irrespective of sex, ASA grade I & II, NYHA functional class I & II and ejection fraction 35-65% were eligible for study. However, patients with severely impaired liver and kidney function, emergency operation and reoperation were excluded. A total of 60 patients were consecutively included in the study and were randomly allocated into the study and control groups. Patients of the study group were treated by vecuronium, fentanyl and magnesium sulphate infusion, while those of the control group were treated by vecuronium and fentanyl infusion.

All patients were examined pre-operatively, and were advised to take tab. Midazolam 7.5 mg at the night before operation. After entering into OT pre-oxygenation was done with face mask for 5-6 minutes with oxygen flow 5-6 L/min. Baseline blood pressure, heart rate, SPO2 all were recorded. Intravenous cannulation was done and an isotonic fluid started. Intraarterial cannulation was done usually at radial artery with 20G cannula and blood pressure was recorded. Induction was done by propofol 1-2.5 mg/kg IV, fentanyl 1-2 mg/kg & vecuroneum 0.08-0.1 mg/kg. Intubation was done 3 min after the administration of vecuroneum. Right internal jugular venous cannulation was done for monitoring the central venous pressure and administration of drugs. Temperature probe and urinary catheter were introduced subsequently. After intubation patients were kept on ventilator and intermittent positive pressure ventilation (IPPV) was started. Patients of both groups were then maintained with oxygen (O2) 50%, Nitrous Oxide (N2O) 50% and propofol infusion (200 mg propofol diluted in 100 ml normal saline & given IV at the rate of 20-25 micro-drop/min). Patients of study group were maintained with magnesium sulphate infusion

(2.47 gm Magnesium sulphate diluted in 100 ml normal saline and given through microbore at the rate of 20-25 micro- drop/min, i.e., 1.0-1.25 mg/kg/hr), Fentanyl infusion 0.4-0.5 mg/kg/hr, vecuroneum bromide infusion 0.04-0.05 mg/kg/hr. Patients of Control group were maintained with fentanyl & vecuroneum bromide infusion (without magnesium sulphate). Arterial blood gas (ABG) and electrolytes were measured every 15 minutes interval. Other causes of perioperative arrhythmia such as hypoxia, hypercarbia, electrolyte imbalance, etc. were corrected. Blood pressure, heart rate, CVP was maintained within acceptable range by adding ionotropes and vasodilator-ionotropes-Dopamine, adrenaline and noradrenaline, vasodilators-GTN. Arrhythmia was managed by several antiarrhythmic drugs such as-Lignocaine, Digoxin & Amiodarone (Cordarone). At the end of the operation all patients were transferred to Cardiac Intensive Care Unit (ICU) and were kept on ventilator. Patients were extubated in ICU when criteria of extubation fulfilled.

Collected data were entered into the computer program SPSS (Statistical Package for Social Science), version 11.5. Both descriptive and inferential statistics were used in data analysis. The descriptive statistics were frequency, mean and standard deviation from the mean (SD), while the inferential statistics were Chi-square (χ^2) Test, Fisher's Exact Test and Repeated Measure ANOVA. The level of significance was set at 0.05 and p < 0.05 was considered significant.

RESULTS:

Age distribution shows that half of the magnesium group was found to lie between 50-60 years followed by 36.7% below 50 years and 13.3% 60 or > 60 years. A similar age distribution was also found in the control group (p=0.636). Males demonstrated their predominance in both magnesium (90%) and control (93.3%) groups. The two groups did not differ in terms of sex distribution (p=0.613) (Table I). The use of calcium channel blockers was identical between groups (50% in each group). Over one-third (36.7%) of patients in Magnesium had a history of receiving beta-blockers compared to 16.7% in Control (p=0.080) (Table II). None of the

risk factors like diabetes, previous MI, hypertension and ejection fraction were found to be significantly different between the study groups (p=0.432, p =0.542, p=0.584 and p=0.143 respectively) (Table III). Classification of ischemic heart diseases by NYHA functional class demonstrates that class-I disease was 30% in Magnesium group and 53.3% in Control, while NYHA class-II was 70% in the former group and 46.7% in the latter group. The Chi-square (χ^2) test revealed that distribution of NYHA functional class between the study groups was statistically different (p=0.037) (Fig.1). Two-thirds (53.3%) of patients in the magnesium group and 53.3% in the control group required 3 grafts. Number of 4 grafts in magnesium and control groups was 20% and 30% respectively and that of 2 grafts was 13.3% and 16.7% respectively. The groups were not statistically different in terms of number of grafts (p=0.301) (Table IV). Three (10%) of 30 patients in magnesium group developed arrhythmia compared to 5(16.7%) patients in control group. Two-third (66.7%) of patients of magnesium group developed arrhythmia between 1-1.5 hours and 33.3% between 1.5-2 hours of initiation of operation, where as 80% of control group developed arrhythmia between 1-1.5 hours and 20% between 1.5-2 hours. Three patients in the magnesium group and 4 patients in the control group developed atrial fibrillation. All arrhythmiarelated variables were identical in the both groups (p > 0.05) (Table V). Table VI & Fig 2 shows the comparison of changes in systolic blood pressure at different time intervals. The mean systolic blood pressure of magnesium and control groups exhibited a sharp decrease from around 138 mmHg at baseline to about 110 mmHg and 105 mmHg respectively at 2 hours interval. It then again began to increase in the both groups reaching a mean blood pressure of 120.3 mmHg in the former group and 126.5 in the latter group at 4 hours intervals. Table VII & Fig 3 demonstrates the changes in diastolic blood pressure between groups. The mean diastolic blood pressure of magnesium group was 85.2 mmHg at baseline which gradually fell to 78.3 mmHg at 2 hours interval. The control group also experienced a similar decrease up to 2 hours. Then

both the groups assumed a sharp increase reaching 82.2 and 82.9 mmHg at 3 hours interval. At 4 hours interval the DBP was significantly less in the magnesium group than that in the control group (p=0.007). Table VIII depicts that the heart rate of control group increased from 74 bpm at baseline to 90 bpm at 1 hour. Then it declined up to 2.5 hours and again took a U-turn to reach 86 bpm at 4 hours interval. The heart rate of magnesium group experienced a sharp fall and rise from baseline to the end of observations. Table IX shows the comparison of changes in mean CVP at different time intervals. At baseline the mean CVP of magnesium group was 10 cm and that of control group was 11.9 cm of water. Then both groups experienced a fall and rise up to 4 hours of observation.

TABLE I. Comparison of demographic characteristics between two groups

Demographic	Group		
characteristics	Magnesium (n = 30)	Control (n = 30)	p-value
Age (years)			
<50	11(36.7)	8(26.7)	
50 – 60	15(50.0)	16(53.3)	0.636
≥ 60	4(13.3)	6(20.0)	
Mean ± SD	51.0 ± 6.9	53.8 ± 6.2	
Sex			
Male	27(90)	28(93.3)	p = 0.613
Female	3(10)	2(6.7)	

Figures in the parentheses indicate corresponding %; (χ^2) Test was employed to analyse the data.

TABLE II. Comparison of preoperative drugs used between two groups

Preoperative	Group		
drugs used	Magnesium (n = 30)	Control (n = 30)	p-value
Calcium channel			
Blocker #	15(50.0)	15(50.0)	0.897
Beta-blocker #	11(36.7)	5(16.7)	0.080

Figures in the parentheses denote corresponding **percentage**. # Chi-square (χ^2) Test was employed to analyse the data.

TABLE III. Comparison of preoperative characteristics between two groups

Preoperative	Group			
characteristics	Magnesium (n = 30)	Control (n = 30)	p-value	
Diabetes#	16(53.3)	19(63.3)	0.432	
Previous MI#	6(20.0)	8(26.7)	0.542	
Hypertension#	21(70.0)	19(63.3)	0.584	
Ejection fraction*	56.2 ± 8.5	53.5 ± 5.4	0.143	

Figures in the parentheses indicate corresponding percentage. **# Chi-square** (χ^2) **Test** was employed to analyze the data. *Data were analysed using **Student's t-Test** and were presented as **mean** \pm **SD**.

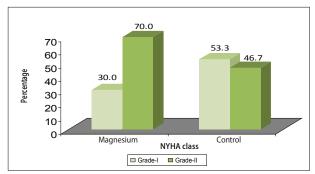


Fig. 1: Comparison of NYHA class between groups

TABLE IV. Number grafts used between two groups

No. of graft required	Gro	Group	
	Magnesium (n = 30)	Control (n = 30)	p-value
2	4(13.3)	5(16.7)	
3	20(67.7)	16(53.3)	0.421
4	6(20.0)	9(30.0)	

Figures in the parenthesis denote corresponding %; χ^2 **Test** was employed to analyse the data.

TABLE V. Comparison of arrhythmia profile between two groups

Arrhythmia	Group		
profiles	Magnesium (n = 30)	Control (n = 30)	p-value
Arrhythmia (developed) #	3(10.0)	5(16.7)	0.353 ^{NS}
Timing of arrhythmia develope	d*		
1 – 1.5 hours	2(66.7)	4(80.0)	
			0.673 ^{NS}
1.5 – 2 hours	1(33.3)	1(20.0)	
Type of arrhythmia*			
Supraventricular tachyca	rdia 00	1(20.0)	
			0.408 ^{NS}
Atrial fibrillation	3(100.0)	4(80.0)	

Fisher Exact Test was done to analyse the data; NS = Not significant *Chi-square (χ^2) Test was employed to analyse the data.

TABLE VI. Comparison of systolic BP between two groups

	Group		
Systolic BP#	Magnesium (n = 30)	Control (n = 30)	p-value
At baseline	138.4 ± 7.3	137.5 ± 8.1	0.665
At 30 minutes	131.1 ± 7.6	128.4 ± 7.2	0.170
At 1 hour	118.5 ± 9.4	115.9 ± 7.5	0.250
At 1.5 hour	111.5 ± 10.3	107.5 ± 5.1	0.060
At 2 hours	109.5 ± 9.5	105.3 ± 6.7	0.051
At 2.5 hours	110.6 ± 7.1	109.1 ± 8.9	0.485
At 3 hours	116.9 ± 10.2	119.3 ± 8.0	0.321
At 3.5 hours	115.5 ± 23.3	122.0 ± 7.9	0.157
At 4 hours	120.3 ± 10.7	126.5 ± 5.6	0.007

Data were analysed using Repeated Measure ANOVA & were presented as mean \pm SD.

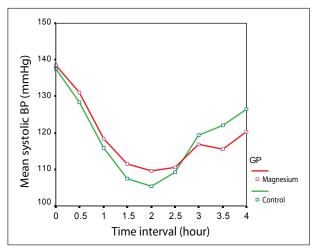


Fig 2. Monitoring of SBP at different time interval

TABLE VII. Comparison of diastolic BP between two groups

	Group		
Diastolic BP # (mmHg)	Magnesium (n = 30)	Control (n = 30)	p-value
At baseline	85.2 ± 4.5	82.9 ± 5.1	0.077
At 30 minutes	82.1 ± 3.0	81.9 ± 4.1	0.859
At 1 hour	78.5 ± 5.9	79.3 ± 4.1	0.545
At 1.5 hour	78.8 ± 4.6	78.1 ± 5.9	0.612
At 2 hours	78.3 ± 7.2	77.9 ± 6.8	0.841
At 2.5 hours	80.8 ± 4.7	80.0 ± 6.1	0.559
At 3 hours	82.2 ± 3.6	82.9 ± 2.9	0.413
At 3.5 hours	80.5 ± 6.6	83.7 ± 3.3	0.020
At 4 hours	80.5 ± 5.2	84.5 ± 3.2	0.001

Data were analysed using Repeated Measure ANOVA & were presented as mean \pm SD.

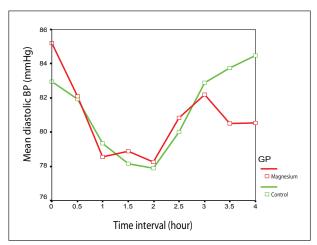


Fig 3. Monitoring of DBP at different time interval

TABLE VIII. Comparison of heart rate between two groups

Heart rate* (bpm)	Group		
	Magnesium (n = 30)	Control (n = 30)	p-value
At baseline	72 ± 4	74 ± 5	0.037
At 30 minutes	79 ± 14	85 ± 6	0.031
At 1 hour	87 ± 6	90 ± 5	0.013
At 1.5 hour	82 ± 5	85 ± 6	0.014
At 2 hours	80 ± 6	84 ± 5	0.002
At 2.5 hours	83 ± 6	83 ± 15	0.912
At 3 hours	88 ± 5	84 ± 5	0.005
At 3.5 hours	80 ± 5	85 ± 5	0.001
At 4 hours	82 ± 6	86 ± 6	0.025

Data were analysed using Repeated Measure ANOVA & were presented as mean \pm SD.

TABLE IX. Comparison of CVP between two groups

	Group		
CVP# (cm of water)	Magnesium (n = 30)	Control (n = 30)	p-value
At baseline	10.0 ± 0.2	11.9 ± 0.9	0.050
At 30 minutes	8.4 ± 0.7	7.7 ± 0.9	0.001
At 1 hour	4.9 ± 0.8	4.8 ± 0.8	0.636
At 1.5 hour	7.9 ± 0.8	7.7 ± 0.8	0.252
At 2 hours	8.9 ± 0.8	8.5 ± 0.9	0.109
At 2.5 hours	10.3 ± 0.7	8.8 ± 0.8	0.007
At 3 hours	8.3 ± 0.6	6.1 ± 0.7	< 0.001
At 3.5 hours	11.5 ± 0.6	9.7 ± 0.9	0.001
At 4 hours	12.0 ± 0.6	10.8 ± 1.0	0.001

Data were analysed using Repeated Measure ANOVA & were presented as mean \pm SD.

DISCUSSION:

Arrhythmia is not uncommon after coronary bypass grafting surgery (CABG). Publications as early as 1930s documented that magnesium deficiency can precipitate ventricular arrhythmias and that treatment with magnesium antiarrhythmic has potency on the supraventricular as well as ventricular level.6 Based on this concept, the present study was conducted to see whether peroperative magnesium infusion could reduce the incidence of arrhythmia in patients undergoing CABG surgery. present study all the baseline characteristics except NYHA functional class were almost identical between the study and the control groups. The NYHA class II subjects demonstrated their significant presence in the Magnesium group (70%) compared to that in the Control group (46.7%). Males were predominant in both the groups. Kaplan⁷ also reported a male predominance in either group. Toraman8 reported no difference in the use of preoperative calcium channel blocker use (p=0.420). Kaplan9 showed that there was no difference between the magnesium and control group in terms of preoperative use of beta-blockers (p=0.717) and calcium-channel blockers (p=0.661). None of the factors like diabetes, previous MI, hypertension and ejection fraction was found to be significantly different between groups. Kaplan⁷ also reported distribution of previous myocardial infarction, hypertension, diabetes mellitus in the magnesium and control group to be almost identical. Toraman⁸ found no significant difference in NYHA functional class between magnesium and control group. There was no difference between the groups in terms of number of grafts required.

All peroperative variables like development of arrhythmia, timing of arrhythmia and types arrhythmia encountered were almost similar in magnesium and control group (p > 0.05). Majority of the patients in both groups experienced atrial fibrillation. Three patients in the magnesium group and four patients in the control group developed atrial fibrillation. Only one patient in the control group exhibited supraventricular

tachycardia. Fanning¹⁰, Karmy-Jones associates¹¹ in a similar study did not find any significant differences between treatment and control groups in terms of incidence of atrial development. Kaplan⁷ fibrillation reported supraventricular tachycardia in magnesium and control group in 2% and 4% cases respectively and artrial fibrillation in 15% and 16% The reported respectively. incidence supraventricular arrhythmia ranges from 40-47%, wher eas ventricular arrhythmia was over 30%.12 There are reports suggesting that magnesium reduces the incidence of ventricular arrhythmia & supraventricular arrhythmias including atrial fibrillation. 13,14

Harris and associates¹⁵ found an incidence of arrhythmia of 22% after 16 mmol of magnesium chloride infusion, compared with 63% in control patients. The authors measured plasma and urine magnesium.² In another study administration of 2 gm of magnesium chloride after termination of CPB resulted in a reduction in the incidence of ventricular arrhythmia from 34 to 16%.1 This group first used ultra filterable magnesium as a reflection of ionized and chelated magnesium, thus excluding the protein-bound fraction. Casthely and colleagues¹⁶ administered four different regimens of magnesium sulfate during CPB and found that the highest magnesium regimen was associated with the least incidence of postoperative cardiac arrhythmia. In these studies, magnesium administration prevented ventricular, but not supraventricular, rhythm abnormalities. Other authors found a greater effect on supraventricular arrhythmia: Wistbacka¹⁷ demonstrated an incidence of AF in 24% of patients who received a high magnesium infusion regimen compared with 45% in patients receiving a low-magnesium regimen. Fanning¹⁰ demonstrated a decrease in the frequency of postoperative AF in magnesium- treated patients compared with placebo but found no difference in the incidence of ventricular arrhythmia. Balser¹⁸ demonstrated that small dose of postoperative magnesium supplementation reduced the incidence ventricular arrhythmia, but larger doses of magnesium were needed to prevent AF. Thus, the findings of the present study and those of other investigators discussed so far suggest that magnesium could reduce the incidence arrhythmia during peroperative period acceptable level in patients undergoing CABG. The systolic and diastolic blood pressures, heart rate and central venous pressures in patients receiving magnesium also did not go beyond normal range during the whole period of observation.

CONCLUSION:

The use of magnesium as an antiarrhythmic drug for extrasystole, supraventricular tachycardia and atrial fibrillation has been a matter of increasing interest and controversy over recent years. In view of the influence of magnesium on electrical stability and function of myocardial cells as well as the myocardium as a whole, the drug appears valuable in a wide array of arrhythmias. Arrhythmia developed after CABG surgery is a serious cause of morbidity. The incidence of arrhythmia could be lowered with magnesium supplement in Off-Pump Beating Heart CABG surgery. However, as the present study was carried out on a small sample, it is difficult to generalize the findings to the reference population. Further study with large sample is recommended to draw a generalizable conclusion.

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