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Prophylactic Magnesium and Rhythm Disorders after Open Cardiac Surgery

Abstract

Objective: To evaluate the effect of intravenous magnesium, on prevention of postoperative cardiac arrhythmias after open cardiac surgery.

Methodology: Prospective interventional study was conducted at Department Of Cardiac Surgery Punjab Institute Of Cardiology, Lahore from 1st August 2011 to 31st March 2012. Study groups included 260 consecutive patients undergoing CABG having normal sinus rhythm. They were classified as group I receiving magnesium supplementation perioperatively & group II not receiving magnesium supplementation. Intravenous Magnesium was administered before weaning from CPB and on 1st postoperative day. Twelve-lead electrocardiograms were obtained immediately after operation and daily until detection of new onset arrhythmias. The distribution of both groups in CABG patients was compared for rhythm disorders.

Results: The mean age of patients was 51.73±10.16 years. A total of 41 patients developed arrhythmias postoperatively. There was no mortality during the study in that specific group. Other analysis indicates there is an effect of intravenous Mg on the prevention of post cardiac arrhythmia after open heart surgery.

Conclusion: Prophylactic administration of intravenous magnesium is associated with low incidence of postoperative cardiac arrhythmias.

Keywords: Arrhythmias; Magnesium; CABG

Research Article

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Abbreviations: CABG: Coronary Artery Bypass Grafting; MVR: Mitral Valve Replacement; AVR: Aortic Valve Replacement; DVR: Double Valve Replacement; OPCAB: Off-Pump Coronary Artery Bypass Grafting; CPB: Cardiopulmonary Bypass, SPSS: Statistical Package for Social Science; RRR: Relative Risk Reduction

Introduction

Magnesium is the second most abundant intracellular cation, which stabilizes cell membrane function. It is secreted in urine in high amounts when there is elevation of adrenal hormones secondary to stress. This leads to decrease in Mg concentration in blood thus inducing stress at cell membrane level "magnesium vicious circle" that may lead to severe complications [1-3] including cardiac dysrhythmias especially supraventricular, atrial fibrillation, prolonged P-R and Q-T segments, even ventricular fibrillation [1]. Postoperative cardiac patients in ICU frequently develop dysrhythmias in first 48 hours after surgery. Majority of these dysrhythmias are controlled by timely electrical cardioversion or antiarrhythmic medications. But the medications are not without side-effects [2]. The aim of this study was to investigate the role of prophylactic intravenous magnesium injection on the development of postoperative cardiac dysrhythmias.

Materials and Methods

The prospective interventional study was performed at Department of Cardiac Surgery, Punjab Institute of Cardiology Lahore, Pakistan from August 2011 to March 2012. The sample was randomized in a unique way that the first and third authors were directly involved in surgical treatment of these patients. Cases were randomly assigned to each first assistant in the Department in the morning of daily operative list. None of the authors had any influence on the distribution of cases. Data of all 260 consecutive patients, who were undergoing coronary artery bypass grafting (CABG), Mitral valve replacement (MVR), Aortic valve replacement (AVR), or both AVR & MVR (DVR, the double valve replacement) all with cardiopulmonary bypass, and data from patients who underwent Off-pump coronary artery bypass grafting (OPCAB) was collected. All patients were in sinus rhythm at the time of operation. Patients undergoing redo and emergency CABG, renal insufficiency (serum creatinine greater than 1.5 mg/dl), asthma, chronic obstructive pulmonary disease, or a prior history of cardiac Dysrhythmias were excluded from the study. Echocardiography, coronary angiography, chest x-ray, biochemical and morphological blood analyses were performed. The preparation of the patients before the surgery, premedication, general anesthesia, cardiopulmonary bypass, cardioplegia, surgical technique, and the treatment after the surgery remained as per institutional standard for all patients. Patients were again randomly assigned to two groups. 1300 patients were given 1g of magnesium sulphate ($MgSO_4$) intravenously (iv) during CPB, before weaning, and on postoperative day 1 (Group A). Another group of 130 patients were taken as control group not received magnesium supplementation preoperatively (Group B). The patients operated on Mondays, Wednesdays and Saturdays received iv magnesium, while on rest of the days did not. Patients were continuously monitored in the intensive care unit with bedside monitors. Twelve-lead electrocardiograms were obtained immediately after the operation and also recorded daily for five days or until the onset of new cardiac arrhythmias, the end point of the study. Arrhythmia data were collected and recorded during the first 5 post-operative days. Atrial fibrillation was defined on ECG with no P waves, fibrillating chaotic F waves around baseline, R-R interval constantly varying, as did size of QRS complexes, atrial rate of 350-600, ventricular rate of 100-180 and

irregular. Supraventricular tachycardia had P waves likely to be abnormally shaped with PR interval possibly abnormal, usually regular rhythm, atrial rate of 100-250, while ventricular rate was variable depending on degree of ventricular capture. Ventricular tachycardia was defined as >3 ventricular extra systoles, with broad complexes in a row at >120 BPM. Ventricular fibrillation was broad complex ventricular dysrhythmia with a frequency of 400-600 per min and irregular rhythm with AV dissociation.

Data was analyzed by SPSS (Statistical Package for Social Sciences) Version 20.0 for Windows. Chi square test and Fisher exact test (if cell frequency was less than 5) was applied to observe the association of the qualitative variables with both groups while for quantitative variable independent t test was applied. Binary logistic regression was used to determine the influence of predictors on major adverse cardiac outcome (i.e. cardiac arrhythmia and mortality) after open heart surgery. Level of significance will be considered ≤5%. All tests applied were two tailed.

Results

In our study of 260 patients 179 were males while females were 81 in number. In this study there is no statistical significant difference between gender and groups (p =0.89), the mean age was 51.73±10.164. The sample characteristics for Group A & B are shown in Table 1, whereas the association of these two groups with different arrhythmias is shown in Table 2. The trend toward high post operative Atrial Fibrillation was found in group B as compare to group A (10.8% vs. 3.85%; P-value =0.032).

Table 1: Descriptive and inferential statistics of patient undergoing open heart surgery according to with and without prophylactic Magnesium.

Variables		Group A (Mg+)	Group B (Mg-)	P-value
		89 (68.5%)	90 (69.2%)	0.893
		41 (31.5%)	40 (38.8%)	
Diabetes		43 (31.1%)	33 (25.4%)	0.173
Hypertension		37 (28.5%)	27 (20.8%)	0.15
Obesity		32 (24.6%)	38 (29.2%)	0.402
Smoking		39 (30%)	38 (29.2%)	0.89
Ejection Fraction <40%		66 (50.8%)	62 (47.7%)	0.62
Procedure	CABG	102 (78.5%)	103	0.95
			-79.20%	
	OPCAB	4 (3.1%)	2 (1.5%)	
	MVR	5 (3.8%)	5 (3.8%)	
	AVR	12 (9.2%)	13 (10%)	
	DVR	7 (5.4%)	7 (5.4%)	
Cross Clamp Time >50min		30 (23.1%)	30 (23.1%)	1
Cardiopulmonary Bypass >70 Min		43 (33.1%)	45 (34.6%)	0.793
Left Internal Mammary Artery		89 (68.5%)	84 (65.1%)	0.568
Time On Ventilator >8 Hours		18 (13.8%)	16 (12.3%)	0.713
IABP		6 (4.6%)	6 (4.6%)	1
Mortality		1 (0.8%)	2 (1.5%)	1

Table 2: Association of iv Magnesium with postoperative Cardiac Arrhythmias.

Complications	Group A (Mg+) (n=130)	Group B(Mg-) (n=130)	P-value
Supra ventricular Tachycardia	6(4.6%)	11(8.5%)	0.21
Atrial Fibrillation	5(3.85%)	14(10.8%)	0.032
Ventricular Tachycardia	1 (0.8%)	3 (2.3%)	0.622
Ventricular Fibrillation	0 (0%)	2 (1.5)	0.498

The results show association (p=0.032) of Atrial Fibrillation with Intravenous Magnesium administration, by reduction in former's incidence. Logistic regression results indicate that, whose were older (age > 33 year) (OR:1.643,CI 95%:0.868-3011; P value = 0.127), hypertensive (OR:1.01,CI 95%:0.469-2.17; P value = 0.980), smokers (OR: 1.378, CI 95%:0.631-3.009; P value = 0.422), diabetes mellitus (OR: 1.279, CI 95%: 0.590-2.774; P value = 0.534) were independently predicting major adverse cardiac outcome development after open heart surgery procedures as shown in Table 3, while who were females, obese (BMI>30) and Left IMA were found to be lower risk to develop major adverse outcome.

Table 3: Logistic regression model for predicting the incidence of post operative outcome (i.e. cardiac arrhythmias and mortality) after open cardiac surgery.

Variable	Wald	Sig.	Exp(B)	95.0% C.I for EXP(B)	
				Lower	Upper
Sex (Male)	0.851	0.356	0.712	0.346	1.466
Diabetes Mellitus	0.387	0.534	1.279	0.590	2.774
Hypertension	0.001	0.980	1.010	0.469	2.174
Obesity	0.204	0.652	0.849	0.416	1.730
Smoking	0.646	0.422	1.378	0.631	3.009
Age	2.325	0.127	1.643	0.868	3.110
Left IMA	1.059	0.303	0.681	0.327	1.416
Constant	3.084	0.079	3.001		

Nagelkerke R^2 value in this study analysis was (0.19) which signify that factors in this study contributing (19%) to major adverse cardiac outcome. Other factors contributing to major adverse cardiac outcome in patients undergoing open heart surgery were not included in the study and the classification table shows that the test is (80.7%) correct.

The probability of the occurrence of post operative cardiac arrhythmias after open heart surgery was found to be less likely in intravenous group as compare to non-intravenous group as relative risk of SVT, AF, VT and VF were (0.68, 0.50, 0.50 and 0.0). (Note: because RR is <1). Relative risk reduction (RRR) indicate that iv Mg reduces the risk of SVT (33%), AF (50%), VT (50%) and VF (100%), suggests that Prophylactic Intravenous (iv) Magnesium Administration is better than no administration at all. Note calculated by (1-Relative Risk* 100).

Discussion

Magnesium has a major influence on myocardial tissues. It

plays an essential role in the maintenance of resting membrane potential by inhibiting outward flow of potassium and influx of calcium. Magnesium deficiency can impair cardiac conduction, increase the risk for arrhythmias, predispose to coronary artery spasm, and contribute to neurological irritability [1,2]. Magnesium also has been shown to reduce platelet aggregation, inhibit catecholamine release associated with stress, and reduce systemic and coronary vascular resistance [3,4].

Arrhythmias following cardiac surgery are still a difficult complication to treat. A variety of genetic defects in magnesium transport are associated with cardiovascular disease. Magnesium appears to be important in arrhythmia prophylaxis after heart surgery in adults and may contribute to improved cardiac contractile indices after cardiopulmonary bypass (CPB) [5,6]. It is well known that hypomagnesaemia results in different forms of cardiac arrhythmias. Atrial fibrillation is one of the most spectacular events in patients after cardiopulmonary bypass [7-13].

Many authors have described the intravenous Mg infusion as a good method to correct hypomagnesaemia [10,14-16]. Fanning et al. [17] reported that the infusion of magnesium sulphate at the dose of 84 mmol/96 h reduced AF from 28% to 14.3% [17]; however, the decline was not statistically significant. Likewise, Jensen et al. [18] demonstrated a non-statistical reduction in AF in patients treated with an infusion of 110 mmol Mg per 80 h [18]. In contrast, Nurozler et al. [19] demonstrated a significant reduction in AF (from 20% to 4%) during the infusion of Mg for 5 days (100 mmol/5 days) [19]. Speziale et al. [20] noted a complete elimination of AF in patients who received 1g of Mg in pump priming solution and the infusion of 10 mmol of $MgSO_4$ for the first 24 postoperative hours [20]. According to them such an administration kept the serum Mg concentration at an unchanged level during CPB and in the early postoperative period. In our study 1G of Magnesium was administered at the commencement of CPB and then another 1G single bolus dose on first postoperative day. We have found that the only significant affect was seen on the incidence of atrial fibrillation. Other types of tachyarrhythmias did not show any statistically significant response to prophylactic Magnesium administration by our method of administering Mg.

Although the meta analysis by Miller et al. [21] concluded that prophylactic administration of Mg is effective for prevention of AF after CABG, only 5 of the 20 studies included in the analysis were clearly in favor of Mg administration, with 7 studies showing no reduction in AF with Mg prophylaxis. We agree with his conclusion as our study also showed a clear reduction in incidence of postoperative atrial fibrillation with prophylactic intravenous magnesium administration.

De Oliveria et al. [22] suggested no association between the total dose of magnesium administration and the incidence of supraventricular arrhythmias ($p = 0.19$), also showed no effect of magnesium on the incidence of postoperative stroke, myocardial infarction, and death. In addition, magnesium did not reduce the hospital or intensive care unit lengths of stay (all $p > 0.05$). He concluded that the effect of magnesium sulfate in reducing postoperative supraventricular arrhythmias was significant when examined by lower-quality studies but not when examined by higher-quality studies. Even though De Oliveria et al. [22] showed association of supra ventricular tachycardia and mortality, in our study we found insignificant relation of Magnesium level with mortality. The relation with supra ventricular tachycardia was found to be similar to study by De Oliveria et al. [22].

Though magnesium therapy is indicated in life-threatening ventricular arrhythmias such as Torsades de Pointes and intractable ventricular tachycardia, our study has found only trivial association of intravenous magnesium prophylaxis with prevention of Ventricular tachyarrhythmias [23]. Results of Kiziltepe et al. [24] showed that Magnesium sulfate is an effective and safe antiarrhythmic agent for arrhythmias developed after open-heart surgery. Its antiarrhythmic effect suggested due to its pharmacological properties and unrelated to normalization of the circulating magnesium concentrations. They recommend its use as a first line antiarrhythmic agent without even routine measurement of blood levels [24].

Conclusion

In according to the findings of our study, prophylactic administration of 1G of Magnesium at commencement of CPB and within the first 24 hours has a beneficial effect on the incidence of AF. Supraventricular tachycardia may not be prevented by this method. It is further concluded that a larger prospective randomized trial is required to finally implement this treatment prophylactically.

Limitations

A Potential confounding factor in our study was the use of Magnesium (Mg) both in the cardioplegia and in the ICU. In the case of cardioplegia, the addition of Mg is the standard of care at our institution. The decision was made to allow for use of Mg in the ICU because serum Mg levels are routinely checked in the ICU, and doctors in ICU become uncomfortable with leaving hypo magnesemia untreated. However, adjustment for such a usage did not alter the relationship between treatment and the development of Arrhythmias.

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