ORIGINAL ARTICLE J. Med. Sci. (Peshawar, Print) April 2013, Vol. 21, No. 2: 77-80

INTRAVENOUS MAGNESIUM PREVENTS ATRIAL FIBRILLATION AFTER VALVULAR HEART SURGERY

Nasreen Laiq[1], Riaz Anwar Khan[2], Abdul Mailk[2], Hamid Ahmad[2]

[1]Department of Cardiothoracic Anaesthesia, Postgraduate Medical Institute, Lady Reading Hospital, Peshawar - Pakistan

2 Department of Cardiovascular Postgraduate Medical Institute, Lady Reading Hospital, Peshawar - Pakistan

ABSTRACT

Objective: To evaluate the effectiveness of prophylactic magnesium sulfate in the prophylaxis of atrial fibrillation.

Materials and Methods: It was a prospective randomized placebo-controlled trial in 100 consecutive patients who were scheduled to undergo elective cardiac valvular surgery and had provided informed written consent, were studied from January 2007 to January 2009 at Cardiothoracic Anaesthesia Department of Post Graduate Medical Institute, Lady Reading Hospital, Peshawar. Operations and management of atrial fibrillations were performed by the same surgical team.

Results: In the treatment group (n = 50) 32 (64%) of the patients were women and 18 (36%) were men, the average age was 36 ± 12.9 years (range 20-60 years). The control group consisted of 20 (40%) men and 30 (60%) women, mean age 40 ± 11.35 SD years, age (range 20-60 years). Data collected were the number of patients, preoperative patient characteristics, magnesium sulphate level and length of stay (LOS) in ICU and in the hospital. LOS in ICU as well as in the ward were significantly long in our control group compared to treatment group i-e 20% in magnesium group and 40% in control group. The rest of data were significantly not different in both of our studied groups. Blood magnesium sulfate levels in both groups were not significantly different in Preoperative, perioperative, and postoperative patients. Frequency of atrial fibrillation (AF) in the treatment group was significantly lower (P = 0.05) compare to control group. No mortality was recorded in our studied groups.

Conclusion: Magnesium provides good pre,intra and postoperative control of arrythmias, without any significant adverse effects,therefore it should be encouraged in open heart surgeries.

Key Words: Magnesium sulfate, Arrythmias, valvular, Heartsurgery.

INTRODUCTION

Atrial fibrillation (AF) is a common complication after cardiac surgery, its frequency ranges between 25-40% reaching upto 50% following open heart surgery as reported in previous studies[1,2]. Several reports have indicated that postoperative AF is associated with significantly increased morbidity and mortality[3].

Risk factors of postsurgical AF could be divided into: preoperative, intra-operative and postoperative. Preoperative factors mainly include: Atrial tissue damages due to age[4], Heart diseases, electrolytic imbalance such as hypokalemia, hypomagnesemia, hypothyroidism, preoperative use of digoxin or milrinone[5,6,7]. Finally obesity and male gender may also predispose to AF[7]. Intra-operative risk factors could be attributed to increased sympathetic activation due to stimulation of catecholamines, reflex sympathetic activation from volume loss, anaemia, pain, adrenergic drug administration and extracorporeal circulation[8]. Postoperative AF may be correlated with hemodynamic deterioration (myocardial infarction, heart failure, thromboembolism, bleeding due to anticoagulation), stroke, hypomagnesemia[9] and others as increase in postoperative P-wave dispersion[10] and exaggerated inflammation reaction[4,11]. It has been reported that postoperative atrial fibrillation can occur at any time during the entire postoperative course, but especially between the 2nd and 5th postoperative days[12].

As Hypomagnesemia is one of the most common cause of AF and is common following cardiac surgery because the initiation of extracorporeal circulation during surgery may dilute the circulating blood volume, and because the use of diuretics during and after surgery may promote urinary excretion of magnesium[8]. There are many pharmacologic agents to prevent postoperative atrial fibrillation(POAF) but none of them are effective for all patients nor free of complications[13]. Magnesium

Address for Correspondence:
Dr. Nasreen Laiq
Department of Cardiothoracic Anaesthesia,
Postgraduate Medical Institute, Lady Reading Hospital,
Peshawar - Pakistan
Cell: +92333-9590610
Email: nasreenlaiq@yahoo.com

exerts its antiarrhythmic effects in part by inhibiting L-type calcium channels which reduces sinus node rate firing, prolongs atrioventricular conductance, and increases atrioventricular node refractoriness and promotes inward entry of potassium through potassium channels in the cardiac action potential[14,15,16]. The combination of the treatment effects of correcting magnesium depletion and of increasing atrial refractoriness caused by magnesium administration is probably responsible for the overall beneficial effect of magnesium.

MATERIAL AND METHOD

After Institutional research and ethical board (IREB) approval, 100 patients who were scheduled to undergo elective cardiac valvular surgery and had provided informed written consent were studied from January 2007 to January 2009 at Postgraduate Medical Institute, Lady Reading Hospital, Peshawar.

Fifty patients were enrolled into either of two groups in a randomized study: group M (n = 50) received magnesium sulfate, while group S (n = 50) received normal saline. The sequence of administration of placebo or magnesium sulfate was randomized and the sequence of randomization was concealed using sequentially numbered envelopes provided by an independent investigator. Studies were included only if they met all of the following criteria. The primary outcome measure was the incidence of postoperative AF or atrial flutter. Two other outcome measures,length of stay (LOS) in ICU and in ward were also analyzed. Exclusion criteria included history of atrial fibrillation, history of paroxysmal atrial fibrillation even if the patient was in sinus rhythm just before the operation, preoperative heart rate of less than 50 beats/min, redo surgery, blood pressure of less than 100 mm Hg, history of renal failure (serum creatinine level > 2.0 mg/dL), and severe respiratory function disorder.

Patients were anesthetized with a standard technique including propofol 1-2 mg/kg, morphine 0.1mg/kg, and pancuronium 0.1 mg/kg to facilitate tracheal intubation. Anesthesia was maintained with sevoflurane 2% in 60% oxygen/air mixture together with incremental boluses of pancuronium 1 mg when required. Patients were monitored by five-lead ECG, pulse oximetry, central venous line, invasive arterial blood pressure, capnography, urine output, serial blood gas analysis to monitor oxygenation, ventilation, acid-base balance, and electrolytes including potassium and magnesium. Group 'M' received magnesium sulfate 40 mg /kg in 100 ml 0.9% saline in 30 min preoperatively while S group received normal saline. As the incidence of AF varies between 10 and 42% and depends on the type of surgery, surgical technique, and management, we elected to determine its incidence in our center utilizing same resources, surgical technique, surgical team and management to exclude any confounding factors.

Group 'M' received a magnesium sulfate infusion in a dose of 40 mg/kg in 30 min intraoperatively. Atrial fibrillation was diagnosed on a 5-lead electrocardiogram (ECG). Postoperativly first sample for arterial blood gas analysis was obtained just after arrival in the ICU to check for oxygenation, ventilation, acid-base disturbance and any electrolyte disturbance. Serial samples were then taken regularly every 4 h and as needed. Atrial fibrillation was monitored during the ICU stay through routine hemodynamic monitoring including heart rate and blood pressure as well as daily ECG. Additional ECG was done if the patient complained of palpitation or in the presence of an irregular pulse. Treatment group patients were extubated whenever they fullfiled the extubation criteria (patient should be fully awake, haemodynamically stable, response to vocal commonds, can lift head, regained full muscle strength and breath spontaneously with acceptable oxygenation and ventilation).

Potassium and magnesium supplementation was provided when hypokalemia and hypomagnesemia were diagnosed. In addition the side effects of both drugs were also assessed. After discharge from the ICU, daily ECG and serial blood gas analysis was continuously monitored during the postoperative period and any electrolyte disturbance such as hypokalemia or hypomagnesemia was vigorously corrected during his or her stay in the ward. Onset of atrial fibrillation was considered as sufficient criteria for the initiation of treatment. Amiodarone or β-blocker was used in case of resistant arrythmias. Calculations were done using the SPSS, software package, version 17. The students 't' test was performed to compare two data. P values of 0.05 or < 0.05 were considered statistically significant.

RESULTS

In the treatment group (n = 50), 32 (64%) of the patients were women and 18 (36%) were men, the average age was 36 ± 12.9 SD years (range 20-60 years). The control group also consisted of 50 patients 20 (40%) men and 30 (60%) women, mean age 40 ± 11.35 years, age (range 20-60 years). All patients underwent elective valve replacement surgery. They all had sinus rhythm preoperatively. Data collected were the number of patients, preoperative patient characteristics, Preoperative, perioperative, and postoperative plasma magnesium sulfate levels of patients, frequency of AF in the treatment and control groups and LOS in ICU and in the hospital of both studied groups are summarized in Table 1.

Blood magnesium sulfate levels were measured 12 hours before the operation, 1 hour after the operation and at the first, second, and third postoperative days normal limits of magnesium sulfate level were considered to be 1.8 to 2.5 mg/dL. Potassium replacement was routinely done to keep potassium levels between 4.0 and 5.0 mmol/L to

Table 1: Comparison of magnesium level, frequency of AF, and LOS in ICU in two groups

	Magnesium sulfate (n=50)	Control (n=50)	P value
Preoperative (Mg level) mg/dL	1.76 ± 0.21	1.66 ± 0.023	0.464 (NS)
Perioperative, (Mg level)	2.50 ± 0.25	1.79 ± 0.10	0.471 (NS)
First postop day(Mg level)	2.6 ±0.096	1.80 ±0.044	0.658 (NS)
Second postop day (Mg level)	2.64 ± 0.24	1.83 ± 0.10	1.210 (NS)
Third postop day (Mg level)	2.50 ± 0.26	2.52 ± 0.08	0.083 (NS)
Frequency of AF	10 (20%)	20 (40%)	0.05 (significant)
ICU stay (h)	48 ± 4.4	60.8 ± 2.89	0.038 (significant)
Hospital stay (days)	6.2 ± 1.03	8.1 ± 0.99	0.002 (significant)

prevent electrolyte imbalance. There was no difference between groups in terms of timing of extubation,only two patients in our saline group showed resistant arrthymias,which were treated with amiodarone infusion @ 500ug/kg for two days. No mortality was recorded in our studied groups.

DISCUSSION

The incidence of Atrial fibrillation is higher in patients who have valvular surgery alone or combined with coronary artery bypass. Our study showed significant difference (P = 0.05) regarding frequency of AF in two groups, frequency of atrial fibrillation was decreased from 40% in control group to 20% in magnesium group. Our study was comparable to previous studies done by Miller et al[18] in one of their meta-analysis and Rasmussen et al[19] who found that magnesium sulfate prophylaxis provided a decrease from 47% to 21% in all arrhythmias. Similarly Maslow and colleagues[20] reported that intraoperative administration of magnesium sulfate decreased the incidence of postoperative atrial tachyarrhythmia. We started magnesium preoperatively and found very good control of fibrillation in M group. As indicated from previous studies preoperative administration of magnesium was more effective in prevention of postoperative AF then intraoperative or postoperative prevention, mortality and LOS were not affected significantly[2]. Drug intervention was done preoperatively through intravenous route instead of the oral route to attain a rapid and effective results in our treatment group.One problem with the use of antiarrhythmic agents (β-blockers,calcium channel blockers, amiodarone etc) to prevent postoperative AF is that the majority of patients are exposed to drugs for which there is no actual need. However, its administration alone is not sufficient for the prophylaxis of atrial fibrillation, other causes for atrial fibrillation must be excluded and treated. The reason for selecting magnesium in our study was to avoid unnecessary side effects of other antiarrythmics.

Individual studies have shown that a high dose of magnesium was significantly more effective than a low dose in preventing AF[21]. Examination of the dose-response effect of magnesium on the prevention of arrhythmias may be necessary. Abraham et al[22] reported that administration of a single dose of 2.4 g of magnesium sulfate during the early phase of acute myocardial infarction decreased ventricular arrhythmia incidence from 34.8% to 14.6%. We used a dose of 40 mg/kg preoperatively which is considered a high dose and got very promising results in our studied group.

Demographic bias for example in one study showed that patients in the magnesium group had a higher ratio of male gender (98% versus 86% *P* = 0.02). This characteristic male gender has been consistently a risk factor for the development of Post Operative Atrial Fibrillation POAF, most of our patients in both groups were female but there was no significant difference regarding sex in both treatment groups. Mean duration of hospitalization after atrial fibrillation extended the duration of hospitalization in some studies[23]. We observed significantly prolonged stay in ICU as well as in ward in our control group compared to treatment group.(P<0.05).

Mathew et al[24] demonstrated that atrial fibrillation is a major predictor of longer hospitalization, atrial fibrillation which develops early after open heart surgery is a serious cause of morbidity and extends the duration of hospitalization. Thus prevention of atrial fibrillation would not only provide physiologic and hemodynamic benefits but will also cause cost savings.No mortality was seen in our studied groups.

CONCLUSION

Magnesium provides good pre, intra and postoperative control of arrhythmias without any significant adverse effects, therefore it should be encouraged in open heart surgeries.

REFERENCES

1. Forlani S, De Paulis R, Notaris DS, Nardi P, Tomai F, Proietti I, et al.Combination of sotalol and magnesium prevents atrial fibrillation after coronary artery bypass grafting. Ann Thorac Surg. 2002; 74: 720-26.
2. Maisel WH, Rawn JD, Stevenson WG. Atrial fibrillation after cardiac surgery. Ann Intern Med. 2001; 135: 1061-73.
3. Vaporciyan AA, Correa AM, Rice DC, Roth JA, Smythe WR, Swisher SG. Risk factors associated with atrial fibrillation after noncardiac thoracic surgery: analysis of 2588 patients. J Thorac Cardiovasc Surg. 2004; 95: 537-43.
4. Solomon AJ, Berger AK, Trivedi KK, Hannan RL, Katz NM. The combination of propranolol and magnesium does not prevent postoperative atrial fibrillation. Ann Thorac Surg. 2000; 69: 126-29.
5. Hazelrigg SR, Boley TM, Cetindag IB. The efficacy of supplemental magnesium in reducing atrial fibrillation after coronary artery bypass grafting Ann Thorac Surg 2004; 77: 824-30.
6. Booth JV, Phillips-Bute B, McCants CB. Low serum magnesium level predicts major adverse cardiac events after coronary artery bypass graft surgery Am Heart J 2003; 145: 1108-13.
7. Treggiari-Venzi MM, Waeber JL, Perneger TV, Suter PM, Adamec R, Romand JA. Intravenous amiodarone or magnesium sulphate is not cost-beneficial prophylaxis for atrial fibrillation after coronary artery bypass surgery Br J Anaesth 2000; 85: 690-95.
8. Geertman H, van der Starre PJA, Sie HT, Beukema WP, van Rooyen-Butijn M. Magnesium in addition to sotalol does not influence the incidence of postoperative atrial tachyarrhythmias after coronary artery bypass surgery J Cardiothorac Vasc Anes 2004; 18: 309-12.
9. Toraman F, Karabulut EH, Alhan HC, Dagdelen S, Tarcan S. Magnesium infusion dramatically decreases the incidence of atrial fibrillation after coronary artery bypass grafting Ann Thorac Surg 2001; 72: 1256-62.
10. Sparicio D, Landoni G, Cerchierini E, et al. A randomized controlled trial on high dose magnesium supplementation to prevent atrial fibrillation after off pump CABG Minerva Anestesiol 2004; 70: 532-33.
11. Wilkes NJ, Mallett SV, Peachey T, Di Salvo C, Walesby R. Correction of ionized plasma magnesium during cardiopulmonary bypass reduces the risk of postoperative cardiac arrhythmia Anesth Analg 2002 ; 95: 828-34.
12. Chelazzi C, Villa G, De Gaudio AR. Postoperative atrial fibrillation. ISRN Cardiol. 2011; 20: 317-19.
13. Ho KM, Lewis JP. Prevention of atrial fibrillation in cardiac surgery: time to consider a multimodality pharmacological approach. Cardiovasc Ther. 2010; 8: 59-65.
14. Christiansen EH, Frost L, Andreasen F. Dose-related cardiac electrophysiological effects of intravenous magnesium: a double-blind placebo-controlled dose-response study in patients with paroxysmal supraventricular tachycardia. Europace 2000; 2: 320-6.
15. Speziale G, Ruvolo G, Fattouch K, Macrina F, Tonelli E, Donnetti M, et al. Arrhythmia prophylaxis after coronary artery bypass grafting: regimens of magnesium sulfate administration. Thorac Cardiovasc Surg. 2000; 48: 22-26.
16. Bert AA, Reinert SE, Singh AK. A beta-blocker, not magnesium, is effective prophylaxis for atrial tachyarrhythmias after coronary artery bypass graft surgery. J Cardiothorac Vasc Anesth. 2001; 15: 204-09.
17. Klevay LM, Milne DB. Low dietary magnesium increases supraventricular ectopy. Am J Clin Nutr 2002; 75: 550-54.
18. Miller S, Crystal IE, Garfinkle IM, Lau IC, Lashevsky II,Connolly ISJ. Effects of magnesium on atrial fibrillation after cardiac surgery: a meta-analysis. Heart. 2005 May; 91(5): 618-23.
19. Rasmussen HS, McNair P, Norregard P, Becker V, Lindeneg O, Balslev S. Intravenous magnesium in acute myocardial infarction. Lancet. 1986; 1: 234-36.
20. Maslow AD, Regan MM, Heindle S, Panzica P, Cohn WE, Johnson RG. Postoperative atrial tachyarrhythmias in patients undergoing coronary artery bypass graft surgery without cardiopulmonary bypass: a role for intraoperative magnesium supplementation. J Cardiothorac Vasc Anesth. 2000; 14: 524-30.
21. Wistbacka JO, Koistinen J, Karlqvist KE. Magnesium substitution in elective coronary artery surgery: a double-blind clinical study. J Cardiothorac Vasc Anesth 1995 ; 9 : 140-46.
22. Abraham AS, Rosenmann D, Kramer M, Balkin J, Zion MM, Farbstien. Magnesium in the prevention of lethal arrhythmias in acute myocardial infarction. Ann Intern Med. 1987; 147: 753-55.
23. Hamid M, Kamal RS, Sami SA, Atiq F, Shafquat A, Naqvi HI. Effect of single dose magnesium on arrhythmias in patients undergoing coronary artery bypass surgery. J Pak Med Assoc. 2008; 58: 22-27.
24. Mathew JP, Fontes ML, Tudor IC. A multicenter risk for atrial fibrillation after cardiac surgery JAMA 2004; 291: 1720-29.