ROLE OF MAGNESIUM IN PREVENTING POST-OPERATIVE ATRIAL FIBRILLATION AFTER CORONARY ARTERY BYPASS SURGERY

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Objective: To assess the role of 3 days of magnesium infusion after coronary artery bypass graft (CABG) surgery in preventing postoperative atrial fibrillation (AF). **Place and Duration of Study:** Armed Forces Institute of Cardiology (AFIC) & National Institute of Heart Diseases (NIHD), Rawalpindi, from July 2006 to June 2007. **Design:** Prospective, randomized, non-blinded. **Methods:** All patients undergoing isolated, initial CABG surgery, and having sinus rhythm before surgery were alternatively randomized into the study or the control group. The exclusion criteria included: history of AF, implanted pacemaker, myocardial infarction postoperatively, use of left ventricular assist devices and renal failure. The patients in the study group received 10 mmol of magnesium sulphate (2.47 gm) dissolved in 100 ml of saline solution infused intravenously over 4 hours, for 3 days. The end point was development of AF for at least 15 minutes or more, or if an episode of AF had to be treated because of symptoms. **Results:** A total of 220 patients were included in the study, 110 in each group. The incidence of AF was 9% in patients who received the three days of magnesium infusion. The patients without magnesium had an AF incidence of 23% ($p<0.001$). The hospital stay was also less in the treated group ($p=0.055$). **Conclusion:** A 3-days postoperative infusion of magnesium is safe and effective in reduction of possibly life-threatening AF, in patients undergoing primary coronary artery bypass surgery.

Keywords: Coronary artery bypass surgery; Postoperative Atrial fibrillation; Magnesium.

INTRODUCTION

After coronary artery bypass grafting surgery (CABG), the postoperative stay in the intensive care unit (ICU) is often complicated by atrial fibrillation (AF) in up to 40% of cases.[1] This type of AF, although may start immediately after surgery, usually becomes prominent on the second or third postoperative day, when the patient is most vulnerable.[2,3] AF at this time leads to prolonged occupation of precious intensive care beds, and apprehension for the surgeons and intensivists on account of its effect on haemodynamics, with an increased risk of thromboembolism.[2,4,5]

In spite of vigorous research, the aetiology of postoperative AF still evades us,[6] the cause probably being multifactorial. Magnesium has been shown to be effective in reducing the incidence of AF in these patients.[7] It may have this effect by inhibiting L-type calcium channels, which may in turn reduce sinus firing and increase AV node refractoriness.[8] However, a number of other theories are also quoted.[6]

In 2006, 571 CABG surgeries were performed in AFIC.[9] In spite of the fact that two local studies have shown that AF is the commonest arrhythmia after CABG (up to 13.3%), the use of magnesium in our cardiac surgery units does not conform to any set protocols, with varying doses and schedules.[10,11] Internationally, also, a number of different protocols are followed.[6] The objective of this study was to assess the efficacy of three days postoperative infusion of low dose magnesium in reducing postoperative AF in our patients.

PATIENTS AND METHODS

This was a prospective, randomised, controlled, non-blinded study conducted in the surgical intensive care unit (ICU) of AFIC, Rawalpindi. The study was for one year commencing in July 2006. All patients undergoing isolated, initial CABG, and having sinus rhythm before surgery were alternatively randomised into the study group or the control group.

A number of exclusion criteria had to be incorporated because of their bearing on the outcome.[6] These were patients with: previous history of AF or other arrhythmias, implanted pacemakers, those suffering myocardial infarction postoperatively or patients who needed left ventricular assist devices.[6] Patients in renal failure or on haemodialysis were also excluded.

The patients in the study group received 10 mmol of magnesium sulphate (2.47 gm). Five ampoules of 500 mg of magnesium sulphate were dissolved in 100 ml of saline solution infused intravenously over 4 hours, once daily for 3 days starting when the patient was shifted to ICU.

The anaesthesia and surgical procedures were standardised for all patients. Same medical staff was involved in the anaesthesia, surgery and postoperative care of these patients. Preoperative clinical information and patients demographics were recorded to ensure that the two groups were grossly similar. Besides the routine variables like age and sex, other more specific variables were also recorded; like left ventricular ejection fraction, number of diseased vessels, their NYHA (New York Heart

Association) grades and stay in the ICU after surgery. Any side effects attributed to magnesium were also noted (bradycardia, hypotension, respiratory depression).

The logical end point of this study was development of AF after surgery. Based on previous studies, this was considered significant if it continued for at least 15 minutes or more, or if an episode of AF had to be treated because of symptoms or haemodynamic instability.[6]

The data was recorded on a performa and analysed using SPSS-12. The results are presented as Mean±SD or percent of patients. For proportions, Pearson test or Fisher's test is used. Student's *t*-test being used for quantitative variables. A *p*-value of <0.05 is considered to show statistical significance and <0.1 to show a definite trend.

RESULTS

There were a total of 220 patients who fulfilled the criteria and were included in the study, 110 in each group. In this study the incidence of AF was 9% in patients who received the three days of magnesium infusion. In contrast the patients without magnesium had an overall incidence of 23% ($p<0.001$). However, no difference was noticed regarding age, sex, number of diseased vessels, ejection fraction and NYHA grades, among the two groups. The hospital stay was less in the treated group showing a definite trend, but not significance ($p=0.055$), (Table-1).

In 2 patients of the treatment group, the magnesium was discontinued on the second day because of severe and unexplained bradycardia, thus making the number in this group to be 108.

Table-1: Details of demographics of the two groups

Variable	Magnesium n=108	Control n=110	*p*-value
Age (years)	62.1±9.9	63.0±8.9	$p>0.05$ NS
Male Sex	98 (91%)	102 (92.7%)	$p>0.05$ NS
Number of vessels			
- Single	7 (6.5%)	7 (6.2%)	
- Two	11 (10.3%)	12 (10.9%)	NS
- Three	66 (61.1%)	67 (61.0%)	
- Four	23 (21.2%)	23 (21.0%)	
- Five	1 (0.9%)	1 (0.9%)	
NYHA			
- Grade 1	22 (20%)	24 (22%)	
- Grade 2	44 (41%)	48 (44%)	NS
- Grade 3	30 (28%)	28 (25%)	
- Grade 4	12 (11%)	10 (9%)	
Preoperative LVEF	0.421±0.16	0.412±0.156	$p>0.05$ NS
Length of stay in ICU	2.58±1.3 days	2.96±1.8 days	$p=0.055$ Trend
Development of side-effects of Mg	2 patients (excluded from the study)		
Atrial fibril.	9 (8.3%)	23 (21%)	$p<0.01$

NS=Not significant, HS=Highly significant

DISCUSSION

A number of advances in anaesthetic and surgical techniques have reduced risks in cardiac surgical patients.[1] AF maybe associated with an increased risk of heart failure, renal insufficiency and stroke, which may prolong hospital stay.[1,5] International literature reports the incidence of postoperative AF as between 16% and 46% of cardiac surgeries.[12] A previous paper[10] from our own department gave an incidence of 13.3% of AF, based on 42 patients operated in 2001. However, their criterion of AF was an arrhythmia which needed treatment. Based on our criteria given in materials above, the total incidence of AF in our untreated group was 23%. This was reduced, remarkably to 9% in our magnesium group. This being the only study of its type in our indigenous population.

In some international studies the incidence of AF is reported as high as 50%.[6] This maybe because AF of very short duration, like 30 seconds, are also included. Most of these AFs are usually harmless and may not benefit from prophylaxis.[6] Hence the definition of 'significant' AF maybe the reason for many trials not showing a significant benefit. This, as Henyan[13] mentions, maybe due to the heterogeneity between the trials, making a meta-analysis less powerful.

The dosage of magnesium is another factor which may be the reason for differing results.[7,13] In literature this has ranged from 2.5 gm[14] to 18 gm[15], and varied with respect to perioperative loading time and duration. According to the meta-analysis of Henyan,[13] in the trials that used low dose magnesium, the incidence of AF was significantly reduced. This also has minimal side effects, and precludes the need for serum levels. Hence the use of lower dose in our study.

Given the consequences, numerous other studies have been done to support the efficacy of a number of different pharmacological interventions. Beta-blockers have been widely studied and is currently the most common medication used in AF prophylaxis, being fiercely supported by some centres.[14–16] Our study may help to purport the wider use of magnesium in our ICUs. Other drugs like amiodarone[17], sotalol, nondihydropyridine calcium channel blockers, and magnesium sulphate have been associated with a reduction in the occurrence of postoperative AF[14], but their results are still pending confirmation by other studies.

Reduction in the occurrence of AF not only reduces the morbidity, but more importantly for the clinicians may reduce the length of hospital and ICU stay.[13,14] Many trials mention the length of hospital stay as another variable studied.[18,19] This, although was not the main objective of this study, the reduction of ICU stay in the study group showed a definite trend towards reduction in the days of ICU stay for the magnesium

group. This further supports the prophylactic postoperative use of magnesium.[20]

It is most interesting that still after more than 15 years since the role of magnesium was first reported[8] there is controversy in its use, with papers both in favour and against the use of magnesium.[13,21,22] In spite of the differing opinions there are recent powerful papers which fully support the prophylactic use of magnesium in reduction of AF as well as in reduction of hospital stay.[7,13,14,23]

Our own findings fully support the use of magnesium. It significantly reduced the incidence of postoperative atrial fibrillation, reduced the morbidity and hence reduced the time spent by these patients occupying scarce ICU beds.

CONCLUSION

A 3-days postoperative infusion of magnesium is safe and effective in reduction of possibly life-threatening AF. This is as effective in our patients as reported in studies from abroad. It is cheap, effective, easily available and with minimal side-effects even when used in the low doses.

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