Use of Magnesium Sulphate in the Prophylaxis of Atrial Fibrillation Post Cardiac Surgery, is it Effective?

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ABSTRACT

Objective: To assess the effectiveness of magnesium sulphate in the prophylaxis of postoperative atrial fibrillation in patients undergoing elective coronary aortic bypass grafting or valvular heart surgery in terms of reducing its incidence and decreasing the length of hospital stay.

Methods: This study which was conducted at Queen Alia Heart Institute from June 2009 to June 2010 on 308 patients who underwent elective coronary artery bypass grafting or valvular heart surgery. Patients were divided into two equal groups, the magnesium-treated and control groups (154 each). Then each group was subdivided into patients who underwent coronary artery bypass grafting alone (n = 102), and patients underwent valvular surgery with or without coronary artery bypass grafting (n = 52). In the treatment group, patients were given 3.0gm of magnesium sulphate intra-operatively, and later on for the first 4 consequent post operative days.

Results: About 8.4% developed atrial fibrillation in the treatment group in contrast 23.3% in the control group ($P < 0.001$).
In the subdivided groups, those patients who underwent only coronary artery bypass grafting, 7.8% and 23.5% developed atrial fibrillation in the treatment and control group respectively. In the group of patients who underwent valvular heart surgery with or without CABG, 5 patients (9.6%) developed atrial fibrillation in the treatment group compared to 15 patients (28.8%) in the control group.
Atrial fibrillation developed after 34 ± 10.52 hours in the treatment group in comparison to 38 ± 11.23 hours which is statistically non-significant. The length of hospital stay was 6.01 ± 2.15 days in the treatment group while it was 5.95 ± 1.85 days in the control group which was also found to be statistically non-significant.

Conclusion: Use of magnesium sulphate, both intraoperativley and postoperatively proved to be safe and effective in reducing the incidence of post operative atrial fibrillation in patients undergoing elective coronary artery bypass grafting or valvular heart surgery, but with no obvious significant effect on hospital stay.

Key words: Magnesium sulphate, Post operative atrial fibrillation, Prophylaxis.

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Introduction

Atrial Fibrillation (AF) is a relatively common postoperative arrhythmia seen early after cardiac surgery with a frequency ranging between (6-40%).[1-3] It commonly occurs between 0-4 days,[4,5] with peak incidence on the second to third postoperative day.[2,3,5] Its onset may be associated with hemodynamic instability, increased

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risk of thromboembolism or stroke, prolonged hospitalization and significant increase of hospital morbidity.[6,7] The aim of this study was to assess the effectiveness of magnesium sulphate in the prophylaxis of AF in patients undergoing elective CABG or valvular heart surgery in terms of reducing its incidence and decreasing the length of hospital stay.

Methods

This was a prospective, randomized, controlled trial of intravenous magnesium sulphate ($MgSO_4$) vs. intravenous saline in patients undergoing elective cardiac surgery for the first time at Queen Alia heart institute conducted over one year between June 2009 and June 2010. The study was approved by the local ethical committee of Jordanian Royal Medical Services.

The study primary endpoint was the occurrence of an episode of AF lasting ≥ 30 minutes or hemodynamic instability due to AF regardless of episode duration. Secondary endpoint was the length of hospital stay.

The age, history of hypertension or diabetes mellitus, total pump and aortic cross clamp time, time onset of AF and hospital stay duration were recorded.

Exclusion criteria included: Emergency surgery (within 12 hrs), previous history of AF or other arrhythmias, permanent pacemaker, renal failure, intolerance to β- blockers, respiratory airway disease requiring regular β-adrenergic agonists such as salbutamol.

All patients were randomized into either the study or control group, had normal sinus rhythm prior to surgery.

Patients were divided into two major equal groups, each consisted of 154 patients i.e. the magnesium (study group) and saline one (control group). Then each group was subdivided into patients undergoing isolated CABG (n=102), and patients undergoing valve surgery with or without CABG (n = 52).

Patients in the study group received 3 gm of $MgSO_4$ while the control group received a 100 cc of 0.9% intravenous saline intra-operatively by the anaesthesiologist after removal of the cross clamp; then the same dose for the next 4 postoperative days. Patients stopped receiving either choice if AF occurred. Regarding general anaesthesia, surgical techniques and patient monitoring were standardized for all patients. All patients were monitored with continuous ECG monitoring (telemetry) for the first 2 days post operatively either in ICU1 or step down ICU2.

Values are presented as means ± standard deviation and percentages. Chi-square was used to analyze the results, differences were considered to be statistically significant when P value < 0.05, in addition to that, the test was used for comparison of patients in terms of duration of hospitalizations.

Results

The demographic data did not differ significantly between the two groups. The mean age of the treatment and control groups was comparable 60.1 vs. 60.5 years respectively as well as the gender, 74.6% vs. 75.3% being males. Hypertension was found in 63.6% (98 patients) of the magnesium group and in 62.3% (96 patients) of the control group. DM was found in 33.7% and 33.1% of the magnesium and control group respectively.

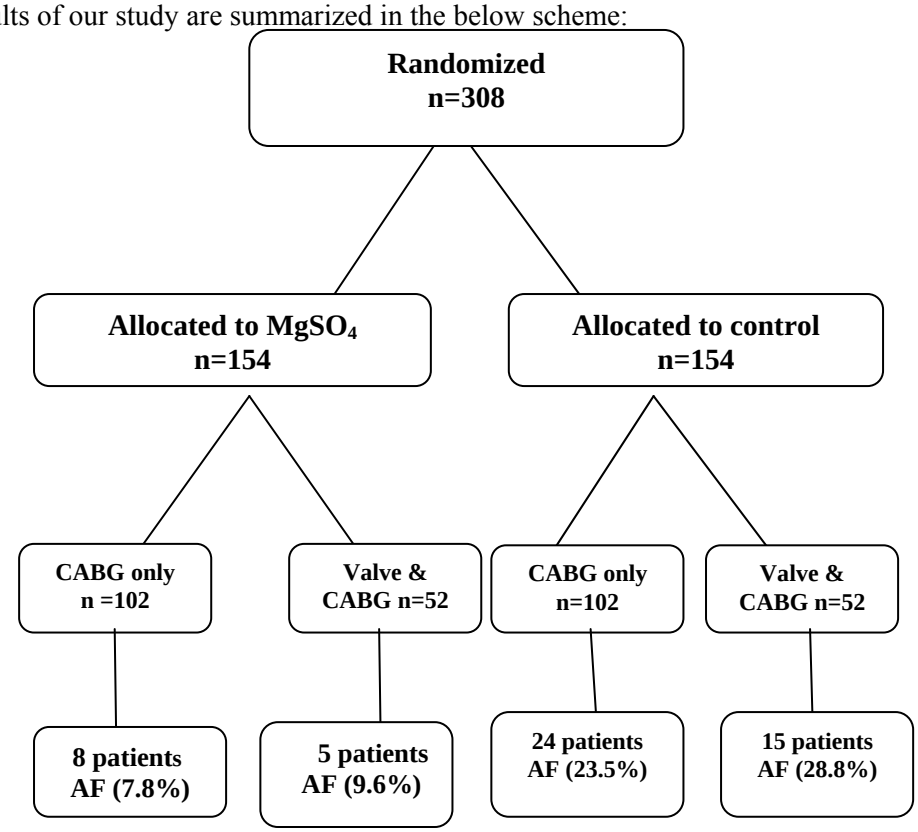
Regarding mean aortic cross clamp time in the magnesium group was 55.7+14.2 minutes (Range 38 – 106 min) vs. 56.2+13.5 minutes (Range 40-104) in the control group whereas the average total pump time was 103+23 minutes (Range 56-156) vs. 103.4 minutes (Range 56-157). Both parameters were found to be statistically non-significant (P > 0.05) (See Table I & II).

The incidence of postoperative AF was 8.4% in the magnesium treated group (N=13) while it was 25.3% in the control group (N=39), which is statistically significant (P < 0.001 -See Table II).

When dividing the patients into those who underwent CABG only and those who underwent valve surgery with or without CABG, the incidence of AF was 7.8% vs. 23.5% (P value < 0.01) in the magnesium and control groups respectively. On the other hand, the incidence of AF in the CABG plus valve group was 9.6% vs. 28.8% (P < 0.05) in both the magnesium and control groups respectively. It was seen that the incidence of AF is more in the valve patients than the CABG group with or without $MgSO_4$ treated, which is due partly to the effect of valve pathology.

Concerning the timing of onset of AF and hospital stay, the onset of AF in the magnesium treated group occurred in 78% of patients on the second day, 15% on the first day, with mere 7% in the third day, in contrast to the control group with 75% on the second day, 10% on the first day, 15% on the third day.

The results of our study are summarized in the below scheme:



The onset of AF was 34.6±10.5 hrs in the treatment group while it was 38±11.2 hrs in the control group which found to be statistically non-significant. The length of hospital stay was 6.0 ± 2.2 days in the treated group while it was 5.6 ± 1.9 days in the magnesium group, when comparing it with patientswho developed AF, it was found to be statistically non-significant, so AF did not have an impact on the length of hospital stay (Table III).

Discussion

Despite the significant advances in the peri-operative management of postoperative AF, its incidence has not decreased during the last decade with consequent morbidities and increased risk of heart failure, renal failure and strokes.

The mechanism behind the occurrence of post operative AF has not been clearly identified, but the most likely cause is multi-factorial in origin which might include advanced age,[4,5,8,9] preoperative withdrawal of β-blockers,[5,7,8] impaired cardiac function,[5,8] myocardial ischemia and reperfusion,[5,8] chronic obstructive lung disease,[5,8] excessive catecholamines[5,8,9] and electrolyte imbalances particularly hypomagnesaemia which has been considered as an independent predictor of postoperative AF.

Almost 80% of patients undergoing cardiac surgery have reduced both ionized and total serum magnesium levels postoperatively,[5,8] which might be attributed to several causes, mainly hemodilution related to cardiopulmonary bypass,[5,9] elevated catecholamine levels, which may be caused by abrupt withdrawal of β-blockers,[9] advanced age in addition to increased urinary magnesium loss due to diuretic use.[5]

Changes in magnesium concentration have significant effects on cellular metabolism and structure, as well as stabilizing the cellular transmembrane potential of myocardial cells, suppressing excessive cellular calcium influx, and reducing the severity of reperfusion injuries,[5,9,10] this can be done by inhibiting L and T type calcium channels, which will reduce sinus firing and increase AV (atrioventricular) node refractoriness.[3,8,11,12]

For these reasons, magnesium has been suggested to be effective in the prophylaxis of AF after cardiac surgery; however a lot of debates on its use and benefits are present, with more necessity to identify the proper dose and timing of magnesium administration.

Table I. Demographic and clinical characteristics

Variable	All Surgeries		CABG (n = 102)		Valve ± CABG		P value
	$MgSO_4$ n = 154	Control n = 154	$MgSO_4$ n = 102	Control n = 102	n = 52 $MgSO_4$ n = 52	Control n = 52	
Male	74.6%	75.3%	77.3%	74.2%	74.2%	72.5%	NS*
Female	25.4%	24.7%	26.7%	25.8%	25.8%	27.5%	NS
Age (median)	60.1 years	60.5 years	60.9%	60.5%	61.2%	61.5%	NS
HT	63.6%	62.3%	62.1%	63.1%	62.4%	62.5%	NS
DM	33.7%	33.1%	33.5%	33.6%	33.8%	32.9%	NS

Table II. Intraoperative and postoperative characteristics of patients

Variable	All Surgeries		CABG (n = 102)		Valve ± CABG		P value
	$MgSO_4$ n = 154	Control n = 154	$MgSO_4$ n = 102	Control n = 102	n = 52 $MgSO_4$ n = 52	Control n = 52	
TPT*	103.4 ± 22.66	102.9 ± 21.95	105 ± 19.52	104 ± 21.62	106 ± 22.52	104 ± 42	NS**
TPT in patients with AF	104.5 ± 21.56	104.8 ± 21.92	106 ± 21.42	105 ± 22.52	106 ± 21.52	103 ± 52	NS
ACX^	55.65 ± 14.25	56.32 ± 13.92	57.42 ± 12.92	55.95 ± 13.52	57.82 ± 12.42	56.92 ± 12.12	NS
ACX in patients with AF	57.42 ± 13.45	56.56 ± 12.82	56.52 ± 13.10	54.95 ± 12.52	56 ± 11.92	54.82 ± 12.60	NS
Patients with AF	13	39	8	24	5	15	P<0.05 significant

* Total Pump Time ** Non-significant ^ Aortic Cross Clamp

Table III. Timing of Atrial fibrillation and length of hospital stay

Variable	Mg $S0_4$ (n = 154)	Control (n = 154)	P value
Onset of AF (hr)	34.65 ± 10.52	38 ± 11.25	NS
Length of hospital stay (days)	6.01 ± 2.15	5.95 ± 1.85	NS

Although the prophylactic use of $MgSO_4$ has not yet verified been of the conflicting evidences,[5,6]

Still it is considered to be attractive tool because of its low cost, safe when administered slowly, moreover the decline in serum Mg with cardiopulmonary bypass which does not recover until the third day coinciding with the period during which AF develops.

In our study, we had an incidence of about 23% AF in the control group, in contrast to just 8% in the treated one $P < 0.001$, which means dramatic and significant decrease in the incidence of AF upon the administration of $MgSO_4$.

It is undoubtly evident that the incidence of AF is within the range reported in the literature (16-40%).[1-3] Fevzi toraman and his colleagues[9] conducted comparative study on 200 patients which showed dramatic decrease in the incidence of post cardiac surgery AF from 24% to mere 2%.

Moreover, another study conducted by Hiroki Kohno and his colleagues[5] on 200 patients illustrated significant decrease in the incidence of post operative AF from 32% to 16%.

Furthermore, a study by Naito Y and his colleagues[13] showed obvious decline in the incidence of postoperative AF from 43.8% to 10%, in addition to the Muhammad Bakhsh study[3] had significant response to $MgSO_4$ administration in that postoperative AF decreased from 23% to just 9%, at the same time, the meta analysis conducted by Miller *et al*[1] concluded that prophylactic $MgSO_4$ is effective for the prevention of AF after CABG with decrease in its incidence from 28% to 18%. The same findings were supported by another meat analysis of Henyan.[14] However, a study conducted by Mehmet Kaplan and his colleagues[4] found no significant difference in the incidence of AF upon the infusion of $MgSO_4$, that is to say $MgSO_4$ infusion alone is not sufficient for the prophylaxis of AF.

Another study by Richard C,[6] found also no difference in the incidence of AF after infusion of $MgSO_4$ between patients who received IV $MgSO_4$ or placebo (26.4% versus 24.3 respectively).

The different results seen from the above mentioned articles might be attributed to the dosage of $MgSO_4$ given, in most clinical trials that have shown effective prophylaxis, the amount of magnesium per day given no greater that 15 mmol with reported mean serum levels after each dose

were within the normal physiological range,[5] in contrast to high magnesium dose >50mmol which had the least effect, hence we use low dose magnesium in our study with less demand or need for serum levels determination.

Since AF usually develops between first post operative days to the fourth one, with associated hypomagnesemia during that, we intended to give $MgSO_4$ during this period which proved to have significant role in the prevention of this arrhythmia.[4,5]

Concerning the risk analysis of post operative AF, we found that age, gander, hypertension, diabetes, total pump time, aortic cross clamp were not significant factors in the development of AF, which is also found in a study conducted by Richard C. cook and his colleagues.[6] We found the same effects of $MgSO_4$ infusion on patients undergoing valve surgery with or without CABG, in comparison to those with CABG only, as in the case of valve with or without CABG, there was 66.6% decrease in the incidence of AF upon administration of magnesium, while there was 66.8% decline in the incidence of AF in patients with CABG only, which is almost the same effect, however the incidence of AF is more in valve patients[15] as seen in our study 28.8% whereas it is 23.5% in the CABG group, on the other hand, meta analysis by S Miller and his colleagues[1] showed that $MgSO_4$ was more effective in trials with CABG surgery alone than that when CABG was combined with valve surgery.

Regarding the length of hospital stay, no statistically significant difference was found between the treatment and control group, which is also seen in other studies;[1,9] in contrast to the study by Kaplan that found significant change in the length of hospital stay with Mg SO_4 in fusion.

Furthermore, the timing of onset of AF was found to be insignificant when comparing both groups, meanwhile the majority of patients developed AF on the second day, then the first day which indicated that $MgSO_4$ infusion has no effect on the timing of onset of AF.

Limitations of the Study

First limitation is the absence of continuous ECG monitoring, except for the first and second day for both the treated and control group, after that the arrhythmia was usually detected either by early morning routine ECG or symptomatic patients with clinical signs or even asymptomatic accidental findings. Because this limitation was the same in each group, it is unlikely that this affected the results of our study.

The second limitation of our study was the definition of significant AF, as several definitions exist according to the duration of AF; therefore we attempted to select relatively long duration (> 30 minutes) because it is likely that the longer the AF duration, the more prominent the benefits of the magnesium treatment will be.

Conclusion

Use of magnesium sulphate, both intra-operatively and postoperatively proved to be safe and effective in reducing the incidence of post operative AF in patients undergoing elective CABG or valvular heart surgery, with no obvious significant effect on hospital stay.

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