Journal of Anesthesia & Clinical Research

Mohamed et al., J Anesth Clin Res 2018, 9:3
DOI: 10.4172/2155-6148.1000810

Research Article Open Access

Magnesium Sulfate for Prophylaxis against Postoperative Atrial Fibrillation after Isolated Cardiac Valve Replacement Surgery in Adult Patients with Rheumatic Heart Disease: A Randomized Controlled Trial

Fatma Nabil Ahmed Mohamed*, Esam Eldin M Abdallah, Abdelrady Shehata Ibrahim, Ahmed MK El-Minshawy and Tarek Taha Hanafy Elmelegy

**Department of Medicine, Assiut University, Anesthesiology, Egypt*

***Corresponding author:** Fatma Nabil Ahmed Mohamed, Department of Medicine, Assiut University, Anesthesiology, Egypt, Tel: +20 1003633992; E-mail: fatmanabil2012@gmail.com

Received date: February 19, 2018; **Accepted date:** March 29, 2018; **Published date:** April 03, 2018

Abstract

Objectives: To evaluate the role of prophylactic magnesium sulfate administration in preventing postoperative atrial fibrillation (POAF), attenuating the inflammatory response and promoting myocardial protection after isolated cardiac valve replacement surgery in adult patients with rheumatic heart disease.

Design: Prospective randomized, double-blind placebo-controlled trial.

Methods: Sixty-four adult patients undergoing isolated cardiac valve replacement surgery were divided into two equal groups (32 patients in each). Patients in magnesium group (group M) received 2.5 gm of magnesium sulfate (dissolved in 100 mL of isotonic saline and infused over 2 h), twelve h preoperatively, within the first hour of ICU arrival, and on the 2nd and 3rd postoperative days (group M). Patients in the control group (group C) received a placebo of isotonic saline at the same time periods.

Results: Prophylactic magnesium sulfate significantly decreased the incidence of POAF compared to the placebo group (P=0.005). White blood cell (WBC) count showed no significant difference between the two groups. C-reactive protein (CRP) level showed significant reduction during the 3rd, 4th, and 5th postoperative days in group M compared to group C (P=0.001, 0.001 & 0.012 respectively). Serum level of interleukin-6 (IL-6) showed a significant reduction on the 5th postoperative day in group M compared to group C (P=0.001). Both groups showed no significant differences in serum levels of troponin I during the study.

Conclusion: Prophylactic use of magnesium sulfate in patients with rheumatic heart disease undergoing isolated cardiac valve replacement surgery can decrease the incidence of POAF. It may play a role in attenuating the inflammatory process associated with the use of cardiopulmonary bypass (CPB).

Keywords: Magnesium sulfate; Postoperative atrial fibrillation; Cardiac valve surgery; Rheumatic heart disease

Introduction

Cardiovascular diseases represent significant health challenges worldwide. Most heart disease patients are subject to surgical intervention [1]. Despite advances in cardiac surgery, both in surgical techniques and perioperative care, patients are still at risk of postoperative complications resulting in bad prognoses and high financial burdens [2]. Among major post-cardiac surgery complications are arrhythmias especially atrial fibrillation (AF) [3]. AF is characterized by irregularly irregular rhythm with high atrial rate (350-500 beats/min) that causes loss of atrial kick and hence reduction of left ventricular filling. Consequently, stroke volume decreases leading to hemodynamic instability [4]. Conventional management of postoperative atrial fibrillation (POAF) usually focuses on atrial conduction, refractory period, and the role of the sympathetic nervous system, while novel therapies target the relationship between the occurrence of POAF and the inflammatory process, oxidative stress, and atrial remodeling [5]. Magnesium is fourth most common cation in the body and the second most abundant one inside the cells. It is an important factor in different enzymatic reactions involving nucleic acid synthesis and energy metabolism. Several studies attributed its membrane stabilizing, anti-arrhythmic and anti-inflammatory actions to its effect as a calcium antagonist [6]. During stress, magnesium appears in a relatively high amount in urine resulting in a decrease in its serum level. This depletion in the serum level of magnesium causes stress at the cell membrane level which further decreases its serum level "vicious circle" resulting in severe complications such as cardiac dysrhythmias, which appear in the form of supraventricular tachycardia, atrial fibrillation, prolonged P-R and Q-T segments, and even ventricular fibrillation [7].

The primary outcomes were to evaluate the effect of prophylactic magnesium sulfate administration on the incidence of POAF after isolated cardiac valve surgery in adult patients and to detect its anti-inflammatory and cardioprotective effects.

Patients and Methods

This prospective randomized, double-blind placebo-controlled trial was carried out from September 2017 to February 2018, after approval from the ethics committee for research of faculty of medicine, Assiut

University (Assiut, Egypt) and after written informed consents from the patients.

Sixty-four adult patients (18-50 years) with rheumatic heart disease, moderate to severe mitral and/or aortic valve lesion (stenosis and/or incompetence) scheduled for elective isolated cardiac valve replacement surgery were included in this study. Inclusion criteria included preoperative sinus rhythm, normal white blood cell (WBC) count, preoperative troponin I (cTnI)<0.01 ng/mL, and preoperative C-reactive protein (CRP)<3 mg/L. Excluded patients were those with a history of atrial fibrillation, any degree of atrioventricular (AV) block, prior use of antiarrhythmic drugs, underlying heart failure or Left ventricular ejection fraction <0.3, associated renal or liver comorbidities, or diabetes mellitus. Also, patients receiving magnesium supplementation for any reason the week before the surgery were excluded from the study.

Patients were allocated using computer-generated random numbers into two equal groups, each of 32 patients. Patients in magnesium sulfate group (group M) received 2.5 gm of magnesium sulfate (dissolved in 100 mL of isotonic saline and infused over two h) twelve h preoperatively, within the first hour of ICU arrival (1st postoperative day), then on the 2nd and 3rd postoperative days. Patients in the control group (group C) received a placebo of isotonic saline at the same times.

Upon arrival to the operating room and after connecting the patient to the standard monitoring, an arterial line was inserted under local anesthesia. Induction of anesthesia was achieved using fentanyl (3-4 μg/kg) and titrated doses of propofol (1-2 mg/kg), followed by cis-atracurium (0.15 mg/Kg) to facilitate endotracheal intubation with a cuffed endotracheal tube. Volume controlled ventilation was instituted with parameters set to maintain normocarbia. Anesthesia was maintained by Isoflurane (0.4-1%) in oxygen and air (Fio2=0.5), Fentanyl infusion (1 μg/kg/h), and midazolam infusion (50-100 μg/kg/h), which were titrated according to the hemodynamics. Muscle relaxation was maintained by cis-atracurium infusion (1-2 μg/kg/min). All cases were done *via* midline sternotomy incisions with similar surgical techniques as far as possible. CPB management was standardized for all patients. Heart was arrested by infusing cold cardioplegia (CUSTODIOL solution 5-8°C) *via* a special cannula introduced in the aorta proximal to the site of aortic cross-clamp, in a dose of 15-20 ml/kg (maximum 2000 ml for any given body weight) and a pressure of 100-110 mmHg initially, to be reduced to 40-50 mmHg after the onset of cardiac arrest.

At the end of surgery, patients were transported to the postoperative ICU where they stayed for at least the 1st three days of the study. Patients were extubated according to standard criteria. Continuous ICU monitoring included hemodynamic parameters (invasive arterial blood pressure, heart rate, and central venous pressure), automated ECG with alarmed arrhythmia detection, and oxygen saturation by pulse oximetry. Input and output with the calculation of fluid balance were recorded. Twelve leads ECG and arterial blood gas (ABG) were done at ICU arrival, every 6 h and during any attack of arrhythmia. Hemodynamic changes were managed by optimizing the intravascular volume and the inotropic support with a targeted systolic blood pressure ≥ 100 mmHg and hematocrit of 30-35%. By the end of the 3rd day, patients who met criteria of discharge from ICU were transferred to an intermediate care unit for two more days where hemodynamic parameters were recorded, and 12 leads ECG and ABG were done every 6 h and during any clinical manifestation suggestive of arrhythmia.

In this study, we used a definition of POAF as any episode of AF lasting for more than five minutes with or without symptoms or any episode of AF that required intervention to maintain hemodynamic stability [8]. Any attack of POAF starting from ICU arrival and for the first five postoperative days was planned to be managed according to a preset protocol; whenever POAF episode is detected, 12-leads ECG is recorded, and arterial blood gas sample is taken for correction of any acid-base or electrolyte disturbance. If the episode of POAF is associated with hemodynamic instability, direct cardioversion is used. If the patient is hemodynamically stable, intravenous amiodarone is used (150 mg over 10 min, then 1 mg/min for 6 h, then 0.5 mg/min for 18 h) followed by oral amiodarone (400 mg twice daily for five days followed by 200 mg once daily for seven days). If sinus rhythm is not established within 24 h of medical treatment, then external electrical cardioversion is performed.

Study measurements

Occurrence of POAF starting from ICU arrival and for the first five postoperative days; serum levels of potassium and magnesium, serum level of CRP, and WBC count 12 h preoperatively (just before administration of the first dose of magnesium sulfate or placebo) as baselines, then on the 1st , 2nd, and 3rd postoperative days (two h after the end of drug infusion from an intravenous line other than the infusion line), then 24 and 48 h later (the 4th and 5th postoperative days); serum level of interleukin-6 (IL-6) post-induction, at the end of CPB, 6 h after CPB, then 24 and 120 h after induction of anesthesia; serum level of cTnI 12 and 24 h after induction of anesthesia. Duration of inotropic support was recorded with the calculation of the mean 24 h and the maximum 24 h inotropic scores. Inotropic score (IS) per hour=[dopamine dose (μg/kg/min)+dobutamine dose (μg/kg/min) +100 X epinephrine dose (μg/kg/min)] [9]. The mean 24 h IS was obtained by averaging the hourly scores for 24 h, while the maximum 24 h IS is the highest value during the first 24 h of the study.

Statistical analysis

Data were analyzed using SPSS (version 23). Normality of data was tested by Kolmogorov-Smirnov test. The incidence of POAF was presented as numbers and percentages and analyzed using Fisher's exact test. Other categorical data were presented as numbers and percentages and analyzed using Chi-square test. Continuous numerical variables were presented as mean ± SD and analyzed using independent samples t-test for normally distributed data, or presented as median and interquartile range and analyzed using Mann-Whitney test for non-parametric data. P-value<0.05 was considered statistically significant.

The sample size was calculated based on a previous study of patients undergoing CABG surgeries on CPB, in which the incidence of POAF was 10% in patients receiving prophylactic magnesium sulfate versus 43.8% in the control group [10]. The sample size was estimated to be 26 patients in each group, with a power of 80% and an α error of 0.05. We enrolled 32 patients in each group to compensate for dropouts.

Results

Figure 1 shows the CONSORT flow chart of the study. The intervention was discontinued for one patient in Group M (AV block that required postoperative pacing) and two patients in group C (one with AV block that required postoperative pacing, and the other with postoperative renal impairment). So, analysis included 31 patients in

group M versus 30 patients in group C. There were no significant differences between the two groups regarding age, sex, weight, body mass index (BMI), preoperative left ventricular ejection fraction (LVEF), left atrial diameter, type of surgery, duration of anesthesia, duration of CPB, cross-clamp time, the lowest hematocrit (HCT), or the lowest temperature (Table 1).

		Group M (n=31)	Group C (n=30)	P Value
Age (Years)		32.45 ± 9.08	30.27 ± 7.73	0.316
Sex	Male	14 (45.2%)	17 (56.7%)	0.369
	female	17 (54.8%)	13 (43.3%)	
Weight (Kg)		59.77 ± 12.83	65.20 ± 16.46	0.156
Body Mass Index (Kg/m^2)		22.38 ± 4.69	24.07 ± 5.07	0.182
Preoperative LVEF (%)		63.03 ± 5.57	61.33 ± 5.83	0.249
Left Atrial Diameter (Cm)		4.77 ± 0.72	5.17 ± 0.96	0.074
Type of Surgery				
Single MV Replacement		14 (45.2%)	16 (53.3%)	0.794
Single AV Replacement		8 (25.8%)	6 (20.0%)	
Combined MV & AV Replacement		9 (29.0%)	8 (26.7%)	
Duration of Anesthesia (Hours)		6.47 ± 1.05	5.95 ± 1.18	0.075
Duration of CPB (Minutes)		120.26 ± 30.43	115.97 ± 33.72	0.604
Cross Clamp Time (Minutes)		73.97 ± 30.93	71.87 ± 26.92	0.778
Lowest HCT (%)		23.29 ± 1.40	22.83 ± 1.58	0.235
Lowest Temperature (C°)		28.87 ± 1.20	28.43 ± 1.17	0.173

Numerical data are expressed as mean ± SD. Sex and type of surgery are expressed as number and percentage. M: Magnesium Sulfate; C: Control; n: number of patients; LVEF: Left Ventricular Ejection Fraction; MV: Mitral Valve; AV: Aortic Valve; CPB: Cardiopulmonary Bypass; HCT: Hematocrit. P value <0.05 is considered significant.

Table 1: Patient Characteristics, Lesion Characteristics, and Operative Details.

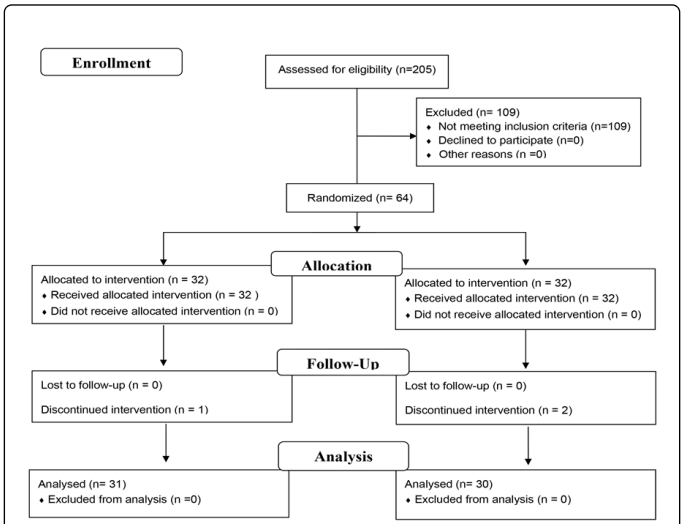

Figure 1: The Consort flow diagram of the study.

Cardiac rhythm

Regarding the cardiac rhythm after declamping, there was no significant difference between the two groups (P=0.806). In group M, we had 19 patients (61.3%) of sinus rhythm, three patients (9.7%) of AF, four patients (12.9%) of AV block, and five patients (16.1%) of ventricular tachycardia or fibrillation (VT/VF). In group C, we had 16 patients (53.3%) of sinus rhythm, four patients (13.3%) of AF, one patient (3.3%) of supraventricular tachycardia (SVT), three patients (10%) of AV block and six patients (20%) of VT\VF (Table 2).

The incidence of POAF during the first five postoperative days was significantly lower in group M compared two group C (P=0.005). Only four cases (12.9%) developed POAF in group M versus 14 cases (46.7%) in group C (Table 2). In group M, POAF cases occurred on the 2nd postoperative day (2 cases) and the 3rd postoperative day (2 cases); Patients were hemodynamically stable during the attacks, so they were managed by amiodarone therapy according to the preset protocol. In group C, POAF cases occurred on the 1st, 2nd, 3rd, and 5th postoperative days (2, 6, 4, and 2 cases respectively). Three out of the 14 cases in group C were associated with hemodynamic instability, so synchronized cardioversion was used to control the attacks, while the remaining 11 cases were hemodynamically stable and managed by amiodarone therapy. In all cases, blood samples were taken for

correction of any electrolyte or acid-base imbalance as a part of the preset protocol.

		Group M (n=31)	Group C (n=30)	P Value
Rhythm after Declamping	Sinus	19 (61.3%)	16 (53.3%)	0.806
	AF	3 (9.7%)	4 (13.3%)	
	SVT	0 (0%)	1 (3.3%)	
	AVB	4 (12.9%)	3 (10%)	
	VT/VF	5 (16.1%)	6 (20%)	
POAF (Day 1-5)		4 (12.9%)	14 (46.7%)	0.005*

Data are expressed as numbers and (percentages). M: Magnesium Sulfate, C: Control, n: number of patients, AF: Atrial Fibrillation, SVT: Supraventricular Tachycardia, AVB: Atrioventricular Block, VT: Ventricular Tachycardia, VF: Ventricular Fibrillation, POAF: Postoperative Atrial Fibrillation. P-value <0.05 is considered significant. *denotes significant difference between both groups.

Table 2: Cardiac Rhythm.

Serum electrolytes

Baseline serum magnesium showed no significant difference between both groups. During the first five postoperative days, serum magnesium levels were significantly higher in group M compared to group C (Figure 2). There were no significant differences between both groups regarding the serum potassium level preoperatively or during the first five postoperative days (Table 3).

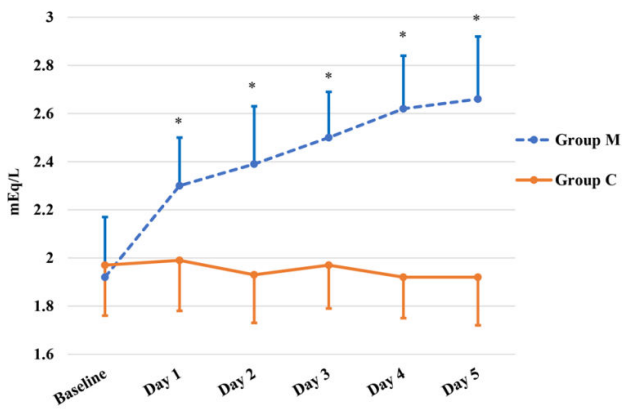

Figure 2: Serum Magnesium with SD (mean ± SD). M: Magnesium Sulfate; C: Control. * Denotes significant difference compared to the control group.

WBC count

There was no significant difference between both groups regarding the baseline WBC count. Postoperatively, the WBC count increased dramatically; however, there were no significant differences between both groups on the first five postoperative days (Table 4).

	Group M (n=31)	Group C (n=30)	P value
Baseline	4.05 ± 0.44	4.21 ± 0.43	0.154
Day 1	4.21 ± 0.44	4.30 ± 0.54	0.477
Day 2	4.28 ± 0.55	4.31 ± 0.54	0.794
Day 3	4.33 ± 0.55	4.23 ± 0.43	0.45
Day 4	4.38 ± 0.51	4.40 ± 0.50	0.862
Day 5	4.33 ± 0.51	4.47 ± 0.50	0.294

Data are expressed as mean ± SD. M: Magnesium Sulfate, C: Control, n: number of Patients. P value <0.05 is considered significant.

Table 3: Serum potassium (mmol/L).

	Group M (n=31)	Group C (n=30)	P value
Baseline	7.08 ± 1.37	7.75 ± 1.69	0.091
Day 1	17.11 ± 2.85	17.40 ± 3.52	0.723
Day 2	16.58 ± 2.57	17.78 ± 3.58	0.139
Day 3	15.97 ± 2.59	17.12 ± 3.39	0.139
Day 4	15.22 ± 2.63	16.30 ± 3.44	0.172
Day 5	13.84 ± 2.95	14.91 ± 4.17	0.252

Data are expressed as mean ± SD. M: Magnesium Sulfate, C: Control, n: number of Patients. P value <0.05 is considered significant. * denotes significant difference between both groups.

Table 4: White Blood Cell Count ($\times 10^3/mm^3$).

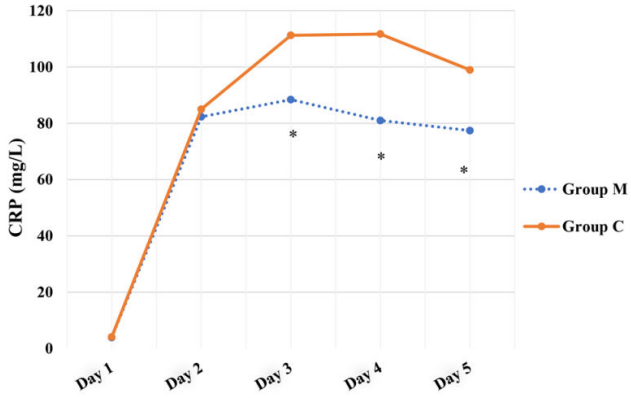

Figure 3: C-reactive protein (Median). M: Magnesium Sulfate; C: Control; CRP: C-Reactive Protein. * Denotes significant difference compared to the control group.

C-reactive protein

No significant differences between the two groups regarding the serum levels of CRP during the 1st and 2nd postoperative days (P1=0.971 and P2=0.812); however, the serum levels of CRP during the 3rd, 4th and 5th postoperative days were significantly lower in group M compared to group C (P3=0.001, P4=0.001 and P5=0.012) (Figure 3).

Interleukin-6

There were no significant differences between the two groups regarding the serum levels of IL-6 post-induction, at the end of CPB, 6 h post-CPB or 24 h after induction of anesthesia (Table 5); however, the serum level of IL-6 was significantly lower in group M compared to group C in the 5th Postoperative day (P=0.001) (Figure 4).

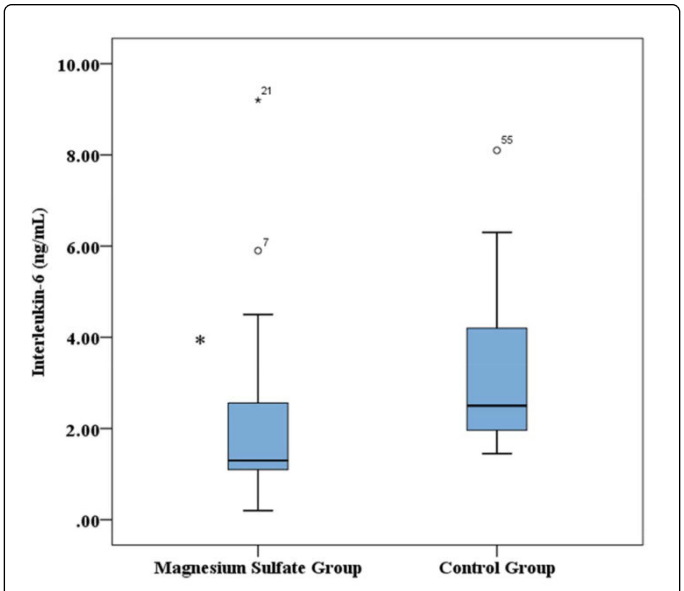

Figure 4: Box plot showing serum Interleukin-6 in the 5th postoperative day. (Median, range, 25th and 75th percentiles). * Denotes significant difference compared to the control group.

		Group M (n=31)	Group C (n=30)	P value
Interleukin-6 (ng/mL)	IL-6 (Ta)	0.9 (0.30-1.20)	1.15 (0.60-1.73)	0.117
	IL-6 (Tb)	6.7 (3.60-8.60)	6.4 (4.28-7.30)	0.857
	IL-6 (Tc)	3.3 (2.60-5.70)	3.8 (3.03-4.75)	0.778
	IL-6 (T24)	3.2 (1.70-6.20)	3.2 (2.80-4.28)	0.812
	IL-6 (T120)	1.3(1.10-2.60)	2.5 (1.96-4.30)	0.001*
Troponin I (ng/mL)	T12	1.92 (1.02-3.30)	1.93 (1.65-3.23)	0.965
	T24	1.9 (1.40-3.10)	1.48 (0.98-2.23)	0.08

Data are expressed as median and (interquartile range). M: Magnesium Sulfate; C: Control; n: Number of Patients; IL-6: Interleukin-6. Ta: Post-induction; Tb: at the end of cardiopulmonary bypass, Tc: 6 h post-cardiopulmonary bypass; T12, T24, & T120=12, 24, & 120 h after induction of anesthesia respectively. P value <0.05 is considered significant. * denotes significant difference between both groups.

Table 5: Interleukin-6 and Troponin I.

Troponin I

The serum levels of cTnI showed no significant differences between the two groups when measured 12 h or 24 h after induction of anesthesia (Table 5).

Inotropic support

There were no significant differences between the two groups regarding the duration of inotropic support, the mean 24 h IS, or the maximum 24 h IS (Table 6).

	Group M (n=31)	Group C (n=30)	P Value
Duration of inotropic support (Hours)	19 (11.0-24.0)	21.5(7.5-27.0)	0.954
Mean 24 h IS	3.1 (0.75-4.70)	3.44 (0.86-6.27)	0.583
Maximum 24 h IS	5 (4.00-7.00)	6.5 (5.00-8.50)	0.07

Data are expressed as median and (interquartile range). M: Magnesium Sulfate; C: Control; n: Number of Patients; IS: Inotropic support. P value <0.05 is considered significant.

Table 6: Inotropic Support.

Discussion

POAF is one of the most common complications after cardiac surgery with a range between 27% and 63%. Its risk increases in combined CABG and valve surgery. POAF gains its importance from its related adverse outcomes as stroke, congestive heart failure, and renal dysfunction which leads to prolonged hospitalization and subsequently high financial burden [11].

Over many years, magnesium was used in the management of atrial and ventricular arrhythmia [12]. Hypomagnesaemia is frequently seen after cardiac surgery, mainly during the 1st postoperative days. It may be related to the perioperative hemodilution, diuretics use, increased anabolic activity and elevation of adrenal hormones due to stress. Whatever the cause of the condition, hypomagnesemia increases the risk of post-cardiac surgery arrhythmia [13].

In this study, we evaluated the effect of prophylactic administration of magnesium sulfate on the incidence of POAF. Also, this study evaluated the anti-inflammatory and cardioprotective effects of magnesium sulfate.

Our results showed that prophylactic administration of magnesium sulfate reduced the incidence of POAF. In agreement to our finding, Nurozler et al. in a controlled double-blind trial that included patients with good left ventricular function and without preoperative arrhythmias who were undergoing CABG surgeries, reported that the use of magnesium sulfate for the first five postoperative days reduced the incidence of POAF [14].

Tiryakioglu et al. compared the prophylactic use of magnesium sulfate versus amiodarone in patients undergoing CABG and reported that both drugs were effective to prevent postoperative arrhythmia and POAF. Also, they stated that the use of magnesium sulfate might counteract the side effects of low postoperative levels of magnesium [15]. In our study, we used a similar protocol of magnesium sulfate

administration but with different doses and for isolated valve replacement surgeries.

Two factors may have impacts on the role of magnesium in the management of POAF; dose and time of administration. Christiansen et al. in a double-blind placebo-controlled trial found that atrioventricular node conduction was prolonged by using intravenous magnesium in a dose of 5 mmol with no further prolongation when using higher dosages. The same study also reported that lower doses of magnesium (defined as a mean cumulative dose of 8.2 gm) were more effective than moderate to high doses (mean cumulative dose of 15 gm) in reducing POAF [12].

Miller et al. in their meta-analysis and Torman et al. in their study reported that administration of magnesium in the preoperative and early postoperative periods reduced the incidence of POAF effectively in CABG surgeries [16,17].

Kiziltepe et al. in their study reported the efficacy and safety of magnesium sulfate for arrhythmias developed after open-heart surgery. Also, they reported that the antiarrhythmic effect of magnesium sulfate might be related to its pharmacological properties and not to normalization of its serum concentration, so they recommended its use as a first line antiarrhythmic agent even without routine assessment of its serum level [18].

It is worth to mention that serum magnesium level, whether total or ionized, is not a reliable indicator of the total body stores of magnesium and that Low myocardial magnesium content may be an indicator of arrhythmia [13]. So, the value of serum magnesium remains questionable and further studies are needed to show the relevance of serum magnesium and arrhythmia.

Carrio et al. in a controlled trial, reported that magnesium supplementation did not decrease the incidence of POAF in cardiac surgery with CPB [19], but, it worth to mention that magnesium was given only in the immediate postoperative period.

Surprisingly, Lancaster et al., in a large observational study, reported that potassium and magnesium supplementations are ineffective for the prevention of POAF and that higher serum levels of potassium and magnesium were associated with increased risk of POAF after cardiac operation. Furthermore, this study suggested that the mechanism of POAF is not related to electrolyte deficit [20].

Inflammatory response syndrome (SIRS) in open cardiac surgery is mainly attributed to the use of CPB. Once initiated, inflammatory mediators including interleukins (IL-1, IL-2, IL-6, IL-8) and tumor necrosis factor (TNF) are released. These mediators can stimulate leukocyte activation, chemotaxis and leukocyte-endothelial adherence which lead to tissue damage and multiple organ dysfunctions [21].

In our study, we evaluated the effect of magnesium sulfate administration on the inflammatory response provoked by cardiac surgery by comparing the WBC count and serum levels of CRP and IL-6 between both groups. There were no significant differences between both groups regarding the WBC count during the first five postoperative days. However, the serum levels of CRP on the 3rd, 4th, and 5th postoperative days; and the serum level of IL-6 on the 5th postoperative day were significantly lower in magnesium group.

In agreement with this result, Aryana et al. reported that magnesium sulfate infusion could suppress part of the inflammatory response after CABG with CPB as demonstrated by reduced postoperative serum level of IL-6 [1].

Many studies reported that magnesium can modulate cellular events involved in inflammation through different mechanisms including inhibition of NMDA dependent cellular pathways and decrease of leukocyte migration to the infarct area. In addition, hypomagnesemia itself can activate inflammatory neurotransmitters, with an inverse relationship between serum level of magnesium and serum levels of some of the inflammatory markers such as CRP and TNF-alpha [1,22-24].

In this study, we used the serum level of cTnI, both 12 and 24 h after induction of anesthesia, to evaluate the cardioprotective effect of magnesium sulfate. Our results showed no significant differences between both groups.

Magnesium supplementation is reported to have cardioprotective effects through inhibition of calcium influx and hence reduction of cellular calcium overload and through the decrease of the release of catecholamines. As well it improves collaterals of coronary circulation by its vasodilator effect [22].

It is worth to mention that magnesium treatment in the acute phase of myocardial infarction was favorable in LIMIT-2 trial [25], but ISIS-4 trial, conducted later with a substantially larger sample, did not find an improved clinical outcome in the group treated with magnesium [26]. Also, De Oliveria et al., in a meta-analysis, reported no effect of magnesium supplementation on the incidence of postoperative myocardial infarction [27].

A limitation of this study was the inability to measure other inflammatory markers such as IL-8 and TNF due to financial obstacles.

We recommend further trials to study the correlation between the intracellular and the serum levels of magnesium and their relation to POAF after cardiac valve replacement surgery.

Conclusion

In conclusion, prophylactic use of magnesium sulfate in patients with rheumatic heart disease undergoing isolated cardiac valve replacement surgery can decrease the incidence of POAF. It may play a role in attenuating the inflammatory process associated with the use of cardiopulmonary bypass.

References

1. Aryana P, Rajaei S, Bagheri A, Karimi F, Dabbagh A (2014) Acute Effect of Intravenous Administration of Magnesium Sulfate on Serum Levels of Interleukin-6 and Tumor Necrosis Factor-alpha in Patients Undergoing Elective Coronary Bypass Graft With Cardiopulmonary Bypass. Anesth Pain Med 4: e16316.
2. LaPar DJ, Crosby IK, Rich JB, Fonner E Jr, Kron IL, et al. (2013) A contemporary cost analysis of postoperative morbidity after coronary artery bypass grafting with and without concomitant aortic valve replacement to improve patient quality and cost-effective care. Ann Thorac Surg 96: 1621-1627.
3. Maisel WH, Rawn JD, Stevenson WG (2001) Atrial fibrillation after cardiac surgery. Ann Intern Med 135: 1061-1073.
4. Kwon CH, Kim SH (2017) Intraoperative management of critical arrhythmia. Korean J Anesthesiol 70: 120-126.
5. Davis EM, Packard KA, Hilleman DE (2010) Pharmacologic prophylaxis of postoperative atrial fibrillation in patients undergoing cardiac surgery: beyond beta-blockers. Pharmacotherapy 30: 274-318.
6. Altura BM (1994) Introduction: importance of Mg in physiology and medicine and the need for ion selective electrodes. Scand J Clin Lab Invest Suppl 217: 5-9.

7. Abbas S, Khan J, Abbas A, Nassery S, Riaz w, et al. (2015) Prophylactic Magnesium and Rhythm Disorders after Open Cardiac Surgery. J Cardiol Curr Res 2: e00081.
8. Carrascal Y, Arnold RJ, De la Fuente L, Revilla A, Sevilla T, et al. (2016) Efficacy of atorvastatin in prevention of atrial fibrillation after heart valve surgery in the PROFACE trial (PROphylaxis of postoperative atrial Fibrillation After Cardiac surgEry). J Arrhythm 32: 191-197.
9. Wernovsky G, Wypij D, Jonas RA, Mayer JE Jr, Hanley FL, et al. (1995) Postoperative course and hemodynamic profile after the arterial switch operation in neonates and infants. A comparison of low-flow cardiopulmonary bypass and circulatory arrest. Circulation 92: 2226-2235.
10. Naito Y, Nakajima M, Inoue H, Hibino N, Mizutani E, et al. (2006) Prophylactic effect of magnesium infusion against postoperative atrial fibrillation. Kyobu Geka 59: 793-797.
11. Klinger RY, Thunberg CA, White WD, Fontes M, Waldron NH, et al. (2015) Intraoperative Magnesium Administration Does Not Reduce Postoperative Atrial Fibrillation After Cardiac Surgery. Anesth Analg 121: 861-867.
12. Christiansen EH, Frost L, Andreasen F, Mortensen P, Thomsen PE, et al. (2000) Dose-related cardiac electrophysiological effects of intravenous magnesium. A double-blind placebo-controlled dose-response study in patients with paroxysmal supraventricular tachycardia. Europace 2: 320-326.
13. Hamid M, Kamal RS, Sami SA, Atiq F, Shafquat A, et al. (2008) Effect of single dose magnesium on arrhythmias in patients undergoing coronary artery bypass surgery. J Pak Med Assoc 58: 22-27.
14. Nurozler F, Tokgozoglu L, Pasaoglu I, Boke E, Ersoy U, et al. (1996) Atrial fibrillation after coronary artery bypass surgery: predictors and the role of MgSO4 replacement. J Card Surg 11: 421-427.
15. Tiryakioglu O, Demirtas S, Ari H, Tiryakioglu SK, Huysal K, et al. (2009) Magnesium sulphate and amiodarone prophylaxis for prevention of postoperative arrhythmia in coronary by-pass operations. J Cardiothorac Surg 4: 8.
16. Miller S, Crystal E, Garfinkle M, Lau C, Lashevsky I, et al. (2005) Effects of magnesium on atrial fibrillation after cardiac surgery: a meta-analysis. Heart 91: 618-623.
17. Toraman F, Karabulut EH, Alhan HC, Dagdelen S, Tarcan S (2001) Magnesium infusion dramatically decreases the incidence of atrial fibrillation after coronary artery bypass grafting. Ann Thorac Surg 72: 1256-1261.
18. Kiziltepe U, Eyileten ZB, Sirlak M, Tasoz R, Aral A, et al. (2003) Antiarrhythmic effect of magnesium sulfate after open heart surgery: effect of blood levels. Int J Cardiol 89: 153-158.
19. Carrio ML, Ventura JL, Javierre C, Rodriguez-Castro D, Farrero E, et al. (2012) Does post-cardiac surgery magnesium supplementation improve outcome? Magnes Res 25: 159-167.
20. Lancaster TS, Schill MR, Greenberg JW, Moon MR, Schuessler RB, et al. (2016) Potassium and Magnesium Supplementation Do Not Protect Against Atrial Fibrillation After Cardiac Operation: A Time-Matched Analysis. Ann Thorac Surg 102: 1181-1188.
21. Jorens PG, De Jongh R, De Backer W, Van Damme J, Van Overveld F, et al. (1993) Interleukin-8 production in patients undergoing cardiopulmonary bypass. The influence of pretreatment with methylprednisolone. Am Rev Respir Dis 148: 890-895.
22. Resatoglu AG, Demirturk OS, Yener N, Yener A (2004) Magnesium decreases cardiac injury in patients undergoing coronary artery bypass surgery. Ann Saudi Med 24: 259-261.
23. Rodriguez-Moran M, Guerrero-Romero F (2004) Elevated concentrations of TNF-alpha are related to low serum magnesium levels in obese subjects. Magnes Res 17: 189-196.
24. Song Y, Li TY, van Dam RM, Manson JE, Hu FB (2007) Magnesium intake and plasma concentrations of markers of systemic inflammation and endothelial dysfunction in women. Am J Clin Nutr 85: 1068-1074.
25. Woods KL, Fletcher S (1994) Long-term outcome after intravenous magnesium sulphate in suspected acute myocardial infarction: the second Leicester Intravenous Magnesium Intervention Trial (LIMIT-2). Lancet 343: 816-819.
26. Lancet (1995) ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. Lancet 345: 669-685.
27. De Oliveira GS Jr, Knautz JS, Sherwani S, McCarthy RJ (2012) Systemic magnesium to reduce postoperative arrhythmias after coronary artery bypass graft surgery: a meta-analysis of randomized controlled trials. J Cardiothorac Vasc Anesth 26: 643-650.