Intravenous magnesium sulfate prophylaxis for atrial fibrillation after coronary artery bypass surgery

Mehmet Kaplan, MD^a
Mustafa Sinan Kut, MD^a
Umit Akif Icer, MD^b
Mahmut Murat Demirtas, MD^a

Objective: Atrial fibrillation is a rhythm disorder commonly seen early after coronary artery bypass grafting, and it increases morbidity.

Methods: To investigate the effectiveness of magnesium sulfate in the prophylaxis of atrial fibrillation, we conducted a prospective, randomized, placebo-controlled clinical study on 200 consecutive patients in whom we performed elective and initial coronary artery bypass grafting operations. In each group 50% of patients underwent beating-heart operations. In the treatment group 100 patients (76 men and 24 women; mean age, 57.63 ± 9.68 years) received 24.34 mEq (3 g) of magnesium sulfate in 100 mL of saline solution that was administered over 2 hours (50 mL/h) preoperatively, perioperatively, and at postoperative days 0, 1, 2, and 3. In the control group 100 patients (74 men and 26 women; mean age, 59.96 ± 9.29 years) received only 100 mL of saline solution according to the same administration schedule as the treatment group.

Results: Atrial fibrillation developed in 15 patients from the treatment group and in 16 patients from the control group. The arrhythmia developed after 37.87 ± 12.76 and 45.26 ± 15.27 hours in the treatment and control groups, respectively. Although a significant relationship was found between low magnesium sulfate levels and increased incidence of atrial fibrillation ($P < .05$), when the incidence of postoperative atrial fibrillation is concerned, no significant difference was found between the 2 groups ($P > .05$). Also, no significant difference was found between operations with cardiopulmonary bypass and beating-heart operations in terms of atrial fibrillation incidence ($P > .05$). However, atrial fibrillation extended the duration of hospital stay in both groups ($P < .05$).

Conclusion: Our findings indicate that magnesium sulfate infusion alone is not sufficient for the prophylaxis of atrial fibrillation.

From the Departments of Cardiovascular Surgery^a and Biochemistry,^b Siyami Ersek Thoracic and Cardiovascular Surgery Center, Istanbul, Turkey.

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Address for reprints: Mehmet Kaplan, MD, 67. Ada Kardelen 4-4, D: 11 Atasehir, 81120 Istanbul, Turkey (E-mail: mehmetkaplan@superonline.com).

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trial fibrillation is among the common complications seen early after coronary artery bypass grafting (CABG). Its mechanism of development has not been clearly defined, and its frequency increases with older age. The frequency of atrial fibrillation has not decreased despite recent developments in cardiac surgical techniques, anesthetic management, and myocardial protection. It generally occurs between 24 and 96 hours postoperatively, being seen most commonly on the second postoperative day. Atrial fibrillation potentially leads to complications, including early and midterm thromboembolic events, hemodynamic disorders, extended duration of hospitalization, and increased costs. It is not only a rhythm disturbance, but also quite a serious morbidity factor because of its complications, and therefore prophylaxis is very important.¹

Until now, many pharmacologic agents have been used to prevent atrial fibrillation. In most but not all studies, β -blockers² and amiodarone¹ have been shown to

decrease the development of postoperative atrial fibrillation. In only 3³⁻⁵ of the randomized controlled clinical magnesium sulfate trials¹⁻¹⁰ relevant to this issue, magnesium sulfate was suggested to decrease the postoperative development of atrial fibrillation.

In this study we aimed to investigate the effectiveness of magnesium sulfate in the prophylaxis of atrial fibrillation and discuss the subject in light of published data.

Patients and Methods

To investigate the effect of magnesium sulfate on the development of postoperative atrial fibrillation, we conducted a prospective, randomized, placebo-controlled trial in 200 consecutive patients who underwent elective and initial CABG operations in our center. The study was approved by the hospital ethics committee, and informed consent was obtained from all patients. Operations and management of atrial fibrillations were performed by the same surgical team.

In the treatment group (n = 100) 24% of the patients were women, and 76% were men; the average age was 57.63 ± 9.68 years (range, 41-76 years). The control group also consisted of 100 patients (74 men and 26 women; mean age, 59.56 ± 9.29 years; age range, 44-80 years). All patients underwent elective CABG. They all had sinus rhythm preoperatively. Fifty percent of operations in both the treatment and control groups were beating-heart operations.

EuroSCORE (European System for Cardiac Operative Risk Evaluation) was used for preoperative risk scoring. According to EuroSCORE, preoperative mean predicted risk score was 1.75% for the treatment group (0.08% for 54 patients, 3% for 42 patients, and 11.2% for 4 patients), whereas it was 2.15% for the control group (0.08% for 60 patients, 3% for 29 patients, and 11.2% for 11 patients).

There was no difference between the 2 groups in terms of preoperative use of β -blocker ($P = .717$), calcium-channel blocker ($P = .661$), angiotensin-converting enzyme inhibitor ($P = .650$), or digoxin ($P = .470$, binary logistic regression analysis). The 2 groups did not differ in terms of other preoperative characteristics. Data related to cases are summarized in Table 1. For determination of the effect of magnesium sulfate on atrial fibrillation incidence and to provide homogeneity for additional medication use, preoperative β -blockers were continued until 1 day before the operation, they were discontinued by the initiation of magnesium sulfate administration, and β -blocker administration was not used unless it was necessary. No statistically significant difference was found in either group (treatment and control) between patients who used β -blockers preoperatively and those who did not use them in terms of atrial fibrillation development.

Magnesium sulfate was administered each time as an infusion of 24.34 mEq (= 3 g = 2 ampules [1 ampule = 12.17 mEq = 1.5 g]) in 100 mL of saline solution for a duration of 2 hours and with a rate of 50 mL/h. This dose was administered 12 hours before the operation to all patients, after termination of cardiopulmonary bypass in patients who were operated on with cardiopulmonary bypass, and after anastomosis of the last graft in patients who underwent beating-heart operations (perioperative dose), and it was repeated in all cases at postoperative days 0 (first dose administered postoperatively in the intensive care unit), 1, 2, and 3.

TABLE 1. Preoperative characteristics of patients and analysis of influence of these parameters on atrial fibrillation development

Variables	Treatment group (n = 100)	Control group (n = 100)	P value
Age*	57.63 ± 9.68	59.56 ± 9.29	—
Patients >60 years, of age (%)	47	54	
Patients >60 years, of age among patients with AF (%)	62.5	77.7	.174
Sex			
Male	76	74	—
Female	24	26	.183
Previous myocardial infarction (%)	62	58	.637
Hypertension (%)	45	54	.608
Diabetes mellitus (%)	17	23	.550
Hypercholesterolemia (%)	36	38	.155
LVEF (%)			
>50	36	41	—
30-50	40	38	—
<30	24	21	—
<50			.620
Mean magnesium sulfate level*	1.95 ± 0.38	1.96 ± 0.42	
Effect of low MgSO ₄ level (<1.8 mg/dL) on development of AF			.003

AF, Atrial fibrillation; LVEF, left ventricular ejection fraction.

*Mean ± SD.

The timing and dosage of magnesium sulfate administration were as follows. Because preoperative magnesium sulfate levels were close to the lower limit of normal in both groups, magnesium sulfate was administered preoperatively to all patients. Magnesium sulfate was administered perioperatively to patients who undergo cardiopulmonary bypass because hypomagnesemia is generally observed in these patients, and it was also administered perioperatively to patients who underwent beating-heart operations to provide a standard. Because magnesium sulfate decreases to its minimal level usually at the first postoperative day and it usually does not return to normal levels before the fourth postoperative day, magnesium sulfate was also given at days 0, 1, 2, and 3. Dosage was determined in the view of the current literature and clinical experience.

We preferred the intravenous route instead of the oral route to attain a rapid and effective result. Because we had to administer the drug in the operating room through the intravenous route, we preferred the intravenous route during both the preoperative and postoperative periods to provide a standard for administering magnesium sulfate.

Only 100 mL of saline solution was administered to the control group for the placebo effect. In addition to magnesium sulfate replacement, patients were also given potassium so as to keep

TABLE 2. Intraoperative and postoperative characteristics of patients

Variables	Treatment group (n = 100)	Control group (n = 100)	P value
With CPB (%)	50	50	
On beating heart (%)	50	50	
No. of grafts*	1.33 ± 0.68	1.69 ± 0.63	
Duration of CPB (min)*	78.46 ± 29.14	77.66 ± 29.23	.891
In patients with AF*	85.14 ± 19.74	85.67 ± 22.97	.751
Duration of aortic CC (min)*	37.76 ± 15.48	38.04 ± 15.43	.928
In patients with AF*	44.00 ± 11.45	43.33 ± 13.24	.958
Blood transfusion (U)			
With CPB*	2.86 ± 1.48	3.02 ± 1.61	.607
On beating heart*	1.90 ± 1.29	2.02 ± 1.33	.649

AF, Atrial fibrillation; CC, aortic crossclamping; CPB, cardiopulmonary bypass.

*Mean ± SD.

TABLE 3. Supraventricular arrhythmias developing perioperatively or postoperatively in intensive care unit and wards

Variables	Treatment group (n = 100)	Control group (n = 100)	P value
Atrial extrasystoles (%)	3	5	.360
Episodes of supraventricular tachycardia (%)	2	4	.341
Atrial fibrillation (%)	15	16	.845

potassium levels at greater than 4 mmol/L. Intraoperative and postoperative characteristics of both groups are summarized in Table 2; supraventricular arrhythmias developed perioperatively and postoperatively (in the intensive care unit or wards), as shown in Table 3. Table 4 shows the timing of atrial fibrillation development and durations of intensive care unit and hospital stay.

Graphic analysis of preoperative, perioperative, and postoperative plasma magnesium sulfate levels of patients in the treatment and control groups are shown in Figure 1. In the treatment and control groups mean magnesium sulfate levels were as follows:

1. Treatment group: preoperative, 1.95 ± 0.38 mg/dL; perioperative, 2.21 ± 0.24 mg/dL; first postoperative day, 2.27 ± 0.19 mg/dL; second postoperative day, 2.39 ± 0.19 mg/dL; and third postoperative day, 2.49 ± 0.14 mg/dL.
2. Control group: preoperative, 1.96 ± 0.42 mg/dL; perioperative, 1.85 ± 0.33 mg/dL; first postoperative day, 1.76 ± 0.32 mg/dL; second postoperative day, 1.91 ± 0.29 mg/dL; and third postoperative day, 2.04 ± 0.31 mg/dL.

Concurrent matrix presentation of the relationships between blood potassium level, blood magnesium sulfate level, and heart rate in 31 patients (in 2 groups) who had atrial fibrillation is shown in Figure 2.

TABLE 4. Timing of atrial fibrillation development and durations of intensive care unit and hospital stays

Variables	Treatment group (n = 100)	Control group (n = 100)	P value
Onset of AF (h)*	37.87 ± 12.76 (15 patients)	45.26 ± 15.27 (16 patients)	.140
Length of ICU stay (h)*	22.40 ± 4.79	23 ± 4.46	.650
Length of hospital stay (d)*	5.16 ± 1.18	5.67 ± 1.31	.004
In patients with AF (d)	6.0 ± 1.2	6.31 ± 0.87	.410

AF, Atrial fibrillation; ICU, intensive care unit.

*Mean ± SD.

Exclusion Criteria

Exclusion criteria included history of atrial fibrillation, history of paroxysmal atrial fibrillation even though the patient is in sinus rhythm just before the operation, preoperative heart rate of less than 50 beats/min, concomitant valve surgery, redo coronary artery 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.

Anesthetic Management

All patients received premedication with midazolam (Dormicum) and scopolamine. Fentanyl, propofol (Diprivan), and pancuronium bromide (Pavulon) were administered for induction of anesthesia. Sevoflurane (Sevorane) 1 to 1.5 vol% was used as an inhalational anesthetic agent.

Operative Procedures

In patients in whom cardiopulmonary bypass was performed, aortic and right atrial 2-staged cannulation, systemic hypothermia (32°C), and antegrade repeated blood cardioplegia were used. In CABG operations on beating hearts, Octopus II and III cardiac stabilizers (Medtronic Inc, Minneapolis, Minn) were used. In all patients who were operated on with cardiopulmonary bypass, a membrane oxygenator (S.p.A. Mirandola, Italy) and centrifugal pump (Sarns Delphin II, Sarns, Inc, Ann Arbor, Mich) were used. During cardiopulmonary bypass, blood flow rate and systemic perfusion pressure were kept at greater than $2.5 \text{ L} \times \text{m}^{-2} \times \text{min}^{-1}$ and 50 mm Hg, respectively. The left internal thoracic artery was used for the left anterior descending artery, and a saphenous vein graft was preferred for other coronary arteries. The intraoperative use rate of the left internal thoracic artery was similar between the 2 groups.

Postoperative Data

After completion of the surgical procedure, patients were taken to the intensive care unit. Treatment group patients were extubated after an average of 4.18 ± 1.15 hours, and control group patients were extubated after an average of 4.0 ± 1.31 hours. There was no statistically significant difference between groups in terms of timing of extubation ($P = .317$, independent-samples *t* test). Patients were taken to the wards when their hemodynamic and respiratory functions were stable.

Figure 1. Graphic analysis of preoperative (*Preop*), perioperative (*Periop*), and postoperative plasma magnesium sulfate concentrations for each group.

Onset of atrial fibrillation was considered as sufficient criteria for the initiation of treatment. In our clinical practice we used amiodarone or β -blocker for patients with atrial fibrillation. In all but 2 patients, sinus rhythm was restored within 24 hours. Examinations done on the fifth postoperative day revealed that these 2 patients also returned to sinus rhythm.

Follow-up Monitoring

Rhythm was monitored continuously during the operation and during the first 2 postoperative days (Datascope 2001A, Datascope Corp, Montvale, NJ). In the wards patients were monitored with a 12-lead electrocardiography and telemetry system (Cardiac Telemetry System, DynaScope, Fukuda Denshi Co, Ltd, Tokyo, Japan) if physical examination revealed a tachycardia attack or the development of an arrhythmia or if a patient had palpitation or any rhythm-related complaint.

Arrhythmia Status

Arrhythmias that developed perioperatively or postoperatively in intensive care units or wards were classified as atrial extrasystole (3% and 5% for the treatment and control groups, respectively; $P = .360$, 2-sided Fisher exact test), supraventricular tachycardia attacks (2% and 4% for the treatment and control groups, respectively; $P = .341$, 2-sided Fisher exact test), and atrial fibrillation (15% and 16% for the treatment and control groups, respectively; $P = .845$, 2-sided Pearson χ^2 test; Table 3).

Laboratory Analysis

Blood magnesium sulfate levels were measured 12 hours and 1 hour before the operation, during the operation, 1 hour after the operation, and at the first, second, and third postoperative days (Table 2). Normal limits of magnesium sulfate level were consid-

ered to be 1.8 to 2.5 mg/dL. Potassium replacement was done to keep potassium levels between 4.0 and 5.0 mmol/L to prevent electrolyte imbalance.

Statistical Analysis

Statistical procedures were done by using SPSS 10.0 (SPSS Inc, Chicago, Ill) and MATLAB 6.0.88 Release 12 (The MathWorks, Inc, Boston, Mass) software. Data are expressed as means $\pm$ SD. The Pearson χ^2 test, the Fisher exact test, log linear analysis, the Levene f test, the independent-samples t test, the Mann-Whitney U test, binary logistic regression analysis, and multivariate linear regression analysis were used for statistical evaluation of the data.

Contribution of operation technique to the development of atrial fibrillation was evaluated with the Pearson χ^2 test. For comparing the treatment and control groups in terms of the frequency of atrial fibrillation the Pearson χ^2 test was used. For evaluating the effect of atrial fibrillation development on the duration of hospitalization in each group, comparison of 2 independent group means was aimed. The Levene f test was used for testing the homogeneity of variances, and variances were found to be homogeneous. Although group variances were homogeneous, the nonparametric counterpart of t test (Mann-Whitney U test) was used because the number of subjects to be compared (patients who did and did not have atrial fibrillation) was not equal. For comparison of mean durations of hospitalization between groups, the independent-samples t test was used (t test for equality of means, $P = .004$; 95% confidence interval of the difference [CID] lower limit of -0.8576 and CID upper limit of -0.1624). For comparison of patients who had atrial fibrillation in terms of duration of hospitalization, the independent-samples t test was used (t test for equality of means, $P = .410$; 95% CID lower limit of -1.0778 and CID upper limit of 0.4528). For comparison of independent group

Figure 2. Concurrent matrix presentation of the relationships between blood potassium level, blood magnesium sulfate level, and heart rate in 31 patients (in 2 groups) in whom atrial fibrillation developed.

ratios for atrial extrasystole and supraventricular tachycardia seen in the treatment and control groups, the Fisher exact test was used, and the Pearson χ^2 test was used for atrial fibrillation.

The Levene f test for equality of variance was done to compare intubation durations in 2 groups. Because the variances were homogeneous, the independent-samples t test was used ($P = .317$, 95% CID lower limit of -0.1710 and CID upper limit of 0.5244). Effects of cardiopulmonary bypass and aortic crossclamping durations on atrial fibrillation were assessed by using the nonparametric Mann-Whitney U test. Because of the dichotomy (nominal) characteristic of atrial fibrillation (dependent variable), the importance of risk factors for the development of atrial fibrillation was determined with binary logistic regression analysis. Independent variables were age, sex, hypertension, previous myocardial infarction, hypercholesterolemia, left ventricular ejection fraction, blood transfusion, and serum magnesium sulfate level. The relationship between atrial fibrillation and other characteristics of patients who had atrial fibrillation and had low and normal-high magnesium levels were investigated by using the log linear analysis test. No statistically significant difference was found in terms of the development rate of atrial fibrillation ($P > .05$). For assessment of the correlation between heart rate and serum magnesium sulfate level in both groups, the dependent variable was heart rate (by days), and the independent variable was serum magnesium sulfate level

(by days). The multivariate linear regression analysis was used, and no statistically significant correlation was found ($P = .158$).

Results

The primary end point of the study was postoperative development of atrial fibrillation, and secondary end points were ventricular rate at the onset of atrial fibrillation, day of onset of atrial fibrillation, and duration of hospitalization. Sex, hypertension, diabetes mellitus, hypercholesterolemia, previous myocardial infarction, disorder of left ventricular function, number of grafts, duration of aortic crossclamping, duration of cardiopulmonary bypass, magnesium sulfate level, preoperative transfusions, and postoperative transfusions did not affect the development of atrial fibrillation. The incidence of atrial fibrillation was increased 1.37 times by female sex ($P = .183$), 1.12 times by hypertension ($P = .608$), 1.11 times by previous myocardial infarction ($P = .637$), 1.12 times by left ventricular functional disorder (ejection fraction $<50\%$, $P = .620$), 1.39 times by hypercholesterolemia ($P = .155$), and 1.03 times by perioperative or postoperative transfusion (treatment group: 2.38 ± 1.47

U, control group: 2.52 ± 1.55 U; $P = .831$, binary logistic regression analysis). Risk factors, including diabetes mellitus ($P = .550$, binary logistic regression analysis), number of grafts, duration of aortic crossclamping ($P = .07$), and duration of cardiopulmonary bypass ($P = .134$, 2-tailed Mann-Whitney U test) did not influence the development of atrial fibrillation. The mean magnesium sulfate level of patients with atrial fibrillation on the day of atrial fibrillation development was 2.31 ± 0.44 mg/dL in the treatment group and 1.74 ± 0.39 mg/dL in the control group. Mean potassium levels of patients with atrial fibrillation (total of 31 patients in the treatment and control groups) were 3.85 ± 0.23 mmol/L, and their mean magnesium sulfate levels were 2.01 ± 0.50 mg/dL. In the treatment group 62.5% of patients with atrial fibrillation were older than 60 years, and in the control group 77.7% of patients with atrial fibrillation were older than 60 years. Although the incidence of atrial fibrillation development over 60 years of age was high, statistical analysis of these data revealed a P value of .174 (2-sided Pearson χ^2 test).

Magnesium sulfate administration did not cause severe bradycardia or hypotension in any of the patients. According to the EuroSCORE risk scoring system, predicted mortality rates were 1.75% and 2.15% in the treatment and control groups, respectively. The observed mortality rate was 1% in both groups (one patient in each group).

In the treatment group magnesium sulfate levels of patients with atrial fibrillation (15 patients) were low in 2 patients (both patients were operated on with cardiopulmonary bypass), normal in 9 patients (4 with cardiopulmonary bypass and 5 beating-heart operations), and high in 4 patients (1 with cardiopulmonary bypass and 3 beating-heart operations). In the control group magnesium sulfate levels of patients with atrial fibrillation (16 patients) were low in 9 patients (6 with cardiopulmonary bypass and 3 beating-heart operations) and normal in 7 patients (3 with cardiopulmonary bypass and 4 beating-heart operations).

No statistically significant difference was found when other characteristics of patients with atrial fibrillation, despite a normal or high magnesium sulfate level, were compared with the characteristics of patients with atrial fibrillation and had low magnesium sulfate levels ($P > .05$, log linear analysis).

Preoperative, perioperative, and postoperative infusion of magnesium sulfate did not cause a difference compared with that seen in the control group in terms of atrial fibrillation development ($P = .845$, Pearson χ^2 test). Low serum magnesium sulfate levels (<1.8 mg/dL; normal values, 1.8-2.5 mg/dL) significantly increased (2.66 times) the risk of atrial fibrillation development ($P = .003$, binary logistic regression analysis). However, the relationship between daily magnesium sulfate levels and heart rate was evaluated

by means of the multivariate linear regression method, and no statistically significant correlation was found ($P = .158$).

Atrial fibrillation developed after 37.87 ± 12.76 and 45.26 ± 15.27 hours in the treatment and control groups, respectively. Distribution of patients who had atrial fibrillation according to the type of surgical procedure was as follows: in the treatment group ($n = 15$), 7 (14%) with cardiopulmonary bypass and 8 (16%) beating-heart operations ($P = .78$) and in the control group ($n = 16$), 9 (18%) with cardiopulmonary bypass and 7 (14%) beating-heart operations ($P = .58$, Pearson χ^2 test). The incidence of atrial fibrillation in patients undergoing beating-heart operations was not statistically different from the atrial fibrillation incidence of patients who were operated on with cardiopulmonary bypass (treatment group: $P = .779$, control group: $P = .585$, Pearson χ^2 test).

In the treatment group atrial fibrillation development occurred at the second postoperative day in 80% of patients (12 patients, 5 with cardiopulmonary bypass and 7 beating-heart operations), at the first postoperative day in 13.3% of patients (2 patients, 1 with cardiopulmonary bypass and 1 beating-heart operation), and perioperatively in 6.7% of patients (1 patient with cardiopulmonary bypass; variable with the highest frequency = 2, 95% confidence interval = 1.4046-2.0621). In the control group, atrial fibrillation development occurred at the second postoperative day in 75% of patients (12 patients, 7 with cardiopulmonary bypass and 5 beating-heart operations), at the first postoperative day in 12.5% of patients (2 patients, 1 with cardiopulmonary bypass and 1 beating-heart operation), and at the third postoperative day in 12.5% of patients (2 patients, 1 with cardiopulmonary bypass and 1 beating-heart operation; variable with the highest frequency = 2, 95% confidence interval = 1.7248-2.2752). In the treatment and control groups, respectively, 97% and 96% of patients were discharged from the intensive care unit at the first postoperative day. Thus atrial fibrillations occurred after discharge from the intensive care unit, and therefore the effect of atrial fibrillation development on the duration of intensive care unit stay was not considered ($P = .650$, independent-samples t test). The mean duration of hospitalization was 5.16 ± 1.18 days in the treatment group and 5.67 ± 1.31 days in the control group. The difference was statistically significant ($P = .004$, independent-samples t test). The mean duration of hospitalization for patients who had atrial fibrillation was 6.0 ± 1.2 days in the treatment group and 6.31 ± 0.87 days in the control group. Development of atrial fibrillation extended the duration of hospital stay in both groups (treatment group: $P = .005$, control group: $P = .013$, 2-tailed Mann-Whitney U test). However, when patients with atrial fibrillation in each group were compared, 2 groups did not differ in terms of hospital stay ($P = .410$, independent-samples t test).

Discussion

The incidence of atrial fibrillation after CABG surgery is 10% to 40%. Although its causes are not clear, it is multifactorial; advanced age and low magnesium sulfate levels are substantial risk factors.^{11,12}

In atrial fibrillation with high ventricular response, cardiac output decreases, and oxygen consumption of the heart increases. This situation might lead to severe hemodynamic problems, particularly in patient with left ventricular dysfunction. Cardiopulmonary bypass is not responsible alone for the development of postoperative atrial fibrillation because atrial fibrillation might also be seen after CABG operations performed on the beating heart, and its incidence is not low in this group of patients. In addition to cardiopulmonary bypass, metabolic changes, body temperature, right atrial temperature, cardioplegia content and its pattern of administration, insufficient right atrial protection with cardioplegia during aortic crossclamping, electrolyte imbalances, anesthetic agents, durations of cardiopulmonary bypass and aortic crossclamping, suture technique for atrial cannulation, stress, atrial enlargement, atrial infarction, local surgical trauma, local pericardial inflammation, pericardial dissection, age-related atrial atrophic changes, and discontinuation of preoperatively used β -blockers might also contribute to the development of atrial fibrillation.^{10,13} In our study atrial fibrillation developed in 16% ($n = 8$) and 14% ($n = 7$) of patients (treatment and control groups, respectively) undergoing beating-heart operations. However, no statistically significant difference was found between patients who were operated on with cardiopulmonary bypass and those undergoing beating-heart operations in terms of postoperative atrial fibrillation development.

Atrial fibrillation alone does not cause mortality; however, it might lead to hemodynamic disorders, thromboemboli and severe arrhythmia, perioperative morbidity (eg, myocardial infarction and stroke), early and midterm mortality, extended duration of intensive care unit stay and hospitalization, and increased costs.^{8,14} No thromboembolic complications developed in our series, despite development of atrial fibrillation in 15% of the treatment group and 16% of the control group. In the treatment group 97% of patients and in the control group 96% of patients were discharged from the intensive care unit at the first postoperative day. Development of atrial fibrillations occurred after discharge from the intensive care unit in the wards, and therefore influence of atrial fibrillation development on the duration of intensive care unit stay was not evaluated. In the treatment group 80% of atrial fibrillations developed at the second postoperative day, whereas in the control group 75% of them occurred at the second postoperative day (at an average of 37.87 ± 12.76 and 45.26 ± 15.27 hours in the treatment and control groups, respectively).

The mean duration of hospitalization was 5.16 ± 1.18

and 5.67 ± 1.31 days in the treatment and control groups, respectively. For patients who had atrial fibrillation, the duration was 6.0 ± 1.2 days in the treatment group and 6.31 ± 0.87 days in the control group. As a result, atrial fibrillation extended the duration of hospitalization in both groups.

The effectiveness of β -blockers and amiodarone in the prophylaxis for atrial fibrillation has been proved.^{1,2} For magnesium sulfate, however, it was suggested that it decreases³⁻⁵ or does not affect^{1,2,9,10} the incidence of atrial fibrillation after CABG operations; some authors even suggested that atrial fibrillation was provoked, and its incidence was increased in patients with high magnesium sulfate levels.⁸ We concluded, in our study, that magnesium sulfate is not solely effective in the prophylaxis of atrial fibrillation.

A low magnesium sulfate level is arrhythmogenic because a decrease in magnesium sulfate level increases the sensitivity of atrial myocardium, and arrhythmias such as atrial fibrillation might develop. In patients who had atrial fibrillation with a low magnesium sulfate level, this arrhythmia is managed with magnesium sulfate infusion.¹⁵

Patients who undergo cardiopulmonary bypass have hypomagnesemia. Postoperative hypomagnesemia is frequently associated with atrial arrhythmias and extended duration of intubation. Magnesium sulfate reaches its minimum level at the first postoperative day. Magnesium sulfate deficiency is due to hemodilution and intraoperative and postoperative cellular depletion. Diuretic use, secondary hyperaldosteronism, high levels of epinephrine, increased anabolic activity, extreme stress caused by sympathetic activity, and increased urinary loss contribute to this decrease. Magnesium sulfate reaches its preoperative values at the fourth postoperative day.^{1,10} These findings indicate the need for magnesium sulfate supplementation after and during cardiac surgery.^{16,17}

Some literature data suggest that preoperative high-dose magnesium sulfate administration protects the cell during ischemia and decreases the reperfusion injury. It was also suggested that it also decreases the incidence of myocardial infarction and supraventricular arrhythmia seen after cardiac surgery. Magnesium sulfate decreases afterload, provides coronary vasodilatation, decreases platelet aggregation, and protects the cell against ischemia and reperfusion.² Low magnesium sulfate levels are also associated with the development of postoperative ventricular arrhythmias.^{2,18}

Magnesium sulfate suppresses the cardiac arrhythmia seen during acute myocardial infarction.¹⁹ Rasmussen and colleagues²⁰ found that magnesium sulfate prophylaxis provided a decrease from 47% to 21% in all arrhythmias. Abraham and associates²¹ 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%. Hypomag-

TABLE 5. Studies investigating the effect of magnesium sulfate on the incidence of atrial fibrillation that develops after coronary artery bypass grafting operations

Reference	Study groups (n)	Total Mg dosage (g)	AF/AT (%)	Effect of Mg on AF or AT
Fanning et al ⁷	Mg, n = 49 C, n = 50	21 g, during 4 d	Mg: 14.2% C: 28%	No significant difference; only total number of AF episodes decrease
England et al ⁶	Mg, n = 50 C, n = 50	2 g, over 30 min	Mg: 34% C: 40%	No significant difference; if Mg is normal, AT incidence decreases
Parikka et al ⁸	Mg, n = 69 C, n = 71	17.5 g, during 48 h	Mg: 29% C: 26%	No significant difference; if Mg increases, AF incidence increases
Colquhoun et al ⁵	Mg, n = 66 C, n = 64	12 g, during 48 h	Mg: 16.7% C: 37.5%	Significant difference
Karmy-Jones et al ⁹	Mg, n = 46 C, n = 54	14.4 g, over 24 h	Mg: 26% C: 24%	No significant difference
Nurozler et al ³	Mg, n = 25 C, n = 25	25 g, during 5 d	Mg: 4% C: 20%	Significant difference
Solomon et al ¹⁰	P + Mg, n = 85 P, n = 82	18 g, over 24 h	P + Mg: 10% P: 18.5%	No significant difference
Treggiari-Venzi et al ¹	Mg, n = 47 A, n = 49 C, n = 51	12 g, during 72 h	Mg: 23% A: 14% C: 27%	No significant difference
Bert et al ²	Mg, n = 63 C, n = 60 D, n = 62 D + Mg, n = 62 P, n = 71 P + Mg, n = 69	12 g, during 96 h	Mg: 38% C: 38% D: 31% D + Mg: 37% P: 18% P + Mg: 19%	No significant difference
Toraman et al ⁴	Mg, n = 100 C, n = 100	7.3 g, during 5 d	Mg: 2% C: 21%	Significant difference

Mg, magnesium; AF, atrial fibrillation; AT, atrial tachyarrhythmias; C, control; P, propranolol; A, Amiodarone; D, digoxin.

The cited studies were clinical randomized controlled trials.

nesemia is frequently seen during acute myocardial infarction. Magnesium sulfate decreases the mortality in 2 to 4 weeks after acute myocardial infarction.¹⁰

In our study the incidence of postoperative atrial fibrillation in the treatment group for hypomagnesemic patients was 13.3% (2/15, 1.4 ± 0 mg/dL). In addition, atrial fibrillation also developed in 9 (60%) patients with normal or 4 (26.7%) patients with high levels of magnesium sulfate. In the control group 9 (56.25%) of 16 patients who had atrial fibrillation had low magnesium sulfate levels (1.43 ± 0.125 mg/dL), whereas 7 (43.75%) of them had normal levels. When the incidence of atrial fibrillation was compared between patients with low and normal magnesium sulfate levels, it was found that atrial fibrillation incidence was significantly increased in patients with low levels.

Maslow and colleagues²² reported that atrial fibrillation could develop in CABG surgery done on beating hearts and intraoperative administration of magnesium sulfate decreased the incidence of postoperative atrial tachyarrhythmia; they recommended intraoperative supplementation of magnesium sulfate. In our study the incidence of atrial fibrillation in patients undergoing beating-heart operations was not statistically different from that of patients operated on with cardiopulmonary bypass.

A study by Jensen and colleagues²³ that investigated electrolyte changes in right atrial and skeletal muscles (pre-operative, intraoperative, and postoperative) found that magnesium sulfate did not decrease in skeletal muscle and atrial muscle, but its serum level was decreased.

England and colleagues⁶ demonstrated that hypomagnesemic patients had higher supraventricular arrhythmia incidence. We found that a low magnesium sulfate level (significant when < 1.8 mg/dL) increases the incidence of atrial fibrillation 2.66 times. Parikka and associates⁸ found that magnesium sulfate was not helpful in the prophylaxis of atrial fibrillation, and they even demonstrated that atrial fibrillation became more prevalent in patients with a high magnesium sulfate level. Fanning,⁷ Karmy-Jones,⁹ and their associates could not find a significant difference between treatment and control groups in terms of incidence of atrial fibrillation development. Fanning and coworkers⁷ only found in their study that the total number of atrial fibrillation episodes was decreased. We also could not find any difference between treatment and control groups with this respect. Studies related to the effect of magnesium sulfate on the incidence of supraventricular arrhythmia after CABG are summarized in Table 5.¹⁻¹⁰

In conclusion, atrial fibrillation, which develops early

after CABG 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. Although low blood magnesium sulfate level increases the incidence of atrial fibrillation, a significant benefit for prevention of atrial fibrillation could not be attained with only routine administration of magnesium sulfate. Intravenous magnesium sulfate administration has a role in the treatment of atrial arrhythmia; however, its administration alone is not sufficient for the prophylaxis of atrial fibrillation.

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