

# Magnesium Sulfate Reduces Incidence of Atrial Fibrillation after Coronary Arterial Bypass Surgery: What Is the Proper Dose? A Randomized Trial

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**Background:** Atrial fibrillation (AF) is a common complication after cardiac surgery and impacts length of hospital stay, greater utilization of health care resources, and increases morbidity and mortality. Magnesium sulfate ( $MgSO_4$ ) has been well documented in its effect of AF reduction after cardiac surgery especially in coronary artery bypass grafting (CABG) but the dosages are still not settled.

**Material and Method:** Eighty-eight elective CABG cases were randomized to receive a high dose (10 gm) or low dose (5 gm)  $MgSO_4$  and were blinded into bottle 1 ( $n = 46$ ) and bottle 2 ( $n = 42$ ). Patients were closely observed with continuous ECG monitoring in the first 24 hours then observed for clinical symptoms until discharge.

**Results:** The demographic data were comparable except for a higher body weight in the high dose group ( $60.21 \pm 11.32$  kg vs.  $65.85 \pm 12.2$  kg,  $p = 0.03$ ) and higher incidence of diabetes in high dose group (52.4% vs. 28.3%,  $p = 0.02$ ). Intraoperative data were similar. No complications were related to  $MgSO_4$  except one patient in the high dose group that experienced flushing and abdominal discomfort during administration. Immediate postoperative serum magnesium was higher in the high dose group but rapidly returned to similar level one day postoperatively. AF occurred in nine patients (10.23%), four in the low dose and five in the high dose group and there was no statistical significance ( $p = 0.62$ ).

**Conclusion:** Current data suggested the safety and effectiveness of  $MgSO_4$  for the reduction of the incidence of AF during postoperative CABG surgery. However, there was no statistical difference between the dosages of  $MgSO_4$  supplement. The 5-gm- $MgSO_4$  supplement was effective in AF prevention and could avoid the adverse effect from high dose  $MgSO_4$  infusion.

**Clinical trials registration number:** TCTR20140122001

**Keywords:** Magnesium sulfate, Atrial fibrillation, CABG, Cardiac surgery

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Atrial fibrillation (AF) is a common complication after cardiac surgery with incidence ranges between 25 and 40%. AF impacts on length of hospital stay (LOS), greater utilization of health care resources, increases morbidity, and mortality<sup>(1)</sup>.

Despite improving myocardial protection and surgical techniques, the incidence of AF after coronary artery bypass grafting (CABG) remains essentially unchanged. Multiple types of medications have been used to reduce the risk of AF. Magnesium sulfate ( $MgSO_4$ ) is an effective medication with fewer side effects when compared to other medications. Magnesium (Mg), the second most abundant

intracellular cation, is central to the viability of all cells. It acts as a co-factor of more than 260 enzymes in the body especially ATPase, phosphatase and kinase<sup>(1)</sup>. In patients after cardiac surgery, the serum Mg level was well documented as low in many studies and associated with increased morbidity and mortality. The cardiopulmonary bypass (CPB) machine was one of the most significant factors of low serum Mg level because of hemodilution from the priming volume of the CPB system and renal loss from hypervolemia<sup>(2,3)</sup>. Even when the effect of CPB in off-pump coronary artery bypass grafting (OPCAB) was eliminated, the incidence of AF was significantly reduced in one study but remained high compared to other types of surgery<sup>(4)</sup>. The pathophysiologic cause of AF remains unclear. Mg supplement has been postulated as effective and has less adverse effects as an AF prophylaxis medication<sup>(5)</sup>. Many meta-analyses have been published about the

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effectiveness of Mg supplements<sup>(5,6)</sup> but when focused on the OPCAB group, only one study had been published and the results showed no effect in preventing AF<sup>(7)</sup>.

A milestone review regarding pros and cons of MgSO<sub>4</sub> administration documented the percentage of AF reduction but there is no published randomized controlled trial directly designed to compare dosage and timing<sup>(1,8)</sup>. The present study was designed to determine whether high dose (10 gm) or low dose (5 gm) was more effective.

## Material and Method

### Patients

The study was approved by the Institutional Human Investigation Committee, Faculty of Medicine, Chiang Mai University, Clinical trials registration number TCTR20140122001, and written informed consent was obtained from all subjects.

We prospectively recruited 88 patients with coronary artery disease that required an elective coronary arterial bypass grafting operation without any excluded cases between August 2008 and February 2012 at Maharaj Nakorn Chiang Mai Hospital. The exclusion criteria included the following:

1. Sick sinus syndrome
2. Second or third degree atrioventricular block
3. History of AF
4. Any other surgical procedure during the current admission
5. Q-wave myocardial infarction in the preceding six weeks
6. Ongoing treatment with amiodarone, digoxin, or warfarin
7. Permanent pacemaker implantation
8. Valvular regurgitation
9. Renal failure (serum creatinine >2.0 mg/dl)
10. Preoperative serum Mg level >4.0 mEq/L

Sample size was calculated according to meta-analysis by Miller et al<sup>(6)</sup> in 2005 using the two proportion formula ( $n/\text{group} = 2P(1-P)(Za+Zb)^2/(PT-PC)^2$ ). The result is 3,518 cases per group. However, the authors also mentioned about high heterogeneity in the study, which might not be able to use as reference. We designed this study as pilot study and institute's Ethic Committee allowed to recruit 40 to 50 cases per group for this study.

All patients were stratified and computerized randomized according to surgeons performing the operation into bottle 1 and bottle 2 groups. The demographic characteristics of patients, preoperative

echocardiographic data, preoperative serum potassium and Mg levels, types of operation and operative data were summarized in Table 1. Most of demographic and preoperative characteristics were not different, except higher body weight and more diabetic patients in the high dose group with statistical significance (low dose group: 28.3% and high dose group: 52.4%,  $p$ -value = 0.02).

### Drugs preparation and administration

MgSO<sub>4</sub> was transferred to a new bottle without a printed label by the hospital pharmacist, so, all study personnel and participants were blinded to treatment assignment for the duration of the study. The high dose MgSO<sub>4</sub> solution was mixed from 10 gm of MgSO<sub>4</sub> in NSS 25 ml per bottle and low dose was mixed from 5 gm of MgSO<sub>4</sub> in NSS 25 ml per bottle. The drug was mixed with 100 ml. normal saline solution by blinded on-duty nurses at common ward then given to patient intravenously by infusion pump within four hours the night before the operation. The concealed letter will be opened after all the subjects were recruited and the analytic process was completed.

### Data of operation

All patients underwent general anesthesia with central line insertion and arterial line monitoring. In the cases with left ventricular dysfunction or more severe disease (more than double vessel disease) or unstable preoperative clinical status, a Swan-Ganz catheter was inserted for close and precise hemodynamic monitoring.

Due to differences in our surgical staffs' preference in the types of CABG (OPCAB, on-pump beating heart technique, or completely arrested heart CABG), all patients were stratified into three groups according to surgeons performing the operation and then randomized into the low dose group or high dose group. All patients underwent isolated elective coronary arterial bypass surgery using a standard sternotomy approach. The decision to proceed with OPCAB versus conventional on-pump or on-pump beating heart revascularization was based on the surgeon's judgment. In the cases that required CPB, we used direct ascending aortic cannulation and two-stage venous cannulation through the right atrial appendage in all cases with additional left ventricular venting through the right superior pulmonary vein for emptying the left ventricle. In the conventional arrested heart CABG, we used both antegrade (via aortic root vent) and retrograde cardioplegia in all cases. In all

**Table 1.** Demographic data and preoperative patient characteristics

Parameters	Low dose (n = 46)	High dose (n = 42)	p-value
Male:female, n (%)	29 (63.00):17 (37.00)	30 (71.40):12 (28.60)	0.40
Age (years), mean ± SD	62.02±9.57	60.17±10.00	0.37
Weight (kg.), mean ± SD	60.21±11.32	65.85±12.20	0.03*
Height (cm.), mean ± SD	156.65±8.69	158.86±7.41	0.21
Diabetes, n (%)	13 (28.30)	22 (52.40)	0.02*
Fasting blood sugar (mg/dl), mean ± SD	102.93±28.79	109.71±29.58	0.27
Dyslipidemia, n (%)	41 (89.10)	36 (85.70)	0.63
LDL level (mg/dL), mean ± SD	100.20±24.62	112.21±82.87	0.35
Renal insufficiency, n (%)	3 (6.50)	5 (11.90)	0.38
Creatinine (mg/dl), mean ± SD	1.13±0.19	1.20±0.28	0.22
Smoking history, n (%)			0.55
Non-smoker	26 (56.50)	22 (52.40)	
Ex-smoker	19 (41.30)	20 (47.60)	
Current-smoker	1 (2.20)	0 (0.00)	
COPD, n (%)	0 (0.00)	1 (2.38)	0.29
Percutaneous coronary angioplasty (PTCA), n (%)	0 (0.00)	2 (4.80)	0.13
Severity of coronary artery disease, n (%)			0.93
Single vessel	3 (6.52)	2 (4.76)	
Double vessels	6 (13.04)	6 (14.29)	
Triple vessels	37 (80.43)	34 (80.95)	
CCS angina grading, n (%)			0.49
1	8 (17.40)	7 (16.70)	
2	27 (58.70)	25 (59.50)	
3	11 (23.90)	8 (19.10)	
4	0 (0.00)	2 (4.80)	
NYHA, n (%)			0.67
I	18 (39.13)	19 (45.24)	
II	24 (52.17)	18 (42.86)	
III	4 (8.70)	5 (11.90)	
IV	0 (0.00)	0 (0.00)	
Ejection fraction (%), mean ± SD	0.59±0.13	0.58±0.12	0.68
LVESD (cm), mean ± SD	3.05±0.80	3.19±0.85	0.43
LVEDD (cm), mean ± SD	4.82±0.88	4.89±0.81	0.71
Left atrium size (cm), mean ± SD	3.68±0.65	3.87±0.59	0.16
Preoperative potassium (K) (mmol/L), mean ± SD	3.72±0.66	3.78±0.66	0.66
Preoperative magnesium (Mg) (mEq/L), mean ± SD	2.03±0.21	2.16±1.15	0.44

COPD = chronic obstructive pulmonary disease; CCS = Canadian Cardiovascular Society grading of angina; NYHA = New York Heart Association functional classification; LVESD = left ventricular end-systolic diameter; LVEDD = Left ventricular end-diastolic diameter

\* Statistically significant p-value <0.05

cases that required CPB, additional MgSO<sub>4</sub> may have been added in the circuit by the perfusionists that may not be recorded clearly in the database. However, according to randomization method, the chance of receiving additional MgSO<sub>4</sub> by perfusionist should be similar in both groups. Overall data such as types of

operation, operative time, and numbers of bypass vessels were not statistically different (Table 2).

#### **Postoperative follow-up**

At the end of the surgical procedure, all of patients were transferred to the ICU, and were weaned

**Table 2.** Operative data, comparing between groups

Parameters	Low dose (n = 46)	High dose (n = 42)	p-value
Operation, n (%)			0.43
OPCAB	26 (56.52)	18 (42.86)	
On-pump beating heart CABG	11 (23.91)	14 (33.33)	
Conventional CABG	9 (19.57)	10 (23.81)	
Number of anastomosis, mean ± SD	3.75±1.29	3.70±0.82	0.92
Operative time (minutes), mean ± SD	246.26±64.99	258.14±69.83	0.41
CPB time in minute (included only on-pump group), median (IQR)	81 (59.50)	83 (70.00)	0.54
Aortic cross clamp in minute (included only conventional CABG), median (IQR)	70 (27.00)	79 (18.00)	0.25

OPCAB = off-pump coronary artery bypass grafting; CABG = coronary artery bypass grafting; CPB = cardiopulmonary bypass; IQR = interquartile range

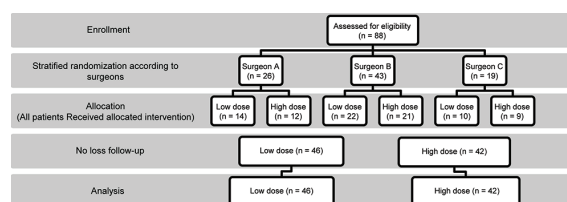
from the ventilator as soon as they met the following criteria: hemodynamic stability, no major bleeding, normothermia, and consciousness with adequate pain control. Weaning from catecholamine infusions was guided by standard hemodynamic criteria. Intravenous potassium was given to maintain a serum concentration greater than 4 mmol/L. Additional doses of Mg were also given to maintain serum concentration greater than 2.0 mEq/L. In all patients, antiplatelet drugs were started within the first 24 hours after surgery. Patients received general standard postoperative care that included routine immediate Mg and potassium levels, which were repeated the first postoperative morning. All patients were extubated and hemodynamically stable before returning to the general ward. The patient electrocardiogram (ECG) was monitored continuously for at least 48 hours postoperatively. The study primary end point was any episode of documented (12-lead ECG) postoperative in-hospital AF, defined as an irregular rhythm with an irregular fluctuating baseline, without well-defined P-waves and irregular RR intervals. Only sustained episodes (>10 minutes) or those requiring medical attention because of patient instability were considered. If AF or flutter occurred, a 12-lead ECG was performed and reviewed by the research staff. AF was managed by the attending physician. Prescription of drugs for rate control or cardioversion was routinely performed, and not influenced by the study investigators. Amiodarone will be given only if there is AF occurred and no patient would receive amiodarone from the other indications. The technique of conversion depended on each individual patient's clinical status and hemodynamics. After discharge, patients were followed-up at two weeks with a 12-lead ECG performed at that visit.

### Statistical analysis

The authors intended to analysis as per protocol. If there is any protocol violation or deviation, that subject will be excluded from the analysis. The data were recorded and processed with STATA version 11 (STATA Corporation, College Station, TX). The categorical data were calculated with Chi-square test and reported as percent. The continuous data were calculated depended on its distribution. Parametric and non-parametric distributions were analyzed by student t-test and Mann-Whitney U test respectively. Comparison between groups was analyzed by logistic regression. Significant differences between groups were considered when the p-value was less than 0.05.

### Results

Between August 2008 and February 2012, 88 patients were randomly assigned to receive either perioperative high dose Mg supplementation (10 gm) or low dose Mg supplementation (5 gm) blinded as bottle 1 and bottle 2 groups. Baseline demographic data and clinical characteristics of the two groups were similar (Table 1). The two groups of patients had a similar Canadian classification, NYHA functional class, severity of disease (number of vessel involvement), preoperative serum Mg and potassium, and preoperative echocardiographic results. The



**Fig. 1** Flow diagram of research method.

**Table 3.** Postoperative data, comparing between groups

Parameter	Low dose (n = 46)	High dose (n = 42)	p-value
Inotrope usage, n (%)	17 (36.96)	23 (54.76)	0.09
Immediate postoperative K (mmol/L), mean ± SD	3.84±0.44	3.84±0.52	0.99
Immediate postoperative Mg (mEq/L), mean ± SD	2.62±0.54	3.13±0.67	0.01*
K level next morning (mmol/L), mean ± SD	4.19±0.47	4.17±0.38	0.83
Mg next morning (mEq/L), mean ± SD	2.49±0.49	2.57±0.43	0.40
AF occurrence, n (%)	4 (8.7)	5 (11.9)	0.62
Median postoperative length of stay in days (range)	4 (3-36)	4 (4-19)	0.35
Median postoperative length of ICU stay in days (range)	1 (1-5)	1 (1-3)	0.79

AF = atrial fibrillation; ICU = intensive care unit

preoperative Mg plasma level was not different between the groups (2.03±0.21 mEq/L in low dose group and 2.16±1.15 mEq/L in high dose group). One patient in the high dose group experienced flushing and abdominal discomfort during administration, which gradually resolved with a decrease in the infusion rate.

Intraoperative data are shown in Table 2, and postoperative data in Table 3. Both groups have similar intraoperative data including types of operation, numbers of coronary arterial anastomosis and operative time. The mean number of grafts per patient was 3.75±1.29 in the low dose group and 3.7±0.82 in the high dose group.

Both groups also had similar postoperative data including immediate and next morning postoperative serum Mg and potassium level. The immediate postoperative serum Mg was statistically higher in the high dose group (low dose group: 2.62±0.54 mEq/dl, high dose group: 3.13±0.67 mEq/dl,  $p = 0.01$ ) but rapidly returned to a similar level the morning after surgery. The length of ICU stay and LOS were also similar.

AF or flutter developed in nine of 88 patients (10.23%) during their hospital stay. Both groups of patients had a similar incidence of postoperative in-hospital AF: four of 46 patients (8.7%) in the low dose group and five of 42 (11.9%) in the high dose group ( $p = 0.62$ , Table 3). The onset of AF in all nine patients occurred within four days after surgery (eight cases occurred within 72 hours, and one case occurred on the fourth postoperative day). All of them were converted with intravenous amiodarone and then prescribed oral amiodarone continuously for three months. At 2-weeks follow-up, all patients were performed 12-lead ECG and the results showed normal sinus rhythm in every cases.

**Table 4.** Atrial fibrillation occurrence in each subgroup

Parameter	Low dose (n = 46)	High dose (n = 42)	p-value
Atrial fibrillation, n (%)			
No	42 (91.30)	37 (88.70)	0.62
Yes	4 (8.70)	5 (11.90)	
Sex, n (%)			
Male	3 (10.34)	3 (10.00)	0.96
Female	1 (5.88)	2 (16.67)	0.35
Operation, n (%)			
OPCAB	3 (11.54)	2 (11.11)	0.97
On-pump beating heart CABG	1 (9.09)	3 (21.43)	0.40
Conventional CABG	0	0	NA
Inotrope usage, n (%)			
No	1 (3.45)	3 (15.79)	0.13
Yes	3 (17.65)	2 (8.70)	0.40
DM, n (%)			
No	3 (9.09)	1 (5.00)	0.58
Yes	1 (7.69)	4 (18.18)	0.39

DM = diabetes mellitus; NA = not available

Subgroup analysis in AF group revealed that five of the nine cases occurred in the OPCAB group (5/46 cases, 10.8%). Surprisingly, no AF occurred in the conventional CABG operation, even in the high dose or low dose group. None of the 88 patients had a stroke or any major neurologic event. No patient died in the hospital. There was no serious adverse drug event. The mean length of postoperative hospital stay was 5.2 days, with a longer stay for the AF group (5.8±3.8 days) than in the non-AF group (4.6±2.8 days).

Calculating the odds ratio of AF (Table 5) revealed the risk factors of AF as female gender, diabetic patients and no inotropic usage. However, all risk factors showed no statistical significance.

**Table 5.** Odds ratio of AF and subgroups patients between treatment groups

Parameter	OR	95% CI	p-value
Female	3.20	0.26-40.05	0.37
Inotrope usage	0.44	0.07-3.01	0.41
DM	2.67	0.26-26.86	0.41

## Discussion

Mg is important in the regulation of vascular tone, heart rhythm, and platelet-activated thrombosis and Mg supplementation may reduce mortality after myocardial ischemia-reperfusion injury. Mg is important in the maintenance of normal cellular and body function and is one of the most important cations in body metabolism. Significant roles for Mg include being an important cofactor for energy metabolism, and secretion of enzymes such as adenylcyclase and hormones such as parathormone. MgSO<sub>4</sub> replacement has cardioprotective and calcium antagonist effects, and increases cardiac output by decreasing systemic vascular resistance and increasing diastolic relaxation. Since Mg is an essential cofactor for the maintenance of myocardial transmembrane potential, its deficiency decreases the threshold for arrhythmias<sup>(8)</sup>.

The CPB machine contributes to a low serum Mg level because of hemodilution from the priming volume of the CPB system and renal loss from hypervolemia<sup>(4,8)</sup>. Even when the effect of CPB in OPCAB was eliminated, the incidence of AF was significantly reduced in data from one meta-analysis but remained high compared to other types of surgery. (The incidence of AF was 19% (1,612/8,265) in the off-pump group vs. 24% (1,976/8,240) in the on-pump group).

Some previous studies had also focused on AF after OPCAB techniques<sup>(9)</sup>. When an OPCAB technique is used to revascularize the heart, the incidence of these arrhythmias remains unchanged despite avoidance of cannulation, aortic cross-clamping, and cardioplegia. There was large multifactor that attributed to rhythm disturbance such as electrolyte shifts related with revascularization, temporary ischemia, perioperative trauma, epicardial inflammatory reactions, transient postoperative increases in sympathetic activity, or withdrawal of preoperative beta-blockers. Hypomagnesemia of multifactorial causes is a frequent finding after multiple types of cardiac surgery and might play a role in cellular damage.

From our result about safety of quite high MgSO<sub>4</sub> supplement was demonstrated no complication or adverse effects<sup>(10)</sup> occurred during infusion or after complete infusion that comparable to other previous studies that provided nearly or larger dose of Mg supplement. During the immediate postoperative period, there were no complications that related to MgSO<sub>4</sub> such as markedly hypermagnesemia, delayed weaning from ventilator from respiratory muscle weakness (overall ICU stay: 1.3 days, *p* = 0.48) or massive bleeding that required re-exploration.

The main result of this pilot study is that either high dose or low dose prophylaxis Mg supplementation have similar effects to the incidence of postoperative AF after coronary arterial bypass grafting surgery. There was no statistical significant difference in incidence of AF, hospital length of stay or major complications in both groups. However, when compared among 25-40%, incidence of postoperative AF after CABG in a previous study, the present study confirms that Mg supplement was also effective to prevent AF after CABG operation.

However, if focused on the on-pump CABG group, both conventional completely arrested heart and beating heart group (Table 6), the incidence of AF decreased to 9.09% (4/44 cases) which was clinically significant when compared to the incidence from previous studies (25-40%). Surprisingly, in conventional arrested heart CABG, no AF occurred postoperatively after giving prophylactic MgSO<sub>4</sub> infusion regardless of dosage, whereas we found the striking higher rate of postoperative AF in the on-pump beating heart CABG group (16%). However, this result may be confounded by intraoperative MgSO<sub>4</sub> that given by perfusionist during running CPB. On the other hand, when specified to OPCAB group, the incidence of AF was 11.36% (5/44 cases). It was slightly higher than on-pump CABG. This result is concordantly matched with previous report from Zangrillo et al, the only study that focused on OPCAB group<sup>(9)</sup>. They performed prospectively randomized 160 OPCAB cases to Mg group (n = 80) (received a 2.5-gm MgSO<sub>4</sub> infusion intraoperatively over 30 minutes), and the placebo group (n = 80). The result showed no effect in preventing AF after off-pump coronary artery bypass. Hence, Mg may be implicated in AF occurrence only in the mechanism caused by CPB could not be clearly explained in the conflicting results of on-pump beating CABG group.

From the results of multivariable analysis, it seemed like a high dose of prophylactic MgSO<sub>4</sub>

**Table 6.** Data comparing between AF and non-AF group

Type of operation	OPCAB (n = 44)	On-pump beating heart CABG (n = 25)	Conventional CABG (n = 19)	All on-pump CABG (n = 44)	p-value
Incidence of postoperative AF, n (%)	5 (11.36)	4 (16.00)	0 (0)	4 (9.09)	0.21

**Table 7.** Data comparing between AF and non-AF group

	AF group (n = 9)	Non-AF group (n = 79)	p-value
Length of ICU stay (days)	1.67	1.10	0.003*
Length of postoperative hospital stay (days)	6.44	5.37	0.54
Total cost of medical care in Thai Baht	174,644.9	158,550.3	0.23

\* Statistically significant is *p*-value <0.05

infusion could prevent AF in female gender, diabetes patients and patient without inotropic usage. Even in non-diabetic patients and patients who needed inotrope, prophylactic high dose MgSO<sub>4</sub> infusion also had a preventive effect but had not a dominant effect as in the previous groups. However, there was no statistical significance in this analysis and the small number of population made these multivariable analytic results questionable.

To determine the impact of AF on the cost of medical care (Table 7), the present study also confirmed that postoperative AF was associated with a longer hospital stay in patients undergoing CABG both length of ICU stay and length of postoperative hospital stay. Hence, the cost of medical care was higher in this group. However, there was no statistical significance in this analysis except in the length of ICU stay.

Limitations of the present study included the very small sample size. We calculated the power of study from our results by two-tailed test and it showed only 7.2% according with very small sample size in our study, which cannot yield a valid conclusion. The incidence of AF was as the reference obtained from previous study with the demonstration of the safety of high dose Mg supplement. The data could also be compared to the case-matched population in our institute for the better comparable reference.

We concluded that preoperative MgSO<sub>4</sub> administration even with high dose was safe and showed a beneficial effect as the prophylaxis of AF after coronary revascularization that seemed to be more obvious in the conventional on-pump arrested heart CABG technique. There was no statistically significant difference between the low dose and high dose group. The result from reduction of AF incidence also seemed to have positive impact on the length of stay and the medical treatment cost. However, a larger sample size is needed to provide valid data.

### What is already known on this topic?

AF is a common complication after cardiac surgery and impacts LOS, greater utilization of health care resources, increased morbidity, and mortality<sup>(1)</sup>. Hypomagnesemia was common after open heart surgery and may be the cause of AF during post-operation<sup>(2,3)</sup>. MgSO<sub>4</sub> was shown as an effective AF prophylaxis medication with less adverse effects<sup>(5)</sup> even in the OPCAB group<sup>(7)</sup>.

### What this study adds?

The dosage of Mg supplement has never been studied directly. Many clinical trials were studied between control and intervention group, however the dosage was not standardized.

A milestone reviewed regarding pros and cons of MgSO<sub>4</sub> administration documented the percentage of AF reduction but there was no published randomized controlled trial directly designed to compare dosage and timing<sup>(1,8)</sup>. This study was designed to determine whether high dose (10 gm) or low dose (5 gm) was more effective.

The result from this study showed no statistical significant difference between high dose and low dose group, so the 5-gm-MgSO<sub>4</sub> supplement was effective in AF prevention and could avoid the adverse effect from high dose MgSO<sub>4</sub> infusion.

### Potential conflicts of interest

None.

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แมกนีเซียมซัลเฟตลดอัตราการเกิด atrial fibrillation หลังการผ่าตัดหลอดเลือดหัวใจโคโรนารี: เปรียบเทียบขนาดที่เหมาะสม

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**ภูมิหลัง:** ภาวะ atrial fibrillation (AF) เป็นภาวะแทรกซ้อนที่พบบ่อยหลังการผ่าตัดหัวใจ และมีผลกระทบต่อระยะเวลาในการนอนโรงพยาบาล ค่าใช้จ่ายที่เพิ่มขึ้นจากการรักษา รวมทั้งยังเพิ่มอัตราการทุพพลภาพ และการเสียชีวิต มีการศึกษาพบว่าแมกนีเซียมซัลเฟตสามารถลดภาวะการเกิด AF หลังการผ่าตัดหัวใจโดยเฉพาะการผ่าตัดทำทางเบี่ยงหลอดเลือดหัวใจ แต่ขนาดของยาที่ใช้ยังไม่ได้ระบุชัดเจน

**วัตถุประสงค์และวิธีการ:** ผู้ป่วยที่เข้ารับการผ่าตัดทำทางเบี่ยงหลอดเลือดหัวใจจำนวน 88 ราย ได้รับการสุ่มแยกผู้ป่วยเป็นสองกลุ่มเพื่อได้รับยาแมกนีเซียมซัลเฟตขนาดสูง (10 กรัม) และขนาดต่ำ (5 กรัม) โดยบรรจุในผลิตภัณฑ์ใหม่ปิดฉลากเป็นขวดที่ 1 (จำนวน 46 ราย) ขวดที่ 2 (จำนวน 42 ราย) ผู้ป่วยได้รับการตรวจคลื่นไฟฟ้าหัวใจอย่างต่อเนื่องเป็นเวลา 24 ชั่วโมงหลังผ่าตัด หลังจากนั้นจะประเมินจากอาการทางคลินิกจนกว่าจะจำหน่ายออกจากโรงพยาบาล

**ผลการศึกษา:** ข้อมูลพื้นฐานของผู้ป่วยสองกลุ่มโดยรวมไม่แตกต่างกันยกเว้นผู้ป่วยในกลุ่มที่ได้รับยาขนาดสูงจะมีน้ำหนักตัวมากกว่า ( $60.21 \pm 11.32$  กก. เทียบกับ  $65.85 \pm 12.2$  กก.,  $p = 0.03$ ) และเป็นโรคเบาหวานมากกว่า (52.4% เทียบกับ 28.3%,  $p = 0.02$ ) ข้อมูลระหว่างผ่าตัดไม่แตกต่างกัน ไม่มีภาวะแทรกซ้อนจากการให้ยา ยกเว้นผู้ป่วยหนึ่งรายที่มีอาการร้อนวูบวาบ ปวดมวนท้อง หลังได้รับยา พบว่าระดับแมกนีเซียมหลังผ่าตัดทันทีจะสูงในกลุ่มที่ได้รับยาขนาดสูงและจะกลับสู่ระดับปกติอย่างรวดเร็วหลังผ่าตัดวันที่หนึ่ง ภาวะ AF พบ 9 ราย (10.23%) โดยพบสี่รายในกลุ่มยาขนาดต่ำ และห้ารายในกลุ่มยาขนาดสูง ซึ่งไม่มีความแตกต่างกันในทางสถิติ ( $p = 0.62$ )

**สรุป:** แมกนีเซียมซัลเฟตมีความปลอดภัย และมีประสิทธิภาพในการลดภาวะ AF หลังการผ่าตัดทำทางเบี่ยงหลอดเลือดหัวใจ อย่างไรก็ตาม ไม่พบว่ามีความแตกต่างระหว่างการให้ยาขนาดที่ต่างกัน

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