RELATIONSHIP BETWEEN SERUM MAGNESIUM LEVEL AND ARRYTHMIAS FOLLOWING POST-CORONARY ARTERY BYPASS GRAFTING

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Abstract

Introduction: Atrial and ventricular arrhythmias are among the most common complications after coronary artery bypass graft (CABG) surgery. It is known that cardiopulmonary bypass reduces serum magnesium level. In this study, we evaluated the relationship between total blood magnesium level (TMG) and the incidence of perioperative arrhythmias.

Methods: TMG was measured in patients who were scheduled for CABG on three occasions: just before anesthesia, on intensive care unit (ICU) arrival and on the first morning after operation. Patients were evaluated for primary cardiac rhythm, serum creatinine, urine output in operating room and diuretic therapy. Supplemental magnesium (SMG) was also recorded in operating room and ICU. Patients were then evaluated for the rate and kind of arrhythmia occurring during the next 3 days.

Results: Mean TMG level in 170 cases was 2.2 (0.5), 2.6 (0.6) and 2.4 (0.6) mg/dl on three occasions respectively. 53 patients developed post-operative arrhythmia (31%) [Atrial Fibrillation (AF) (7.1%), Non-AF Supraventricular arrhythmia (14.7%) and Ventricular arrhythmia (16.5%)]. Although there was a significant difference between TMG on

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three occasions (P <0.001), all values were within normal range. Although TMG was higher in arrhythmic patients compared to non-arrhythmics (2.26 vs. 2.14), both values were in normal range and there was no significant difference between two groups.

Discussion: This study shows that routine magnesium administration has no significant effect on serum magnesium level. We conclude that though routine regimen of magnesium administration has no effect on incidence of perioperative arrhythmia, it is probably necessary for maintaining normal magnesium level.

Key words: Arrhythmia, Coronary artery surgery, Magnesium.

Introduction: Atrial and ventricular arrhythmias are among the most common complications after coronary artery bypass graft (CABG) surgery. The occurrence of arrhythmias, especially atrial fibrillation (AF), as the most common of all, does not increase the risk of patients' mortality, it does, however, increase the length of Intensive Care Unit (ICU) stay and total period of hospitalization[1,2].

Risk factors for developing AF consist of: previous history of AF, advanced age, combined valvular and coronary surgery, preoperative congestive heart failure (CHF) or chronic pulmonary disease, Surgical factors include cross-clamp time, bicaval venous cannulation, and pulmonary vein venting[3]. Further, the protective role of ß-blockers and ACE inhibitors against AF has been recently emphasized[4].

Many methods used in the treatment or prevention of post-surgical arrhythmias lack significant effectiveness beside causing various complications[5,6]. Controversy exists on the effectiveness of magnesium (Mg) sulfate in preventing post surgical arrhythmias. Some studies[7,8] have highly emphasized its role in preventing arrhythmias, to others, however, it is questionable[9,10,11].

Mg serum levels highly change after CABG surgery, such that the rate of hypomagnesemia after cardiopulmonary bypass (CPB) approaches 70% in some studies[12]. Hence, Mg serum levels and the administration of Mg sulfate may play a role as anti- arrhythmic factors. Currently,

measuring peri-operative levels of serum Mg is not routinely done.

The present study aims at determining the peri-operative Mg serum levels in CABG patients, and its correlation with development of post-surgical atrioventricular arrhythmias. The relationship between doses of administered supplemental Mg and post-surgical arrhythmias is studied as well.

Methods and Materials

Candidates for CABG with normal sinus rhythms were included in the study of 170 patients (116 males, 54 females). Exclusion criteria consisted of: presence of any kind of arrhythmias, valvular heart disease, taking anti-arrhythmic medications, past surgical history of CABG (redo), and renal failure.

Patients Mg serum levels were then measured on the three designated times: re-operatively immediately after anesthesia induction; post-operatively on admission to ICU; and in the morning of first day post-operatively.

Age, sex, past medical history of CHF; COPD, drug history of diuretic consumption, serum creatinine level, and duration of cross clamping in all studied patients were recorded and analyzed. The Mg sulfate administration, prescribed doses in operating room and ICU were separately recorded. The dose of administered Mg during CPB, was in the range of 1 ± 0.2g for all patients.

Patients were monitored for supraventricular and ventricular arrhythmias for 3 days from the time of surgery. During this period, any type of arrhythmias appeared on the monitor was reported by the staff nurse and rechecked by a specialist physician then confirmed by 12 lead ECG. Patients were then divided in two groups: arrhythmic and non-arrhythmic for further assessments. Any adverse effects due to rise in Mg serum levels were recorded.

Data variables comparison was done by parametric and non-parametric tests and their relationship was evaluated using correlation

tests. The P-values <0.05 was considered significant for all tests.

Results: Patients details are shown in Table 1.

Table 1
Patients details

Total (n)	170
Men (n)	116 (68%)
Women (n)	54 (32%)
Age (yr)	59.9 (9.3)*
Hx of COPD (n)	4 (2.5%)
Hx of CHF (n)	27 (15.3%)
RCA involvement (n)	140 (82.3%)
Serum creatinine level (mg/dl)	1.2 (0.31)
Urine output during surgery (ml)	1803 (761)
Cross-clamp time (min)	49.8 (21)
Mean administration Supplemental Magensium (g)	2.6 (1.2)

Hx = History, COPD = Chronic Obstructive Pulmonar Disease, CHF = Congestive Heart Failure, RCA = Right Coronary Artery.

* Unspecified numbers in parentheses are SDs.

Only one patient, in whom the duration of CPB was rather long and a total bolus dose of 6g supplemental Mg sulfate was administered exceptionally, had complications due to rise in Mg serum level. However, 2nd time (on admission to ICU) and 3rd time (1st day post-op) Mg serum levels was reported 3.5 mg/dl and 5.3 mg/dl, respectively. On the 1st day post-operation, the patient had weakness and hypotension which could be explained by long duration of CPB and post-operative inotrope intake besides high Mg serum level.

53 (i.e. 31.2%) had at least one type of arrhythmia. Mg serum levels in non-arrhythmic group were higher than the arrhythmic one. Although there was a significant difference (P <0.001) in 1st and 3rd time mg serum levels, the correlation between Mg serum levels and administered Mg sulfate dose (r = 0.37, P <0.001) posed a confounding role of the latter variable. Using Mentel-Haenszel test, it was shown that there were no significant differences between 3 times measurement of Mg serum levels omitting dose-related effect of Mg sulfate administered (P = 0.6).

Detailed information and results of statistical tests are presented in Table 2.

Table 2
Serum magnesium level and arrhythmia data

Arrhythmia (n)			
Total	53 (31.2%)*		
AF	12 (7.1%)		
Other SVAs	25 (14.7%)		
Ventricular	29 (17.1%)		
Seurm Mg level (mg/dl)			
Beginning of the operation	2.2 (0.5)**		
Arrival in ICU	2.6 (0.6)		
First postoperative day	2.4 (0.6)		
	P <0.001		
Serum Mg level (mg/dl)			
	Time 1	Time 2	Time 3
Arrhythmic group	2.26	2.60	2.49
Non-Arrhythmic group	2.14	2.57	2.37
			NS
Serum Mg level (mg/dl)			
	Time 1	Time 2	Time 3
Patients with ventricular arrhythmia	2.26	2.60	2.49
Patients without ventricular arrhythmia	2.14	2.57	2.37
			NS
Serum Mg level (mg/dl)			
	Time 1	Time 2	Time 3***
AF with SVA	1.94	2.34	2.07
AF without SVA	2.26	2.60	2.55
			NS
Hypomagnesemic patients (Serum Mg level <1.5 mg/dl) (n)			
Beginning of the operation			6 (3.5%)
Arrival in ICU			4 (2.4%)
First postoperative day			2 (1.2%)
Age (yr)			
Patients with AF			64 (6.9)
Patients without AF			59.8 (9.3)
			P = 0.1

AF = Atrial Fibrillation.
SVA = Supraventricular Tachyarrhythmia.

IC = Intensive Care Uni.
* Some patients had more than one arrhythmia.
** Unspecified numbers in parentheses are SDs.
*** P value for time 3 is 0.068.

Comparing the average age of patients with AF to patients without AF, showed that the occurrence of AF occurred at higher age, though the difference was not significant (Table 2). None of the patients with AF was below 50 years.

There was no relationship between AF arrhythmias and such factors as history of CHF or COPD, right coronary artery involvement, cross-clamp time, serum creatinine levels and urine output. There were also no meaningful correlation between Mg serum levels and creatinine serum levels or urine output.

Of 12 patients with AF, 5 had other supraventricular arrhythmias (SVA) especially premature atrial contractions (PAC) previously, but none had previous ventricular arrhythmias. Comparing Mg serum levels of these patients on the three designated times showed lower measures in patients with both AF and SVA but the difference was not significant (Table 2).

Discussion

In the present study the average age and male to female ratio of patients studied was lower than many other similar studies[13,14,15]. Although in other studies[3,16] occurrence of AF was observed at higher ages, the difference was not significant (Table 2). Also factors including history of CHF or COPD, right coronary artery involvement, and cross-clamp time of the present study had no correlation with AF. Our studies conform to the studies of Kohno and Neurozler[13,17].

Patients Mg serum levels was raised following surgery but the rise was not beyond normal ranges. Mean Mg serum levels was decreased again on the first postoperative day, but there was no significant difference with preoperative levels. In patients whom CPB had been used during CABG surgery and without having received intra-operative

supplemental Mg sulfate administered, the postoperative Mg serum levels was lower than preoperative levels[9,18,19].

There was also decrease of Mg serum levels in the first postoperative day when a bolus supplemental Mg was administratered[8,19] in post-CPB period. Various etiologies contribute to decreased Mg serum levels following CABG: blood dilution of CPB, fall of intracellular Mg during surgery, following myocardial hypoxia, ionized Mg chellation with heparin or blood preserving solution in case of allogenic transfustion[20,21,22].

Despite the general agreement on post-CABG decrease in Mg serum levels, a controversy exists on the role of hypomagnesemia increasing post-operative arrhythmias and more importantly whether supplemental Mg sulfate in current common doses, could prevent development of those arrhythmias after CABG.

The present study showed there was no difference in post-operative Mg serum levels between patients with AF and those without AF (2.39 vs 2.41). Both groups measures were within normal range.

There was no significant difference between 2nd and 3rd time serum Mg levels in patients with ventricular arrhythmias (Table 2), though the Mg serum levels in patients with ventricular arrhythmias was higher than those without arrhythmia[9,18,23,24,25]. As shown in Table 2, the difference between two groups in 1st time Mg serum levels, (onset of anesthesia, (2.28 vs. 2.15), was continued in 2nd and 3rd times. In addition, Mg serum levels was within normal ranges in all cases and hence was of no clinical importance. Lack of significant difference between two groups in three times of serum Mg measurement supports this idea.. Furthermore, the study by Fanning[9], one of the most valid and cited studies in post surgical arrhythmias[15], has questioned role of Mg sulfate administration in treatment of ventricular arrhythmias.

The high prevalence rate of hypomagnesemia which is reported as high as 71% in some references[8,12] was not confirmed in our study (Table 1); probably due to Mg supplemental administration in cardioplegic solutions.

The dose measurement of administered Mg sulfate and determining its relationship with other variables was one of our objectives. On average, patients received 2.5g of Mg sulfate (Table 1), with the intake dose (including that in cardioplegic solutions) ranging between one to six grams. There were no complaints (except one particular case) of adverse effects due to rise in Mg serum levels. The maximum Mg serum level in the studied patients is also affirmative (4 mg/dl in 2nd time and 4.2 mg/dl in 3rd time).

Studies on complications of Mg serum levels rise have shown that patients develop symptoms when Mg serum levels >4.85 mg/dl[26]. It has also been observed that extra amounts not absorbed into human cells are excreted in the urine[27]. So, one of our exclusion criteria was renal failure to prevent toxic Mg serum level.

There are a few studies on the role of administration of Mg sulfate using bolus doses similar to the current study (administering 2-4g after CPB, excluding amounts of the cardioplegic solution). Evidence has shown that bolus administration of Mg sulfate in rates and doses as used in this study, has no adverse effects[28]. In other studies, using bolus doses of Mg sulfate, post surgical ventricular dysrythmias was decreased compared to control group[8,19,29]. It is only the study by England which has evaluated supraventricular dysrythmias and has emphasized its relationship with Mg serum levels[8], thus emphasizing the importance of Mg serum levels when compared to the administered Mg doses.

The most prominent difference between the present study and others is the rate of post-operative AF. In various studies, the rate of AF has been reported to be from 16 to 42% in non-treated groups and from 20 to 30% in treated groups[4,7,8,9,10,25,30,31,32]. But, there was no significant difference in development of AF compared to the control groups in studies using bolus doses of Mg sulfate[8,33]. In the present study, the rate of AF was much lower than stated and those variation of findings could be explained as follows:

1) In most other studies done, all cases of AF have been considered, but in the present study, only cases of AF that required treatment were

included. Some studies, in which statistics of AF episodes (transient without treatment) were mentioned separately, have such significant differences. Wistbacka et al. reported an AF rate of 7% and AF episodes rate of 24%[33]. In another study, AF rate was 50% of the cases in which only 36% needed treatment[34].

2) Many studies have reported AF as a part of supraventricular dysrythmias and did not report it separately. Precise meta-analytic studies by Alghadmi[15] and Miller[14], however, reported all kinds of SVAs under one category in data compilation.

3) In our study of patients with AF, the exclusion of patients with isolated valvular or combined valvular and coronary surgery, with renal failure, and patients with previous history of CABG, could decrease the overall number of patients with AF.

4) The use of prophylactic methods (ß-blockers), improvement of surgical techniques (by time), routine use of myocardial protection methods (e.g. using warm colloid cardioplegic solutions), using antegrade/retrograde methods for myocardial circulation, using various filters and medications reducing body reaction to CPB, ... Increasing the speed of surgeries and decreasing duration of CPB and cross-clamping, could also be effective in lowering rates of AF.

5) Since advanced age and previous history of AF are major risk factors for development of post surgical AF, the lower mean age of patients in our study compared to many others, could be another reason for the low rate of AF in the present study[14,15].

6) Since all patients were evaluated for just three days post-operatively because of limitations in monitoring, the cases of AF occurring after this time, were ignored.

Conclusion

This study shows that there is a relationship between Mg serum levels and postoperative arrhythmias. The administration of supplemental doses of Mg sulfate seems to play a protective role against occurrence of

arrhythmias by maintaining Mg serum levels within normal limits and preventing hypomagnesemia. These administered amounts, however, do not cause complications due to the rise in Mg serum levels. It appears that the administration of supplemental Mg sulfate does not keep Mg serum in high levels for long time and thus does not prevent AF or other post CABG surgical arrhythmias.

Based on these results, while the authors do administer supplemental Mg sulfate for CABG patients, further studies are needed to define more efficient therapeutic protocols and the pathophysiology of postoperative dysrythmias, particularly AF, is elucidated.

Acknowledgement

The authors wish to thank the operating room and the intensive care nursing staff for their support. This study was financially supported by the Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences.

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