

A comparative study of the effect of metoral and magnesium prophylactic in controlling atrial fibrillation after coronary arteries bypass operation.

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Abstract

Objective: Arterial fibrillation is the most common type of arrhythmia observed after coronary arteries bypass operation and culminates in hemodynamic instability, higher morbidity and mortality rate, longer period of hospitalization, and higher hospital expenditures. The present research seeks to compare the effect of metoral, magnesium prophylactic, and a mixture of both (magnesium and metoral) in reducing the occurrence of CABG (coronary arteries bypass graft).

Methods: This is a double blind clinical trial where 195 patients candidated for CABG were selected based upon exclusion and inclusion criteria and randomly divided into three groups of metoral (receiving 5 mg metoral), magnesium (receiving 1.5 g magnesium), and combined (2.5 mg metoral+1 g magnesium). The resulting information was then analyzed using SPSS v.19 and ANOVA statistical tests.

Results: A significant difference was observed between the three groups in terms of post-operation AF and other types of arrhythmia. Higher rates of post-operation AF were observed in magnesium group than the two other groups (P=0.001). On the other hand, higher rates of post-operation AF were observed in the combined group than what was observed in metoral group (0% vs. 4.5%). The occurrence of other types of post-operation arrhythmia in the combined group was more than what was observed in the other two groups (P=0.001).

Conclusion: Both metoral and magnesium are really useful in reducing post-operation AF among the patients with CABG, while metoral was more effective than magnesium. On the other hand, adding magnesium to metoral can clearly enhance its prophylactic effects.

Keywords: Arterial fibrillation, Coronary arteries bypass graft, Magnesium, Metoral, Prevention.

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Introduction

Arterial Fibrillation (AF) is considered to be one of the most common complaints following coronary operations [1-4]. The occurrence rate of AF is different depending upon the type of operation, (e.g. 20 to 40% following CABG with an average of 30%). The etiology of AF is not clearly specified, but there are three main factors that play a major role in its occurrence: 1) Ischemic atrial tissue; 2) Increased sympathetic activity; 3) Increased inflammatory responses [2].

There is a direct correlation between post-operation AF and hemodynamic instability. Various researches have pointed to the fact that post-operation AF increases hemodynamic instability, Thrombolytic incidents, and result in longer period of hospitalization and higher hospital expenditures [1]. Various pharmacological methods have been proposed to prevent post-operation AF [1-4]. Prescription of beta-blockers before and after operation is used as the first line of treatment for POAF prophylaxis. Sotalol and Amiodarone are used as proper substitutionary treatments among high-risk patients. On the other hand, magnesium supplements also need to be taken into

consideration among patients with hypomagnesemia. As a result of rise in sympathetic tone following CABG, AF risk increases among patients. By influencing catecholamines that affect myocardia, beta-blockers reduce the risk of AF [1,5-7]. Various researches have recently pointed to metoprolol as the most commonly used material [1,8,9]. Metoral is a class 2 beta-blocker. It is usually used to treat hypertension, chest cage pains, migraine headaches, anxiety, tachycardia, and to control arterial rhythm [9-11]. Further to reducing AF, metoral also reduces ventricle rate [6,10,12]. Hypomagnesaemia also acts as a risk factor in order to create supraventricular tachycardia and ventricular tachycardia and it is an independent factor in the progress of POAF [1,12]. Mg is the second intracellular cation whose reduction may make the patient prone to SVT, VT, AF, long term PR, QT-segment, and even VF [12-14]. Mg prophylaxis is safe for the patients, but we do not know if it is useful for preventing AF [13,15]. The advantages of using magnesium include cheap price, the length of AF and VT, cardiac index stabilization, and infraction size reduction [15-17]. In spite of all these advantages, proving the routine utilization of Mg following CABG is a quite challenging task

[15]. The present research seeks to compare the effect of metoral and magnesium and a mixture of both in the form of prophylaxis on POAF.

Materials and Methods

This is a double blind, randomized, clinical trial conducted on 195 patients candidated for CABG resorting to Amir Almomenin Hospital (PBUH) of Arak. Having possessed the inclusion criteria, the participants signed the written consent form. The patients were randomly divided into metoral, magnesium, and metoral and magnesium groups. After entering, the operation room and receiving premedication on the day of operation (25 mg of promethazine and 3 to 5 mg of morphine), the patients entered the operation room. Then, the necessary monitoring including T, Paco 2, EKG, RR, PR, and SPO 2 were carried out. Following a brief sedation (1 mg of midazolam and 1 cc of fentanyl), arterline was taken from non-dominant left ulnar artery. The patients were then inducted and intubated using 5 to 7 mg fentanyl, 5 mg midazolam, 50 mg Atracurium, and 60 to 100 mg lidocaine. The patients then underwent ventilator. Following intubation, 5 mg metoral was used for the first group, while the second and the third groups received 1.5 g magnesium and 2.5 mg mixture of metoral and magnesium, respectively. The drugs were put in syringes and given to an assisting resident of anesthesia who was totally unaware of their contents. These drugs were finally put on syringe pump. Then, CV-line was installed for the patients and the operation began. Having placed the patients on cardiopulmonary pump and after conducting grafts, CBP pump was removed and the intubated patient was relegated to ICU. All signals of the patients were controlled in ICU and in the case of any signs of AF, amiodarone (300 mg) and, then, infusion dose were used to treat them. Finally, the information obtained by completing patients' questionnaire by the interns was analyzed and the frequency rates of AF across all three groups were compared against one another. Patients' V/S after entering ICU and their length of stay there were compared against one another. The resulting information was finally analyzed using ANOVA and χ^2 and presented in tables and statistical figure.

Inclusion criteria

1) All non-emergency patients candidated for CABG resorting to Amir Almomenin Hospital of Arak who agreed to take part in the research. 2) All type 3 and 4 ASA patients. 3) All patients whose length of operation was shorter than 6 h. 4) All

patients without a history of previous arrhythmia and AF prior to CABG. 5) Patients without any history of using antiarrhythmic agent prior to CABG.

Exclusion criteria

1) All patients whose operation had lasted longer than 6 h. 2) Patients candidated for heart valve replacement in addition to CABG. 3) Patients with a previous history of arrhythmia and AF prior to operation. 4) Patients with a history of sensitivity to magnesium or metoral.

According to the following formula, as many as 65 patients were put in each group.

$$N=2\{P1(1-P1)+P2(1-P2)\}^2(Z1-\alpha/2+Z1-\beta)^2/(P1-P2)^2$$

$$P1=5, P2=14, Z1-\alpha/2=1/96, Z1-\beta=1/68 \Rightarrow N=65$$

This clinical trial is approved by university under the ethical code of IR.ARAKMU.1394-296 and (IRCT2016031520258N5) IRCT.

Results

Table 1 presents a comparison of the age and number of grafts of patients candidated for coronary artery bypass graft resorting to Amir Almomenin Hospital of Arak in metoral, magnesium and metoral & magnesium groups.

Table 1. Comparing the age and number of grafts in patients.

Groups	Metoral	Magnesium	Combined	P-value
Average age (y)	64.7 ± 7.7	65.1 ± 8.2	65.4 ± 6.4	P ≥ 0.05 Not significant
Average number of grafts	3.1 ± 1.1	3.5 ± 1.3	3.2 ± 1.8	P ≥ 0.05 Not significant

Considering Table 1, no significant difference was observed between the three groups in terms of their average age and the average age across all three groups was 65 years old. The average number of grafts (3 grafts) didn't show a significant difference ($P \geq 0.05$).

The following table compares the participants in the three groups in terms of their gender. As $P \geq 0.05$, there is no statistically significant difference between the three groups in terms of their gender frequency and the frequency of male participants in all three groups was 65% (Table 2).

Table 2. Comparing patients' gender.

Groups	Metoral		Magnesium		Combined		P-value
	Male	Female	Male	Female	Male	Female	
Gender							
Frequency percentage	0.646	0.354	0.652	0.348	0.661	0.339	P ≥ 0.05 Not significant

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Table 3 compares the length of staying in ICU and the length of hospitalization across the participants in three groups.

No significant difference was observed between the three groups in terms of their length of staying in ICU and the length of hospitalization ($P \geq 0.05$).

Table 3. Comparing the length of staying in ICU and the length of hospitalization.

Groups	Metoral	Magnesium	Combined	P-value
Average length of staying in ICU	3.7 ± 2.1	3.4 ± 1.8	3.4 ± 1.5	$P \geq 0.05$ Not significant
Average length of hospitalization	11.9 ± 5.6	12.5 ± 4.8	12.1 ± 3.7	$P \geq 0.05$ Not significant

According to Table 4, a comparison of mortality rate among the participants in three groups failed to find any significant difference. The mortality rate across all three groups was 9% ($P \geq 0.05$).

Table 4. Comparing mortality percentage among patients.

Groups	Metoral	Magnesium	Combined	P-value
Mortality percentage	0.091	0.096	0.095	$P \geq 0.05$ Not significant

According to Figure 1, a significant difference was observed between the three groups in terms of arterial fibrillation occurrence with the magnesium group exhibiting more arterial fibrillation cases than the other two groups ($P=0.001$). The difference observed between metoral and combined group was also significant with a lower percentage of post-operation arterial fibrillation observed in the combined group. This fact points to the positive effect of all three medicines in reducing arterial fibrillation with beta-blockers (metoral) being more effective. It should also be mentioned that this effect would enhance as a result of combining with magnesium with a lower rate of arrhythmia observed in the combined groups. Other post-operation arrhythmias were less frequent in the combined group compared to what was observed in the other two groups ($P=0.001$).

increases the possibility of AF after CABG. As a result, utilizing prophylactic magnesium may result in the significant reduction of AF after operation [1,2]. The results of previous studies are somehow similar to those achieved in our research. A research conducted by University of Tehran introduced using beta-blockers as the most effective prophylactic method to reduce post-operation AF [1]. This research, conducted by Haghjoo et al. introduced Sotalol and amiodarone as prophylactic agents [1]. These results are in line with those achieved in our research where we discussed the prophylactic effect of metoral.

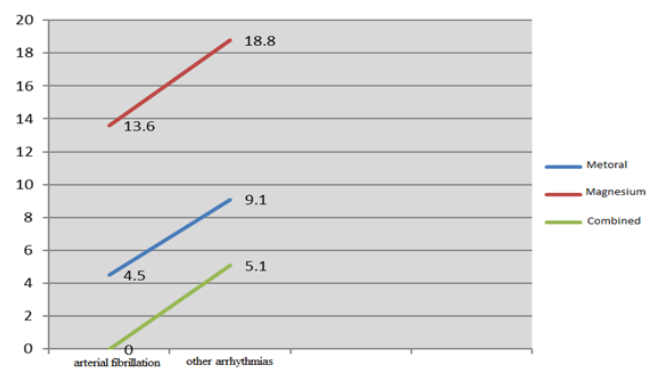


Figure 1. A comparison of the occurrence of arterial fibrillation and other arrhythmias after operation.

Discussion

Achieving a useful combination as prophylaxis to prevent post-operation AF of the patients candidated for CABG is a major step taken towards reducing the costs, death toll and post-operation side effects. As the results of our research indicate, the occurrence of AF following CABG is more in Mg group compared to the other two groups of participants. These results point to the fact that metoral is an effective beta-blocker in preventing post-operation AF among CABG patients. This effect will be enhanced by adding magnesium as an additive. There is a direct link between post-operation AF and hemodynamic instability. AF increases mortality, length of hospitalization, length of staying in ICU, and hospital costs [1,2]. Utilizing beta-blockers or amiodarone is one of the most effective pre-emptive measures [1-3]. On the other hand, existence of hypomagnesemia is also an important factor that

The occurrence of post-operation AF among those in the combined group was significantly more than what was observed in the other two groups where the prophylactic role of metoral is confirmed. On the other hand, the additive effect of magnesium along with metoral is also taken into consideration. Another research by Koniari et al. in Patras University of Greece arrived at the conclusion that beta-blockers need to be used as the first line of prophylaxis to reduce post-operation AF among all patients candidated for CABG [2]. The results of this research are also in line with those achieved in our research. This research has introduced amiodarone as a useful treatment to reduce post-CABG AF following metoral as the second line of treatment [2]. Our researchers found that metoral could reduce post-operation AF and this prophylactic effect could be enhanced in the combined group using magnesium additive. A meta-analysis by Shiga et al. found that magnesium could reduce post operation AF 29% and bring about a 40% reduction in other arrhythmias and has no effect

on secondary infraction and mortality [18]. Another meta-analysis by Miler et al. found that prophylactic magnesium could reduce AF rate from 28 to 18 percent which is in line with the results of our research. Our research also confirmed the effect of magnesium in reducing post-operation AF, but it was less powerful compared to the prophylactic effect of metoral [17]. A research by Echahidi et al. in the USA reported that beta-blockers are more effective and safer in reducing post-operation AF. This research also found that using magnesium along with beta-blockers could enhance their prophylactic effect in reducing post-operation AF [4]. The results of this research are in line with those achieved in our study where metoral was very effective in reducing post-operation AF and magnesium could enhance this effectiveness. Another research conducted by the operation department of Freeman hospital in the UK found that further to reducing post-operation AF occurrence, beta-blockers also played a major role in reducing the length of hospitalization, the length of patient's stay in ICU, mortality, and morbidity rate among patients [5]. However, the results reported in our research showed that metoral reduced post-operation AF rate but it had no influence upon length of hospitalization, length of stay in ICU, morbidity, and mortality period. A study by Crystal et al. in Toronto of 1000 patients candidated for CABG found that prophylactic metoral had reduced AF from 40 to 28.5% while occurrence of post-operation AF in control group was 38%. These results are completely in line with those achieved in our research [8]. A similar project by Abbas et al. found that prophylactic magnesium could reduce post-operation AF and other arrhythmias, but it had no influence upon patients' mortality rate. In our research, magnesium had reduced POAF but it had no influence upon mortality. In a research by Xiaosun et al. 5 RCT's were studied. It was concluded that using magnesium combined with beta-blocker could make no difference in reducing POAF compared to the cases where beta-blocker is used alone. In other words, magnesium doesn't enhance the effect of metoral in reducing POAF [13]. These results are not in line with those achieved in our research because magnesium, in our research, played a reinforcing role in anti-arrhythmic prophylactic effects of metoral.

A research by Gu et al. in Guangxi university of China reported that magnesium had a prophylactic effect in reducing post-operation AF. Clear results indicated a 36% reduction of POAF using prophylactic magnesium which is in line with our research, but the effect of magnesium in reducing POAF was less than the above said research [14]. In a systematic review by Shepherd et al. in Southampton University of the UK, the prophylactic effect of magnesium and Sotalol in reducing POAF was investigated and both medicines were found to have a major effect in reducing POAF compared to placebo, while Sotalol played a stronger role compared to magnesium [16]. The effectiveness of metoral and the combined group in our research was more than magnesium. A research by Kamali et al. in Medical Sciences University of Arak arrived at the conclusion that metoral had a greater influence in reducing POAF compared to Amiodarone (P-value=0.004) which is in line with the current research [19]. In the present research,

metoral played a major role in shortening the period of patients' stay in ICU, but our research found no significant difference between the two groups in terms of this issue. A review of all these researches confirms the great effect of magnesium and beta-blockers in reducing POAF. It is suggested to used beta-blockers such as metoral as very useful factors to reduce POAF. As magnesium is cheap and considering its prophylactic influence in reducing POAF, this medical supplement can be used in the absence of beta-blockers. Our research would also like to recommend using magnesium along with metoral as the reinforcing factor which enhances the anti-arrhythmical effects of metoral. Furthermore, recently various studies using computerised tomography scan have reported on pattern of differential diagnosis and play a major role on diseases [20-26].

Conclusion

Both metoral and Mg are really useful in reducing post-operation AF among patients with CABG with metoral being more useful than magnesium. Adding metoral to magnesium can clearly increase its usefulness. Finally, interested researchers are recommended to compare the effect of metoral and magnesium with metoral and other reinforcing factors such as statins and saturated fatty acids.

Conflict of Interest

The authors report no conflicts of interest related to this study.

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