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Effect of single dose intravenous Amiodarone on post bypass cardiac rhythm in patients with preexisting atrial fibrillation undergoing mitral valve replacement - A prospective, randomized, double blind controlled study

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Abstract

Introduction: Atrial Fibrillation (AF) is the most common arrhythmia found in patients scheduled to undergo mitral valve replacement surgery. Various ablation therapies or pharmacological agents are used to prevent AF. Although ablation therapies can be effective in some patients, these therapies may not be appropriate for all patients, and pharmacological treatments will continue to have an important place in the prevention of AF and maintenance of normal sinus rhythm.

Aim: The aim of our study was to evaluate the effect of single dose intravenous amiodarone on post bypass cardiac rhythm in patients with pre-existing atrial fibrillation undergoing valvular surgery and study if Amiodarone (IV) given prior to cross-clamp release is helpful in preventing the recurrence of Atrial fibrillation.

Materials & Methods: In this prospective randomized, double blind controlled study, patients with pre-existing atrial fibrillation undergoing mitral valve replacement (MVR) were divided into two groups, Group A receiving prophylactic intravenous amiodarone 3mg/kg and their post bypass rhythms were compared with group B (control group). If NSR was established, it's maintenance or recurrence of AF was watched for. If NSR was not established, the need for cardioversion, amount of energy needed for defibrillation and the response to defibrillation was compared in both the groups.

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Results: There was statistically significant difference in the number of patients who reverted to normal sinus rhythm after aortic cross clamp removal when given IV Amiodarone prophylactic ally as compared to the control group. There was statistically significant difference in the number of patients who needed cardioversion. In the control group, 39 patients (54.9%) required cardioversion whereas only 21 patients (29.5%) who received IV Amiodarone group required cardioversion. The duration of ICU stay and duration of hospital stay was comparable between the groups. There was no significant difference in the incidence of complications between Group A and Group B.

Conclusion: Amiodarone given as a single intravenous dose in patients with pre-existing atrial fibrillation undergoing valvular surgery, prior to cardiopulmonary bypass was found to be effective in reducing the incidence of atrial fibrillation after aortic cross clamp release. It decreased the requirement of cardioversion after the release of aortic cross clamp.

Keywords: Amiodarone, Mitral Valve Replacement, Cardioversion, Prevention of Post-operative Atrial fibrillation.

Introduction

In developing countries, rheumatic mitral stenosis (MS) is the most frequent underlying condition in patients with AF. [(1)] It is difficult to achieve and sustain NSR in patients with RHD and it has been stated in a report that mitral valve surgery restored NSR in only 8.5% of patients with chronic AF. Since AF can lead to haemodynamic compromise during the immediate post-operative period, it is recommended to use concomitant anti-arrhythmic procedures or medication for all patients with AF who undergo mitral valve surgery.[(2)]

Many Randomised trials have been conducted to evaluate the efficacy of amiodarone for prophylaxis against POAF after cardiac surgery. [(3-7)] Reversion to normal sinus rhythm (NSR) in patients with AF is a desired outcome as it leads to relief from symptoms, prevention of arrhythmia, improved exercise tolerance, improved quality of life, possible reduction in strokes and in whole improved survival.

Amiodarone is a class III Vaughan-Williams antiarrhythmic drug and has some effects of Class I and II drugs as well as antiadrenergic effects, often used to treat arrhythmias like Atrial fibrillation (AF). Initiation of oral or intravenous amiodarone preoperatively preferably needs monitoring and admission. There are studies which have concluded that a single dose of intravenous amiodarone infused prior to CPB increases the incidence of conversion to NSR.[(8)(9)]

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The aim of our study was to determine if a single loading dose of i.v amiodarone in patients with pre-existing AF, prophylactically before CPB reduced the incidence of atrial fibrillation after aortic cross clamp release. We compared the incidence of conversion of AF to NSR, need for cardioversion, inotropic support and adverse effects in patients who received amiodarone with the patients who received normal saline (control group).

Methodology

With the approval from the Institutional Ethics Committee and a valid written informed consent, the patients undergoing mitral valve replacement with atrial fibrillation were enrolled for the study, whose history and physical examination were done as per routine protocol followed in our institution.

In a similar study by Selvaraj T et al[8], in the amiodarone group the initial rhythm after the release of aortic cross clamp was noted to be AF in 9.5% of patients till the end of surgery, while that in the control group it was 32.5%. Using formula for sample size calculation for comparing proportions in independent groups, sample size $n = (Z_{\alpha/2}+Z_{\beta})^2 * (p_1(1-p_1)+p_2(1-p_2)) / (p_1-p_2)^{2,}$

where $Z_{\alpha/2}$ is the critical value of the Normal distribution at $\alpha/2$ (for confidence level of 95%, α is 0.05 and the critical value is 1.96), Z_{β} is the critical value of the Normal distribution at β (for power of 80%, β is 0.2 and the critical value is 0.84) and p_1 and p_2 are the expected sample proportions of the two groups. Using p_1=0.325 and p_2 = 0.095, 80% power and alpha error of 5%, the sample size calculated was 49 in each group. The total number of mitral valve replacement that took place in our centre, in the year prior to this study was 128. Therefore, considering the number of fallout cases as 10%, the sample size is calculated as a total of 142, with 71 patients in each group.

These patients were randomized into 2 groups, after picking a sealed envelope generated by randomized computer sequence.

Group A: The patients received amiodarone 3mg/kg diluted with normal saline so that the volume becomes 100 ml

Group B: The patients received the same volume (100ml) of normal saline in a similar manner.

The drug was prepared (using computer generated randomization) by a resident doctor not involved in the study. The anesthesiologists recording the patient's data were not aware of the group the patient is allocated. The co-investigator later partook in the intraoperative and the post-operative data collection.

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In the operation theatre, continuous electrocardiography, non-invasive blood pressure and pulse oximetry monitoring was commenced and baseline vital parameters recorded. An arterial and central venous cannulation was done before induction of general anaesthesia. In both groups the infusion was started via the central venous line after induction of general anaesthesia, prior to surgical incision. Haemodynamics was maintained within 20% of the baseline values. It was given over a period of 30 min and completed before onset of Cardiopulmonary bypass (CPB). At anytime during the induction, if the patient (irrespective of the group allotted) has a fast ventricular rate IV Esmolol/ IV Diltiazem/ IV Amiodarone was given as per established OT protocols. Patients receiving amiodarone as the rescue medication were excluded from the study.

In group A, patients received study drug as infusion prior to skin incision and administered through venous line over a period of 30 minutes. If bradycardia (HR <50 beats/min) or hypotension (SBP<90 mm of Hg) was noted, the infusion was temporarily discontinued and fluid or inotropic support instituted to optimize blood pressure. The infusion was continued after hemodynamic stability was achieved. Pre – CPB conversion of AF to NSR, if any, was documented.

After release of aortic cross clamp, initial rhythm was noted. Epicardial pacing was done for patients with severe bradycardia. Inotropes (dopamine +/- noradrenaline) was used to maintain hemodynamic stability. After completion of procedure, patient was shifted to ICU and mechanically ventilated. In the ICU, invasive blood pressure, ECG, Oxygen saturation, ABG and electrolytes were monitored. Weaning from mechanical ventilation and extubation was done when appropriate. Patients were monitored during their complete ICU stay and also after shifting to the step-down ICU facility, from where they were discharged home.

Assessment parameters:

1. Return to Normal Sinus Rhythm OR persistence of Atrial Fibrillation at release of Aortic Cross Clamp.
2. Need for defibrillation, amount of energy needed for defibrillation and the response to defibrillation.
3. Recurrence of Atrial Fibrillation during hospital stay.
4. Need for temporary pacemaker

Statistical Analysis

Quantitative data is presented with the help of Mean and Standard deviation. Comparison among the study groups is done with the help of unpaired t test as per results of normality test. Qualitative data is presented with the help of frequency and percentage table. Association among the study

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groups is assessed with the help of Anova and Chi-Square test. ‘p ’value less than 0.05 is taken as significant.

Results were graphically represented where deemed necessary.

Appropriate statistical software, including but not restricted to MS Excel, SPSS ver. 20 will be used for statistical analysis. Graphical representation will be done in MS Excel 2010.

Results

Patients in both Group A (receiving IV Amiodarone) and Group B (receiving normal Saline) had comparable results with respect to demographic parameters like age, sex, BMI, NYHA classification and ejection fraction. There was statistically significant difference in the number of patients who reverted to normal sinus rhythm after aortic cross clamp removal when given IV Amiodarone as compared to the control group. The initial rhythm after the release of aortic cross-clamp was noted to be ventricular tachycardia/fibrillation (VT/VF) in 21 (29.5%) patients and atrial fibrillation (AF) in 1 (1.4%) patient; all were converted to normal sinus rhythm (SR). In Group B, the rhythm after the release of aortic cross-clamp was noted to be VT/VF in 27 (38.1%) patients and AF in 11 (15.5%) patients; all were converted to normal SR. (Table 1). There was statistically significant difference in the number of patients who needed cardioversion. In the control group, 39 patients (54.9%) required cardioversion whereas only 21 patients (29.5%) who received IV Amiodarone group required cardioversion. (Table 2) The amount of required energy for cardioversion was significantly lesser in the patients receiving IV Amiodarone (20.32±6.62 Joules vs. 29.66±8.71 Joules). (Table 3) The requirement of inotropic support was 23 (32.4%) and 24 (33.8%) patients in Group A and Group B respectively. There was no significant difference between the groups as per Chi-Square test ($p>0.05$).

Table 1: Distribution of patients according to Rhythm after cross-clamp removal

Rhythm after cross-clamp removal	**Group A**		**Group B**		**P-value**
	N	**%**	**N**	**%**	
VT/VF	21	29.5%	27	38.1%	>0.05
Atrial fibrillation (AF)	1	1.4%	11	15.5%	0.002
Sinus rhythm (SR)	49	69.1%	33	46.4%	0.006
Total	71	100%	71	100%	

VT/VF – Ventricular tachycardia / fibrillation

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Table 2: Distribution of patients according to Requirement of Cardioversion

Requirement of Cardioversion	Group A		Group B		P-value
	N	%	N	%	
Yes	21	29.5%	39	54.9%	0.006
No	50	70.5%	32	45.1%	
Total	71	100%	71	100%	

Table 3: Distribution of patients according to Amount of required energy for cardioversion

	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Amount of required energy for cardioversion (Joules)	20.32	6.62	29.66	8.71	0.0001

The incidence of atrial fibrillation postoperatively was significantly lesser in patients receiving IV amiodarone [16.9% (12 out of 71 patients)] compared to the control group [39.4% (28 out of 71 patients)] Symptomatic AF were reported in 4 out of 12 (33.3%) patients who developed AF in Group A and 16 out of 28 (57.1%) patients who developed AF in Group B. (Table 4) None of the patients of both groups required temporary pacemaker. AF occurred at a mean of 3.79 ±1.47 days after surgery in patients receiving IV Amiodarone and 2.65 ±1.14 days after surgery in Control group. (Table 5) This difference was statistically significant. The duration of ICU stay (2.42±1.20 days vs. 2.61±1.28 days) and duration of hospital stay (10.72±3.84 days vs. 11.14±3.93days) was comparable between the groups. (Graph 1) There was no significant difference in the incidence of complications between Group A and Group B. (Graph 2).

Table 4: Distribution of patients according to postoperative parameters

Parameters	Group A		Group B		P-value
	N	%	N	%	
No. of patients who had AF	12	16.9%	28	39.4%	0.002
No. of patients who needed treatment for AF	4	33.3%	16	57.1%	>0.05

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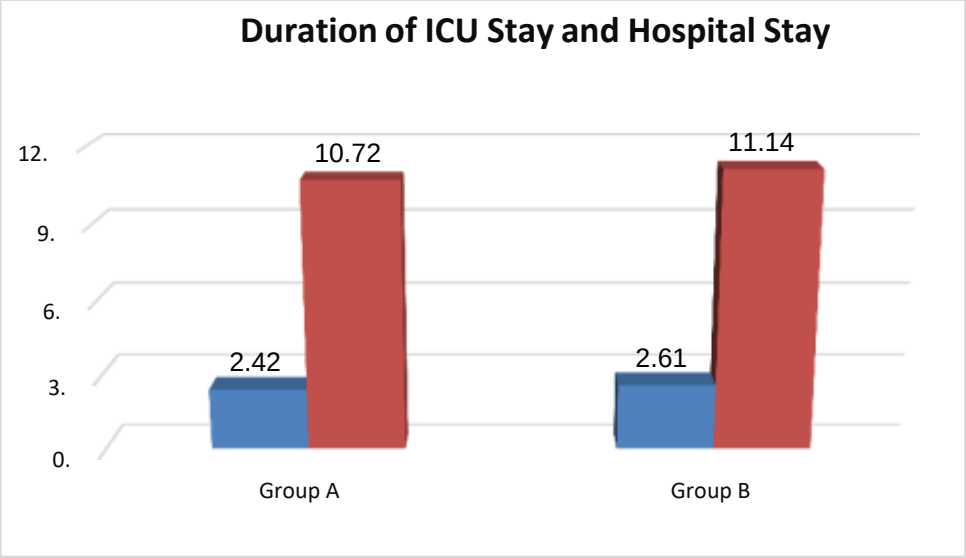
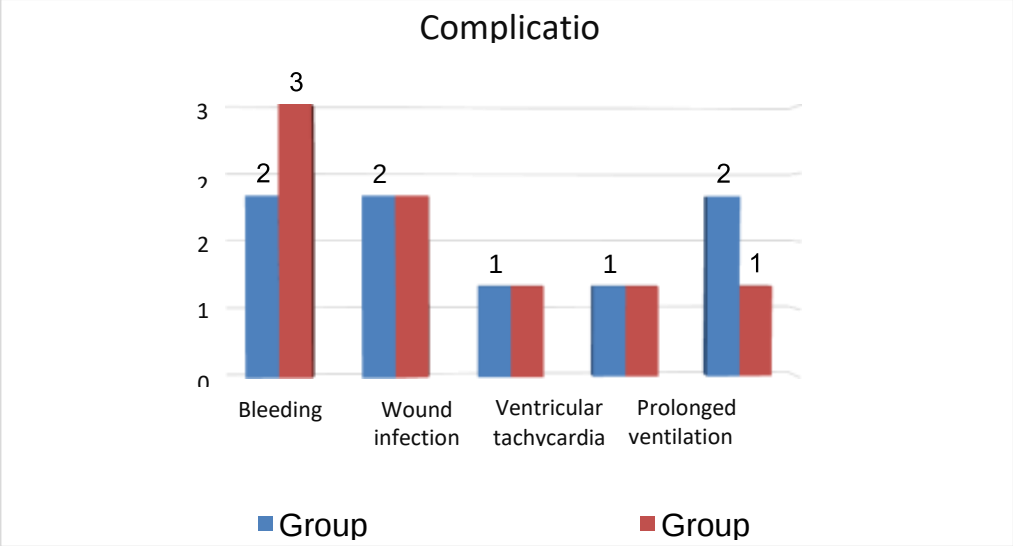
Table 5: Distribution of patients according to postoperative parameters

Parameters	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Occurrence of AF after surgery	3.79	1.47	2.65	1.14	0.0001
Ventricular rate/minute	158.39	21.88	161.06	23.38	>0.05



Graph 1: Distribution of patients according to Duration of ICU Stay and Hospital Stay



Graph 2: Distribution of patients according to Complications

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Discussion

Post operative atrial fibrillation (POAF) is a common occurrence post cardiac surgery.[10] In mitral valve diseases cause dilatation of the left atrium thus resulting in a pre-existing atrial fibrillation.[11] Most patients are haemodynamically stable and are on rate limiting drugs like beta blockers, calcium channel blockers for maintenance of normal sinus rhythm and anticoagulants to prevent complication of AF like stroke. Reversion to NSR in patients with AF is a desired outcome as it leads to relief from symptoms, prevention of arrhythmia, improved exercise tolerance, improved quality of life, possible reduction in strokes and in whole improved survival. Many studies have been done previously to study prevention of post operative AF and the maintenance of a normal sinus rhythm. This study aimed at studying the prophylactic effect of IV Amiodarone in preventing post bypass AF and maintenance of NSR in patients undergoing mitral valve replacement.

Various metanalyses have been done on the benefits of Amiodarone in the restoration of normal sinus rhythm, with similar dosage protocols. Zebis LR et al[6] study assessing Practical regimen for Amiodarone use in preventing postoperative atrial fibrillation showed that post-operative prophylaxis with intravenous infusion (300 mg in 20-minute infusion) and followed by 600 mg oral Amiodarone significantly diminished the occurrence of postoperative AF. Guarnieri T et al[3] study assessing Intravenous amiodarone for the prevention of atrial fibrillation after open heart surgery reported low-dose intravenous Amiodarone (1 g over 24 hours, total 2 g of 48 hours) without loading dose which started 3 hours after surgery.

In this study, a lower dose of Amiodarone (3mg/kg) was given, where patients receiving prophylactic IV amiodarone had a significantly lesser incidence of atrial fibrillation, after release of aortic clamp. This was in concordance with studies of Selveraj T et al[8] and Amr YM et al[9] . Symptoms attributable to AF were reported less in patients who developed AF in Group A than in Group B ($p>0.05$).

Electrical cardioversion is a modality of treatment of AF, however it is resource intensive and is associated with higher procedural risks.[12] It was observed in this study, the number of patients requiring electrical cardioversion was significantly lesser in group receiving prophylactic Amiodarone. This finding was like in the studies of Amr YM et al[9] and Gillinov AM et al[13]. The energy required of cardioversion was significantly lesser as well in Group A. A similar finding in a study of Sagrista-Sauleda et al.[14], Amiodarone was found to reduce the threshold for electrical cardioversion in the study population however the reductions weren't statistically significant. The pretreat-

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ment effectiveness of oral Amiodarone with electrical cardioversion was studied previously by Opolski et al[15] where return of normal sinus rhythm was only in 59% of patients having persistent atrial fibrillation unresponsive to previous treatments.

The requirement of ionotropic support after discontinuation of CPB and return of cardiac activity were also studied, but showed no significant difference in the requirement between the groups.

It was observed in our study that AF reoccurred after a longer duration of NSR which was statistically significant with the maximal ventricular rate during AF being insignificantly lower in Group A than Group B. This is comparable to the studies of Zebis LR et al[6], Amr YM et al[9], Bagshaw SM et al[16], Selveraj T et al[8], Budeus M et al[17] and Guarnieri T et al[3]. Lesser incidence and recurrence of AF was found likely to decrease the incidence of complications thus helping improve patients haemodynamic status, and also comparably decrease the duration of ICU stay and hospital.

Postoperative complications occurred in 9 (12.6%) patients each of Group A and Group B. The limitation posed was that the complications seen in patients of Group A in our study, if at all, could not be definitely attributed to the use of I.V Amiodarone. However, none of the patients showed important side effects of amiodarone, e.g., bradycardia, hypotension, or QT interval prolongation during patient hospitalization. No mortality was noted in our study. Similar observations were noted in the studies of Amr YM et al[9] and Gillinov AM et[13].

Various studies like Sharma et al.[18] have also studied the effect of other anti-arrhythmic drugs like beta blockers, and Magnesium on post bypass rhythm and have found significant reduction in incidence of AF. However, our study excluded patients receiving other anti-arrhythmic therapy and studied solely on the prophylactic efficacy of Amiodarone.

Limitation of our study

The limitation of our study was that we observed the patients only till hospital discharge. Long term follow up would be necessary to analyse if a single prophylactic dose of IV Amiodarone prevents long term recurrence of Atrial Fibrillation. A multicentric trial with a larger sample size and long term follow up would be able to bring out differences that maybe significant.

Conclusion

Amiodarone given as a single intravenous dose in patients with pre-existing atrial fibrillation undergoing valvular surgery, prior to cardiopulmonary bypass was found to be effective in reducing the incidence of atrial fibrillation after aortic cross clamp release. The reduction in incidence of AF in effect means lesser hospital stay and associated complications. In cases with AF after the release

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of cross clamp release, amiodarone was found to decrease the energy required for cardioversion to normal sinus rhythm.

References

1. Kannel WB, Abbott RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation: the Framingham Study. N Engl J Med 1982;306:1018-22.
2. Raine D, Dark J, Bourke JP. Effect of mitral valve repair/replacement surgery on atrial arrhythmia behavior. J Heart Valve Dis 2004;13:615-21
3. Guarnieri T, Nolan S, Gottlieb SO, Dudek A, Lowry DR. Intravenous amiodarone for the prevention of atrial fibrillation after open heart surgery: the amiodarone reduction in coronary heart (ARCH) trial. J Am Coll Cardiol 1999;34:343-7.
4. Beaulieu Y, Denault AY, Couture P, et al. Perioperative intravenous amiodarone does not reduce the burden of atrial fibrillation in patients undergoing cardiac valvular surgery. Anesthesiology 2010;112:128-37.
5. Tokmakoglu H. Amiodarone versus digoxin and metoprolol combination for the prevention of postcoronary bypass atrial fibrillation. Eur J Cardiothorac Surg 2002;21:401-5.
6. Zebis LR, Christensen TD, Thomsen HF, et al. Practical regimen for amiodarone use in preventing postoperative atrial fibrillation. Ann Thorac Surg 2007;83:1326-31.
7. Yagdi T, Nalbantgil S, Ayik F, et al. Amiodarone reduces the incidence of atrial fibrillation after coronary artery bypass grafting. J Thorac Cardiovasc Surg 2003;125:1420-5.
8. Selvaraj T, Kiran U, Das S et al. Effect of single intraoperative dose of amiodarone in patients with rheumatic valvular heart disease and atrial fibrillation undergoing valve replacement surgery. Ann Card Anaesth. 2009;12(1):10-16.
9. Amr YM, Elmistekawy EM et. al Intraoperative loading dose of amiodarone for prophylaxis against atrial fibrillation after valvular heart surgery. Anesth Essays Res.2010;4(2):96-101
10. W. H. Maisel, J. D. Rawn, and W. G. Stevenson. Atrial fibrillation after cardiac surgery. Annals of Internal Medicine, 2001;135(12):1061–1073.
11. Nabauer M., Gerth A., Limbourg T. The Registry of the German Competence NETwork on Atrial Fibrillation: patient characteristics and initial management. Europace. 2009; 11: 423–434.
12. Lucy Y. Lei, Derek S Chew, William Lee et al. Pharmacological Cardioversion of Atrial Tacchyarhthmias Using Single High Dose Oral Amiodarone: A Systematic Review and Meta-analysis.Corc Arrhthm Electrophysiol. 2021; 14:e010321

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE03, 2023

13. Gillinov AM, Bagiella E, Moskowitz AJ et al. Rate Control versus Rhythm Control for Atrial Fibrillation after Cardiac Surgery. N Engl J Med. 2016; 374:1911- 1921.
14. Sagrista-Sauleda J, Permanyer-Miralda G, Soler-Soler J. Electrical cardioversion after amiodarone administration. Am Heart J 1992; 123: 1536–42.
15. Opolski G, Stanislawska J, Gorecki A, Swiecicka G, Torbicki A, Kraska T. Amiodarone in restoration and maintenance of sinus rhythm in patients with chronic atrial fibrillation after unsuccessful direct-current cardioversion. Clin Cardiol 1997; 20: 337–40
16. Bagshaw SM, Galbraith PD, Mitchell LB et al. Prophylactic amiodarone for prevention of atrial fibrillation after cardiac surgery: A meta-analysis. Ann Thorac Surg. 2006; 82: 1927–1937.
17. Budeus M, Hennersdorf M, Perings S et al. Amiodarone prophylaxis for atrial fibrillation of high risk patients after coronary bypass grafting: a prospective, double-blinded, placebo-controlled, randomized study. Eur Heart J. 2006; 27: 1584–1591.
18. Sharma S, Angral R, Saini H. Effect of prophylaxis of amiodarone and magnesium to prevent atrial fibrillation in patients with rheumatic valve disease undergoing mitral valve replacement surgery. Anesth Essays Res. 2020; 14: 189-193.