Comparison of amiodarone and propafenone for maintenance of stable sinus rhythm after bipolar radiofrequency ablation combined with a mitral valve procedure in patients with mitral valve disease and persistent atrial fibrillation

Mitral kapak hastalığı ve uzun süreli atriyal fibrilasyonu olan hastalarda mitral kapak işlemi ile kombine yapılan bipolar radyofrekans ablasyon sonrasında stabil sinüs ritminin devamlılığının sağlanmasında amiodaron ve propafenonun karşılaştırılması

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ABSTRACT
Background: This study aims to examine the effects of amiodarone versus propafenone for maintenance of stable sinus rhythm after left atrial bipolar radiofrequency ablation combined with a mitral valve procedure in patients with mitral valve disease and persistent atrial fibrillation.

Methods: The study included 75 patients (29 males, 46 females; mean age 66.8±7.4 years; range 54 to 82 years) who underwent left atrial bipolar radiofrequency ablation combined with mitral valve surgery between July 2008 and July 2010. Patients were divided into three groups of 25: propafenone group (group 1), amiodarone group (group 2), and control group (group 3). Atrial fibrillation patients with slow ventricular response were excluded from the study.

Results: Data was collected at preoperative period, during surgery, prior to discharge from hospital, and at 3, 6, and 18 months after discharge. Patients from all groups were followed for 18 months. In group 1, the number of patients in sinus rhythm was 18 at discharge, 13 at three months, 15 at six months, and 16 at 18 months. In group 3, the number of patients in sinus rhythm was 21 at discharge, 16 at three months, 14 at six months, and 16 at 18 months. Group 1 had a statistically significantly higher rate of stable sinus rhythm. No hospital mortality was observed in any group.

Conclusion: This study revealed that propafenone was more effective than amiodarone in maintenance of stable sinus rhythm at the postoperative period in patients who underwent bipolar radiofrequency ablation combined with a mitral valve procedure.

Keywords: Amiodarone; mitral valve surgery; propafenone; radiofrequency ablation.

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Atrial fibrillation (AF) is the most common heart rhythm disorder in adults and is responsible for significant cardiovascular morbidity and mortality, primarily due to thromboembolism. Pharmacological therapy, in particular the use of amiodarone, is still the most frequent choice for treating AF during the postoperative period, but according to Calò et al., a medical regimen is unsuccessful in between 50 and 84% of patients with persistent AF. Thus, several surgical techniques, such as left atrial (LA) isolation, catheter ablation of the bundle of His, the corridor procedure, pulmonary button isolation, and the atrial compartment operation have been used to treat this condition. The maze III procedure was developed by Cox et al. and because of its high success rate, it has become the gold standard for the surgical treatment of AF. In this method, various parts of both atria are cut and sewn to block the spread of chaotic electrical activity by forming areas of isolation in the atrial musculature. Unfortunately, since it is a complex and time-consuming procedure, experience is required, and there is a high rate of complications. Recently, alternative energy sources such as radiofrequency (RF), microwave, laser, bipolar cauterization, and cryoablation have been developed that allow for the creation of isolating lines without the need for cutting the tissue, thus making ablation easier.

The aim of this study was to examine the effects of amiodarone versus propafenone for the maintenance of stable sinus rhythm after undergoing LA bipolar RF ablation in conjunction with a mitral valve procedure in patients with mitral valve disease and persistent AF.

**PATIENTS AND METHODS**

The study was comprised of 75 patients who underwent a left atrial bipolar radiofrequency ablation procedure in conjunction with mitral valve surgery between July 2008 and July 2010. The patients were randomly divided into three groups. Group 1 (9 males and 16 females; mean age 66.7±8.1 years) was given propafenone, group 2 was given amiodarone (10 males and 15 females; mean age 66.6±8.02), and group 3 served as the control group (9 males, 16 females; mean age 66.9±7.88 years). The local ethics committee approved the study protocol, and all patients gave their written consent to be included. Patients who required additional surgery, for example coronary bypass grafting or aortic valve surgery, were excluded from the study, but those who needed tricuspid intervention were not excluded.

The primary endpoint was a return to AF. Propafenone was one of the available anti-arrhythmic drugs in our hospital, so it was selected to compare its efficacy against that of amiodarone. The ablation procedure was performed on the study participants in the three groups who had persistent AF plus mitral valve disease, but the AF cases with slow or normal ventricular response (heart rhythm <90/minute) did not undergo this procedure. In addition, standard 12-lead electrocardiography (ECG), Holter ECG, transthoracic echocardiography (TTE), left and right heart catheterization, and coronary angiography were performed preoperatively on all of the patients and controls who were over the age of 40.

After the median sternotomy, the patients underwent aortic and bicastral venous cannulation. Antegrade blood cardioplegia was used for induction, and continuous retrograde blood cardioplegia via the coronary sinus was utilized to maintain myocardial protection. Mitral valve replacement was performed on all of the members of groups 1, 2, and 3. The surgical treatment for persistent AF was accomplished by means of a bipolar radiofrequency irrigated ablation system (Cardioblate®, Medtronic Inc., Minneapolis, MN), and pulmonary vein isolation, LA appendage isolation and plication were also carried out.

In group 1, the propafenone (Rytmonorm, Abbott Laboratuvarları İth. İhr. ve Tic. Ltd. Şti., Istanbul, Turkey) was administered nasogastrically via an infusion (560 mg/day) on the day of the surgery. After extubation, it was given orally (150 mg three times a day) for one month followed by the same dosage twice a day for three months and then once a day for 18 months. In addition, all of the patients were started on anticoagulation therapy (warfarin) for the life span of the mechanical mitral valve.

Group 2 was administered amiodarone (Cordarone) as an intravenous bolus (150 mg) before the completion of cardiopulmonary bypass (CPB) followed by an infusion of 900 mg/day for two days. It was then given orally (3*200 mg) for one month, but the dosage could be adjusted depending on body weight. This was followed by 2*200 mg/day for the next 18 months. In addition, all of the patients were also started on anticoagulation therapy (warfarin).

Warfarin was also given to group 3, and they received cardiac medication without any anti-arrhythmic drugs as well.

**Data analysis**

Statistical analysis was performed using the SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL, USA) software package with a confidence interval (CI) of 95%. Chi-square, Mann-Whitney U, and Wilcoxon
Atrial fibrillation (AF) is a common arrhythmia that affects patients with underlying cardiovascular conditions. It is characterized by an irregular and rapid ventricular rate, often without atrioventricular (AV) synchronization, leading to reduced cardiac output and potential heart failure. AF also increases the risk of stroke and doubles the rate of death. The risk of thromboembolic complications caused by blood stasis in the atria leads to systemic anticoagulation stemming from the associated risk of bleeding. Non-persistent AF usually culminates in persistent AF, the final form of this disease.

In our series, the bipolar RF approach was used because it is less invasive and is associated with a shorter aortic cross-clamp time. In addition, all of the patients and controls were operated on by the same surgical team. In the literature, left atrial (LA) enlargement has been a strong independent risk factor for the failure of the pulmonary vein isolation.
procedure, which has led to a tendency toward it being performed selectively.[6] Isobe and Kawashima[6] reported that the risk of persistent AF after pulmonary vein isolation surgery is higher in patients with an LA diameter of greater than 80 mm. Conversely, Choo et al.[7] recently reported that pulmonary vein isolation surgery was successful in 95% of mechanical ventilation (MV) patients with an LA diameter equal to or greater than 60 mm. Other authors have also joined Choo et al.[7] in recommending a policy of aggressive LA size reduction in persistent AF patients with a dilated LA.[8,9] However, in our series, we found no significant differences between the three groups with respect to LA diameter.

Nevertheless, it remains unclear whether the LA size itself is the only critical issue. It is reasonable to expect that cellular, structural morphological, and parallel electrophysiological changes in the atrial tissue play a more prominent role in the progressive enlargement and hypertrophy of the atria.[10,11] Restoration of sinus rhythm by ablation leads to a greater quality of life (QoL), especially when compared with patients who have persistent AF that experience a sustained abnormal heartbeat and undergo mitral valve surgery.[12] Moreover, Pappone et al.[13] reported reduced mortality and morbidity and an improved QoL in patients who underwent circumferential pulmonary vein ablation for AF versus those treated with medical therapy alone. In our study, no hospital mortality occurred.

Between 30 and 79% of patients who undergo mitral valve surgery have AF, and less than 10% of those will enjoy a spontaneous conversion to sinus rhythm after isolated mitral valve surgery.[14] Patients who are cardioverted following mitral valve repair or replacement have a better survival rate as well as freedom from adverse events.[15-17] Recently, new methods and devices have been available to facilitate the surgical treatment of AF during mitral valve interventions, and sinus rhythm can now be restored in the majority of patients with persistent AF. Our observations suggest that patients who receive treatment for AF during mitral valve surgery have a better QoL. Therefore, we strongly recommend this type of therapy for all patients with persistent AF who are also scheduled for mitral surgery.

Ablation is the gold standard treatment for AF; however, maintaining sinus rhythm in cardioverted patients is actually more important. The cardioversion

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**Table 3. Operative data**

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic clamp time</td>
<td>40.2±3.7</td>
<td>40.5±3.7</td>
<td>35.2±6.1</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time</td>
<td>55.9±5.5</td>
<td>56.2±5.7</td>
<td>50.2±5.0</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Number who had tricuspid annuloplasties</td>
<td>3 12</td>
<td>4 16</td>
<td>4 16</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

SD: Standard deviation.

**Table 4. Postoperative data**

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>At discharge</td>
<td>22 88</td>
<td>18 72</td>
<td>16 64</td>
<td>0.06</td>
</tr>
<tr>
<td>At the 3rd month</td>
<td>20 80</td>
<td>13 52</td>
<td>11 44</td>
<td>0.03</td>
</tr>
<tr>
<td>At the 6th month</td>
<td>21 84</td>
<td>15 60</td>
<td>12 48</td>
<td>0.034</td>
</tr>
<tr>
<td>At the 18th month</td>
<td>21 84</td>
<td>16 64</td>
<td>14 56</td>
<td>0.041</td>
</tr>
</tbody>
</table>

**Figure 1.** Postoperative data.
Anti-arrhythmic drug selection is crucial because of the need to maintain a stable sinus rhythm. Camm[19] determined that amiodarone was the most effective anti-arrhythmic drug but believed that its safety profile limited its usefulness. Freemantle et al.[20] also found that amiodarone was the most effective drug for maintaining sinus rhythm. However, differences in outcomes between anti-arrhythmic drugs have been reported,[21] with sotalol and possibly amiodarone increasing mortality. However, in their study, Feyrer et al.[21] found no significant differences between the amiodarone and non-drug groups in their study on the restoration and maintenance of sinus rhythm in patients who underwent surgical ablation. Similarly, we also determined that there were no significant differences between the controls (group 3) and the patients taking amiodarone (group 2). Furthermore, Ventura et al.[22] reported that patients who were previously medicated with amiodarone had a higher recurrence rate of arrhythmia compared with those who had not been previously medicated with anti-arrhythmic drugs or those who had been medicated with anti-arrhythmic that had short plasma half-lives, in particular propafenone. Additionally, in their series, Sestito and Molina[23] found no differences regarding the side effects of propafenone and a placebo, and Larbuisson et al.[24] suggested that propafenone produces a more prompt effect in converting patients from AF to normal sinus rhythm than amiodarone.

Conclusion

In this study, our findings indicated that propafenone was associated with better outcomes than amiodarone with respect to the restoration and maintenance of sinus rhythm during the postoperative period in patients who underwent valvular surgery in conjunction with ablation therapy for AF. Therefore, we recommend the use of propafenone because of its higher tolerability and effectiveness and its low incidence of side effects. However, more studies are needed to support our results.

Declaration of conflicting interests

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