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Original Article

A randomized placebo-controlled trail with amiodarone for persistent atrial fibrillation in rheumatic mitral stenosis after successful balloon mitral valvuloplasty

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ARTICLE INFO

Article history:
Received 16 December 2015
Accepted 10 February 2016
Available online xxx

Keywords:
Anticoagulant
Atrial fibrillation
Mitral stenosis
Rheumatic heart disease

ABSTRACT

Objective: Atrial fibrillation is the most common sustained arrhythmia in patients with rheumatic heart disease (RHD). This study was conducted to determine the maintenance of sinus rhythm with amiodarone therapy following DC cardioversion (DCCV), early after successful balloon mitral valvuloplasty (BMV).

Methods: Patients were randomized to amiodarone group and placebo group and their baseline characteristics were recorded. DCCV was done 48 h after BMV. After cardioversion, oral amiodarone was started initially 200 mg three times a day for 2 weeks, then 200 mg twice daily for two weeks followed by 200 mg once daily for 12 months. Patients in placebo group received DCCV alone without preloading amiodarone. After DCCV, they were given placebo for 12 months.

Results: The 3 months follow-up period was completed by 77 patients (95%). Of them, 31 (77.5%) patients in amiodarone group and 14 (34.1%) in placebo group remained in sinus rhythm (SR). The 12 months follow-up period was completed by 73 patients (90.1%). Of them, 22 (55%) patients in amiodarone group and 7 (17.1%) in placebo group remained in SR.

Conclusion: We conclude that amiodarone is more effective than placebo in maintenance of SR at the end of 3 months following successful cardioversion and more patients continued to remain in SR even at the end of 12 months without major serious adverse effects.

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http://dx.doi.org/10.1016/j.ihj.2016.02.013

Please cite this article in press as: Vilvanathan VK, et al. A randomized placebo-controlled trail with amiodarone for persistent atrial fibrillation in rheumatic mitral stenosis after successful balloon mitral valvuloplasty, *Indian Heart J.* (2016), http://dx.doi.org/10.1016/j.ihj.2016.02.013

1. Introduction

Atrial fibrillation (AF) is common in patients with rheumatic valvular heart disease.[1] Strategies to maintain sinus rhythm (SR) in nonvalvular AF have been shown to improve functional capacity and quality of life (QoL).[2–4] The failure to reduce the mortality associated with rhythm-control strategies is in part due to the toxicity of the therapies used to maintain SR[5] Attempts to restore SR in rheumatic mitral stenosis (MS) have been rare because the long duration of AF and left atrial (LA) enlargement does not bode well for maintenance of normal SR.[6–9] Successful balloon mitral valvuloplasty (BMV) in MS by reducing LA pressure and chronic atrial stretch has been reported to result in a favorable reversal of electrical remodeling and reduced AF vulnerability.[10] Electrical DC cardioversion (DCCV) following successful BMV may lead to a better chance of successful cardioversion and a better chance of maintaining SR.[11] Large et al. demonstrated that surgical correction of mitral valve disease in patients who have AF resulted in spontaneous conversion to SR in 46%.[12,13] However, the rate of spontaneous conversion was much lower in other reports.[8]

In rheumatic MS after BMV, DCCV combined with amiodarone therapy successfully restored SR and maintained it in 49–81% patients at a mean follow-up of 18–31 months,[7,8] a success rate apparently surpassing that achieved by catheter-based radiofrequency ablation in this particular group of patients.[14,15] Amiodarone is preferred as the antiarrhythmic drug because it has been reported to be more effective than sotalol or class I agents for maintenance of SR in AF[11] and is particularly effective in rheumatic AF patients after mitral valve surgery[6] or BMV.[7,8]

The primary objectives of this study were to determine the maintenance rate of SR at 3 months and 12 months following amiodarone therapy and to assess the improvement in QoL by maintaining SR and also to determine the success rate of DCCV early after successful BMV in patients with symptomatic rheumatic MS with persistent AF.

2. Material and methods

2.1. Study population

From August 2010 to May 2012, we studied 89 patients with rheumatic MS with persistent AF without significant other valvular heart disease who underwent successful BMV. The duration of AF varied from 3 months to more than 2 years. In all patients, transthoracic echocardiographic examinations were performed to measure mitral valve area, mitral pressure gradient; LA diameter and LA pressure gradient were recorded immediately before and 24 h after BMV. LA diameter was measured during the diastolic phase using M-Mode study in the parasternal long axis view. LA pressure and mitral gradient were recorded in catheterization lab before and after BMV.

2.1.1. Inclusion criteria

Patients over 18 years of age who underwent successful BMV and Electrocardiogram (ECG) evidence of AF for more than 3 months.

2.1.2. Exclusion criteria

Prior history of cardioversion, significant mitral, tricuspid or aortic regurgitation, significant tricuspid and aortic stenosis, LA thrombus (detected by transesophageal echocardiography), LA diameter ≥6 cm, inability to comply with 12 months follow-up period or contraindications to anticoagulation and amiodarone. BMV was performed using accura balloon and the transseptal approach.

2.2. Study protocol

All eligible patients provided informed written consent before participation and all procedures followed institutional ethical standards and guidelines. The study complies with Declaration of Helsinki.

Patients were anticoagulated with warfarin and International normalized ratio was required to be between 2 and 3 for at least one month prior to DCCV. Patients were randomized to amiodarone group and placebo group and their baseline characteristics were recorded. DCCV was done 48 h after BMV. All of them were kept fasting through the night before they underwent cardioversion.

Patients in the amiodarone group were given amiodarone IV bolus 150 mg followed by 1 g IV infusion for 12 h prior to DCCV. After cardioversion, oral amiodarone was started initially 200 mg three times a day for 2 weeks, then 200 mg twice daily for two weeks followed by 200 mg once daily for 12 months.

Patients in placebo group received DCCV alone without preloading amiodarone. After DCCV, they were given placebo for 12 months.

Before DCCV, patients were administered IV midazolam or diazepam for sedation and meperidine for analgesia. Synchronized DCCV was given using biphasic defibrillators using the following protocol: 100 J, 200 J, 300 J, and 360 J. Unsuccessful DCCV was considered to include those who did not revert with 360 J.

2.3. Follow-up and assessment

Patients were followed up at 1, 3, 6, 9, and 12 months. During the visits, cardiac rhythm was determined by ECG. QoL was assessed using SF8 questionnaire. The physical component scores (PCS8) as well as the mental component scores (MCS8) were assessed separately. Patients under amiodarone group were assessed for drug side effects and drug interaction. All patients continued to take oral anticoagulants throughout the study period irrespective of their rhythm.

2.4. Endpoints of the study

The primary endpoint was the comparison of amiodarone versus placebo in maintaining SR at 3 and 12 months following successful cardioversion in patients with rheumatic MS with persistent AF undergoing BMV. The secondary endpoints were to identify the success rate of cardioversion following successful BMV, to identify the success rate of IV amiodarone in converting AF to SR, to identify the factors affecting maintenance of SR, changes in the QoL scores at follow-up and frequency of adverse events.

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