

Cardiac Rate Normalization in Chronic Atrial Fibrillation: Comparison of Long-term Efficacy of Treatment with Amiodarone versus AV Node Ablation and Permanent His-bundle Pacing

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ABSTRACT

Chronic atrial fibrillation (AF) is a common arrhythmia with significant morbidity and mortality. AF has been the subject of considerable attention and intensive clinical research in recent years. Current opinion on the management of AF favors the restoration and maintenance of normal ventricular rhythm. This has several potential benefits, including the alleviation of arrhythmia-associated symptoms and hemodynamic improvements. Maintenance of frequent normalization of ventricular rhythm (NVR) can be achieved with antiarrhythmic drug therapy or with AV node radiofrequency ablation (RFA) and permanent ventricular pacing. Recent interest has focused on the use of class III antiarrhythmic agents, such as amiodarone hydrochloride.

This investigation compared amiodarone to AV node RFA and permanent pacing of the His-bundle area in maintaining NVR in patients with resistant chronic AF. After 12 months of treatment with amiodarone (200 to 400 mg/d) 30 % of patients remained in NVR, 30 % were in transitional phase of improvement, and 40 % showed negative effect. Only a few patients in this group developed ocular or hepatic side effects.

On one year follow-up was achieved in 100 % of cases without any clinically significant side effects being seen. In conclusion, analysis of the results of this study suggests that low-dose amiodarone is well tolerated in the management of chronic AF in a selected patient population. The more aggressive interventional radiofrequency ablation technique is significantly more effective and more reliable in the long-term clinical treatment of drug-resistant AF.

INTRODUCTION

Chronic atrial fibrillation (AF) is a common arrhythmia associated with chronic heart failure, poor quality of life and significant morbidity and mortality. AF is the most common dysrhythmia in patients coming to emergency departments and also the most common arrhythmic cause of hospitalization. It has been the subject of considerable attention and intensive clinical research in recent years. Current opinion among

physicians on the management of AF favors the control of normal ventricular rate [1]. This has several potential benefits, including the alleviation of arrhythmia-associated symptoms and an overall hemodynamic improvement. Maintenance of normal ventricular rate (NVR) can be achieved with drug therapy (digoxin, β -blockers, calcium channel blockers) in most of the cases. Recent interest has been focused on the use of class III antiarrhythmic agents in resistant cases, such as amiodarone hydrochloride [2].

Due to high incidence of side effects this medication has been used only when conventional therapy has failed to control the rate [3,4]. Non-pharmacological modalities such as AV node radiofrequency ablation (RFA) with permanent pacing have also been used [5,6]. The efficacy of amiodarone for rate control of AF has not been quantified. No trial to date has compared the use of amiodarone with non-pharmacological modalities. Results of such a comparison will help us select the most effective way to achieve rate control in AF with minimal side effects in patients resistant to conventional therapy. We hypothesize that RFA with permanent pacing of the His bundle is superior to amiodarone for rate control in AF.

METHODS

This trial is an open, randomized and comparative study of the efficacy of pharmacological and non-pharmacological therapy in patients with resistant chronic AF. 76 patient with age range from 45-82 (mean 62 years) were enrolled in the study during a period of three years.

The study included patients of both genders, with AF for more than one year, rapid ventricular rate (bpm >90 at rest and bpm >140 during exertion) unable to be controlled with conventional medications (beta-blockers, calcium blockers and digoxin.) Patients that were treated with amiodarone or other antiarrhythmics except β -blockers, calcium channel blockers and digoxin, were excluded from the study. Patients enrolled were distributed in two groups by a closed envelope randomization.

In the first group of patients we used amiodarone for rate control (Group AM) and these patients received 12 months of treatment with amiodarone (200 to 400 mg/d). The

second group with radiofrequency ablation (RFA Group) underwent AV node RFA with permanent pacing of the His bundle. Patients were then followed monthly for one year and the heart rate at rest and exertion was documented on each visit. Hospitalizations during this period of time were also recorded. Results were analyzed by percentages and frequencies. Differences were compared by χ^2 test, ($p < 0.05$). The local institutional review board approved the study and all the patients enrolled signed an informed consent.

RESULTS and DISCUSSION

The trial included 76 patients all of whom were included in the final analysis. Patients were randomized in two groups (group AM & group RFA) which were homogenous in age, gender, and comorbidities. Thirty eight patients that were randomized in group AM underwent treatment with amiodarone 200-400 mg/d. A normal ventricular rate (50-90 b/min) was achieved in 22 of the patients (57,9%) within 3 weeks after therapy initiation (Table I). The rest of the patients (42,1%) had a slight decrease in the heart rate but were still above the target (heart rate >90 bpm at rest and >130 bpm on exertion). Three patients (7,9%) underwent RFA with pacemaker placement within 6 months of enrollment in the trial. During the follow up, ten of the patients (26,3%), that had a controlled rate initially, experienced intermittent episodes of rapid ventricular response (Table II). No additional patients achieved NVR during the follow up period. No adverse events from amiodarone were encountered during the one year follow up.

Thirty eight patients were enrolled in the non-pharmacological group. All of them were hospitalized for 2-3 days (52h average) for the RFA and pacemaker placement. A normal ventricular rate was achieved in all patients (100%) and was maintained during the one year follow up. No complications were encountered during the procedures.

Statistical analysis was performed with the initial results 3 weeks after treatment. χ^2 value was 20.267, degree of freedom of 1, ($p = 0.00000674$) yielding statistically significant difference between the two groups. Based on this result no χ^2 was calculated with the one year follow up data.

Table I. Results of rate control in two groups of patients after the initial 3 week treatment.

Treatment	Rate controlled (%)	Rate not controlled	Total no. of cases
Group AM	57,9	42,1	38
Group RFA	100	0	38
Total	60	16	76

Table II. Accumulative results of rate control after one year follow up.

Treatment	Rate controlled (%) @ 1 y F/U	Rate uncontrolled (%) 1y F/U	No.
Group AM	33.6	66.4	38
Group RFA	100	0	38
Total	50	26	76

Final analysis shows clearly a superiority of the non-pharmacological modality in the management of AF. Hospitalization for the RFA with pacemaker placement and the cost of the procedure should also be taken in consideration however no cost analysis was included as part of this study. One of the limitations of the study is the small sample size. Larger and multi-center trials will be required to consider RFA with pacemaker placement in the His bundle area as the first choice approach in the patients where conventional therapy for rate control of AF is unsuccessful.

In conclusion, analysis of the results of this study suggests that low-dose amiodarone is well tolerated in the management of chronic AF in a selected patient population with moderate success. RFA with permanent pacing of the His bundle area is more effective and reliable in the long term clinical treatment of drug resistant

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