Rhythm or Rate Control in Atrial Fibrillation: Which Is Better?

Hohnloser SH, Kuck KH, Lilienthal J. Rhythm or rate control in atrial fibrillation—Pharmacological Intervention in Atrial Fibrillation (PIAF): a randomised trial. The PIAF Investigators. Lancet 2000;356:1789–94.

Study Overview

Objective. To determine whether a strategy of rhythm control is superior to rate control alone in patients with symptomatic atrial fibrillation (AF).

Design. Open, randomized clinical trial. Analysis was by intention to treat.

Setting and participants. Patients aged 18 to 75 years who had persistent, symptomatic AF for at least 7 and no more than 360 days. Exclusion criteria were New York Heart Association class IV congestive heart failure, unstable angina pectoris, acute myocardial infarction within 30 days of the trial, average heart rate (with AF) less than 50 bpm, sick-sinus syndrome, Wolf-Parkinson-White syndrome, coronary artery bypass graft or cardiac valvular surgery in the previous 3 months, echocardiographic evidence of an intracardiac thrombus, embolic disease, hypertrophic cardiomyopathy, amiodarone therapy in the previous 6 months, acute thyroid dysfunction, pacemaker, contraindications for systemic anticoagulation therapy, and pregnancy. The study was conducted at 21 sites in Germany (details about location not provided).

Intervention. Group A patients received 90 mg of diltiazem 2 or 3 times daily. Group B patients first underwent pharmacologic cardioversion with 600 mg of amiodarone daily for 3 weeks, after which time patients who did not achieve restoration of sinus rhythm received electric cardioversion and maintenance on 200 mg of amiodarone daily. For patients taking diltiazem who were not rate controlled (group A) or for those with recurrent AF (group B), additional treatment was to be administered at the discretion of their physicians. All patients were anticoagulated to a target INR range of 2.0 to 3.0. Subjects were followed for 1 year, with regular visits scheduled for 3 weeks and 3, 6, and 12 months after randomization.

Main outcome measures. The primary outcome was relief of AF-related symptoms (palpitations, dyspnea, dizziness), which were qualitatively assessed through traditional clinical interviews. Secondary endpoints included change in a 6-minute walk test, change in mean heart rate during AF, stabilization of sinus rhythm, adverse drug effects, number of hospital admissions, and quality of life as measured by the Medical Outcomes Study short-form health survey (SF-36) [1].

Main results. Of the 252 patients enrolled, most were men (73%). Patients had a mean age of 61 years and had symptomatic AF for a mean of 110 days. About half of the study cohort had hypertension, 23% had coronary artery disease, and 15% had no underlying cardiovascular disease. At baseline, about two thirds of patients had palpitations and/or dyspnea and 30% had dizziness; 71% of patients were taking digoxin, and almost half were taking angiotensin-converting enzyme inhibitors. About 10% were receiving β blockers.

During the study, 2 patients died in each group. One patient in group A and 4 in group B were lost to follow-up. A total of 10 subjects crossed from one study group to the other (4 patients from A to B, 6 from B to A). In both groups, almost 60% of patients reported symptomatic relief at all follow-up visits. Sinus rhythm was restored during amiodarone loading in 23% of group B patients, while those remaining received at least 1 electric cardioversion. At 1 year, 56% of group B patients were in sinus rhythm, compared with 10% of group A patients ($P < 0.001$). Both groups experienced a mean decrease in heart rate of about 8 bpm (from 88 to 81 bpm in group A and from 86 to 78 bpm in group B) by the end of the trial. Group B improved in mean 6-minute walk distance by about 50 meters (10% over baseline) compared with no significant change in group A; this difference became apparent at 12 weeks.

In both groups, 17% of patients were admitted for adverse effects of study treatment. Group B had almost 3 times as many hospital admissions, two thirds of which were for electric cardioversion. Overall, 47% of group A patients experienced adverse drug effects compared with 64% of group B patients ($P = 0.001$). Because of these side effects, 14% of group A patients stopped treatment versus 25% of group B patients ($P = 0.036$). Quality-of-life scores for most subscales showed significant increases that were equal between groups.

Conclusion

Rate control and rhythm control appear to be roughly equivalent strategies for managing symptomatic AF.

Commentary

Hohnloser and colleagues designed this as a pilot study; as such, it was successful. Several obvious shortcomings limit the evidence: First, the trial was not blinded in any way. Second, therapeutic strategies were only partially controlled. (Of note, most patients were already rate controlled at baseline.) Third, the primary outcome measure was not assessed through a standardized instrument. Nonetheless, the study provides useful information. Although a type II error may have occurred for clinically significant outcomes, no trends suggested this possibility. The proportion of patients who experienced symptom relief as well as improvement in SF-36 scores were similar between groups. While rhythm-control patients increased their 6-minute walk distance significantly, this was not reflected across groups in terms of quality of life unless adverse drug effects in group B offset gains in exercise tolerance. Rate-control patients seemed to tolerate their medications better, but this was not reflected in quality-of-life scores. Notably, Hohnloser et al's study was conducted in light of the ongoing AFFIRM trial [2], a large (4000- to 5000-patient) multicenter trial examining treatment options for AF.

Applications for Clinical Practice

This study suggests that rhythm control provides no overall advantage in managing AF. Thus, it seems reasonable to make AF treatment decisions on a case-by-case basis, with patient symptoms and preferences taken into consideration. While the authors indicate that rate control alone may be cheaper—because of fewer hospital admissions—this issue must be resolved in future research.

References

1. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care 1993;31:247–63.
2. Atrial fibrillation follow-up investigation of rhythm management—the AFFIRM study design. The Planning and Steering Committees of the AFFIRM Study for the NHLBI AFFIRM investigators. Am J Cardiol 1997;79:1198–202.