

Review: Amiodarone is effective for converting atrial fibrillation to sinus rhythm

Letelier LM, Udol K, Ena J, Weaver B, Guyatt GH. Effectiveness of amiodarone for conversion of atrial fibrillation to sinus rhythm: a meta-analysis. *Arch Intern Med.* 2003;163:777-85.

QUESTION

Is amiodarone effective for converting atrial fibrillation (AF) to sinus rhythm over a 4-week period?

DATA SOURCES

Studies were identified by searching MEDLINE (1966 to February 2001), EMBASE/Excerpta Medica (1980 to September 2000), the Cochrane Controlled Trials Register (issue 3, 2000), Best Evidence (1991 to September 2000); hand-searching abstracts presented at major meetings or cardiology societies (1995 to 2000) and published in supplemental issues of 4 cardiology journals; reviewing reference lists of major cardiology and internal medicine textbooks, UpToDate (volume 8, number 2, 2000), recently published reviews, and all included articles; and contacting experts, authors, and 1 drug company.

STUDY SELECTION

Published and unpublished randomized or quasirandomized clinical trials were included if they compared amiodarone with placebo, digoxin, calcium-channel blockers, or no treatment in patients with AF of any cause or duration. The main outcome was conversion

to sinus rhythm over ≤ 4 weeks. Studies were excluded if $\geq 30\%$ of patients had non-AF supraventricular arrhythmias, the focus was on primary prevention of AF, or insufficient data were available on the primary outcome.

DATA EXTRACTION

2 authors independently extracted data on patient characteristics, drug regimens, rate of conversion to sinus rhythm, mortality, and adverse events. Quality of individual studies was assessed on the basis of allocation concealment, blinding, and completeness of follow-up.

MAIN RESULTS

21 trials met the inclusion criteria (7 abstracts, 14 published articles). Data from 1930 of 2000 patients were included in the analysis (mean age range 58 to 71 y, 43% to 86% men). Control treatments were placebo

(10 trials), no treatment (1 trial), a calcium-channel blocker (4 trials), digoxin (5 trials), and digoxin or diltiazem (1 trial).

Meta-analysis was done based on the intention-to-treat principle and used a random-effects model. Because of heterogeneity of study results, separate meta-analyses were done for studies with a long duration (> 48 h) or short duration (≤ 48 h) of AF. Amiodarone increased rates of conversion to sinus rhythm more than did control treatments (Table).

CONCLUSION

Amiodarone is effective for conversion of atrial fibrillation to sinus rhythm.

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Amiodarone vs control for conversion of atrial fibrillation (AF) to sinus rhythm*

Duration of AF	Number of trials	RBI (95% CI)	NNT (CI)
> 48 hours	5	333% (176 to 577)	4 (3 to 14)
≤ 48 hours	16	40% (25 to 57)	4 (3 to 6)

*Abbreviations defined in Glossary; follow-up periods were ≤ 24 hours (14 trials), 48 to 96 hours (3 trials), and 3 to 4 weeks (4 trials).

COMMENTARY

Clinically, one can divide AF into presentations where treatment priorities differ between rhythm control on the one hand and stroke prevention on the other. Usually, rhythm control is a priority in emergency departments, where intravenous or loading-dose oral medications are required, and a relevant outcome is acute conversion. Stroke prevention is a priority when cardioversion is more "elective," and a separate strategy for reducing stroke risk is used before conversion. In this context, the need for intravenous cardioversion medication is less clear. These issues are especially relevant to amiodarone, an agent with pharmacologic properties that differ when given orally and intravenously. Many of these concerns were addressed by the a priori subgroup analysis by duration of AF done by Letelier and colleagues. An analysis based on these priorities would have been more informative but probably not easily done in this complicated data set. In patients with AF ≤ 48 hours, the placebo or control response rates of 35% to 84% hint at

further areas of heterogeneity within this subgroup and underscore the difficulties of doing and interpreting such a meta-analysis.

Trials have also shown the efficacy of intravenous ibutilide, dofetilide, and procainamide, as well as oral flecainide, propafenone, and dofetilide for acute cardioversion of AF when compared with placebo. Drug-drug comparison trials are needed to guide clinicians in choosing among these potential management options.

In the meantime, amiodarone given intravenously or orally is safe, and the review by Letelier and colleagues provides an estimate of its efficacy despite the significant heterogeneity of the data set. The findings are most relevant to emergency department management of AF.

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