EUROPEAN JOURNAL OF
CARDIO-THORACIC
SURGERY

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*Eur J Cardiothorac Surg* 1994;8:194-198

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European Journal of
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# A comparison of amiodarone and digoxin for treatment of supraventricular arrhythmias after cardiac surgery

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**Abstract. Despite the widespread use of amiodarone in non-surgical patients, its role in the management of supraventricular tachyarrhythmias after cardiac surgery is not clear. We set out to compare the relative efficacy of amiodarone and digoxin in the management of atrial fibrillation and flutter in the early postoperative period. This prospective randomised trial comprised 30 patients, previously in sinus rhythm, who developed sustained atrial fibrillation or flutter following myocardial revascularisation, valve surgery or combined procedures. Amiodarone was administered as an intravenous loading dose followed by a continuous infusion. Digoxin was given as an intravenous loading dose followed by oral maintenance therapy. Electrocardiographic and haemodynamic monitoring was continued for 24 h after the commencement of treatment. There was a marked reduction in heart rate in both groups, mainly in the first 6 h, from 146 to 89 beats per minute in the amiodarone group and from 144 to 95 in the digoxin group. At the end of the 24 h, one of the 15 patients in the amiodarone group and 3 of the 15 patients in the digoxin group remained in atrial fibrillation. No patient in either group developed adverse reactions. We conclude that intravenous amiodarone therapy is safe and at least as effective as digoxin in the initial management of arrhythmias after cardiac surgery. [Eur J Cardio-thorac Surg (1994) 8:194–198]**

**Key words:** Coronary artery bypass – Arrhythmias – Amiodarone – Digoxin – Heart surgery

The development of supraventricular arrhythmias, especially arterial fibrillation, is a common complication after cardiac surgery [15, 18]. These early post-operative arrhythmias are poorly tolerated when the ventricular response is rapid. The goal of pharmacological treatment is rapid reduction in the ventricular rate and early reversion to sinus rhythm.

Amiodarone hydrochloride is highly effective in the management of ventricular and supraventricular arrhythmias. The efficacy of parenteral amiodarone in the management of atrial fibrillation (AF) with rapid ventricular response, has been established in a variety of settings, including coronary artery disease, cardiomyopathy and valvular heart disease [2, 3, 20]. After myocardial infarction, parenteral amiodarone has been shown to be more effective than digoxin in the initial management of AF [5].

A broad spectrum of antiarrhythmic activity makes amiodarone potentially useful after cardiac surgery where transient myocardial irritability predisposes to both atrial and ventricular arrhythmias. Although the efficacy of amiodarone in post-operative cardiac patients has been reported [8, 12, 14], digoxin remains the drug of choice in most cardiac surgical units in the initial management of post-operative supraventricular tachycardias. To our knowledge no previous study has directly compared the efficacy of digoxin with amiodarone in this setting. We therefore undertook a prospective randomised study to compare amiodarone and digoxin in the initial management of AF and flutter in the early period after cardiac surgery. Hypotension and bradycardia have been troublesome side effects in previous studies of post-operative patients, where amiodarone was given as an intravenous bolus [8]. To avoid these problems in the present study, we excluded patients with severe impairment of pre-operative left ventricular function or with post-operative haemodynamic instability and administered amiodarone as a slow intravenous infusion.

Received for publication: October 5, 1993
Accepted for publication: November 22, 1993
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## Methods

### *Study groups*

Patients recovering from open heart surgery were entered into the trial if they developed AF which persisted for more than 20 min with systolic blood pressure of 85 mmHg or above without inotropic support. Patients were randomised (on the basis of their hospital record number) to receive either amiodarone ($n=15$) or digoxin ($n=15$). Patients were excluded from the study on the following grounds: AF prior to surgery; poor ventricular contractility on pre-operative left venticulogram (Grade 5; scale: 1 = normal to 5 = worst); post-operative administration of beta-blocking agents. The characteristics of the two groups and the operations performed are shown in Table 1. The study protocol was approved by the Alfred Hospital Ethics Committee according to the guidelines of the National Health and Medical Research Council of Australia. Written consent to participate in the study was obtained from all patients prior to surgery.

### *Drug regimens*

*Amiodarone.* A loading dose of 5 mg/kg (up to a maximum of 400 mg) in 100 ml of 5% dextrose, was infused intravenously over 30 min. Thirty minutes after completion of the loading dose, an infusion of 25 mg/h was commenced. The ventricular rate was reassessed after 6 h and if this exceeded 120 beats/min, the infusion rate was increased to 40 mg/h. Treatment was continued for 24 h after reversion to sinus rhythm. If reversion had not occurred after 24 h of intravenous amiodarone infusion, digoxin was added to the amiodarone therapy using half the dose detailed below.

*Digoxin.* A loading dose of 1 mg was administered intravenously over 9 h as follows: 0.5 mg over 30 min at the onset of treatment, followed by 0.25 mg after 2 h and 0.125 mg after 5 h and 9 h. Oral maintenance therapy was then commenced within 12 h, at a dose appropriate to body weight and renal function. The serum digoxin level was measured between 6 and 12 h after completion of the loading dose. All patients had therapeutic serum digoxin levels after completion of the loading dose. If reversion had not occurred during the 24-h study period, amiodarone was added as described above and digoxin was continued at one-half the previous dose.

### *Measurements*

At the onset of the arrhythmia, the pulse rate, cardiac rhythm and arterial blood pressure were recorded. A 12-lead electrocardiogram (ECG) was obtained and serum electrolyte and arterial blood gas levels were measured. Electrolyte disturbance or hypoxia was corrected. The cardiac rate and rhythm were monitored continuously throughout the first 24 h following commencement of therapy. The ventricular rate and rhythm and the arterial blood pressure were recorded hourly for the first 6 h, 2 hourly for a further 6 h and then 4 hourly until 24 h had elapsed. A 12-lead ECG was obtained following any change of rhythm.

### *Statistical analysis*

The treatment groups were compared during the first 24 h after the onset of treatment with regard to cardiac rhythm, ventricular rate and blood pressure. Repeated measures analysis of variance was performed to compare the effect of the two agents on cardiac rate, and to evaluate the differences in blood pressure between amiodarone- and digoxin-treated groups at each assessment time. The log-rank test was used to compare the rate of reversion to sinus rhythm in each group.

**Table 1.** Clinical characteristics

| | Amiodarone | Digoxin |
|---|---|---|
| Number of patients | 15 | 15 |
| Mean age (years) | 60.2 | 65.8 |
| Male: female ratio | 11:4 | 10:5 |
| Pre-operative beta-blockade | 7 | 8 |
| Operation | | |
| CABG | 11 | 10 |
| AVR | 3 | 3 |
| Mitral valvotomy | 1 | 0 |
| Combined procedures | 0 | 2 |
| Reoperation | 3 | 2 |

CABG = coronary artery bypass grafting, AVR = aortic valve replacement

## Results

### *Onset of atrial fibrillation*

The mean time from surgery to the onset of atrial arrhythmias was similar in each group (amiodarone 54 h, digoxin 49 h). The mean time from onset of AF to institution of treatment was 72 min in the amiodarone group and 51 min in the digoxin group. The mean initial ventricular rate was 146 beats/min in the amiodarone group and 144 in the digoxin group. At the time of onset of AF there was no significant difference between the two groups in serum electrolyte or arterial blood gas levels or mean arterial blood pressure.

### *Reversion to sinus rhythm*

The percentage of patients in AF throughout the 24-hour observation period is shown in Figure 1. During the 24-h study period, all 15 patients in the amiodarone group reverted to sinus rhythm. However, AF recurred transiently in two patients, after 12 and 16 h of treatment. In another patient, sustained AF recurred after 20 h of treatment; digoxin was added at the end of the 24-h study period with subsequent reversion to sinus rhythm after a further 20 h.

In the digoxin group, two patients failed to revert to sinus rhythm during the study period. Of the 13 patients who initially reverted to sinus rhythm, 3 transiently re-developed AF at 6, 8 and 24 h, respectively.

The probability of remaining in AF throughout the 24-h study period in the two groups was not significantly different ($P=0.87$ log-rank test). During the 24-h period of the study no patient in either group required direct current reversion for arrhythmia control. After the first 24 h, one patient in the digoxin group required cardioversion, having failed to revert to sinus rhythm despite therapy with both agents.

### *Control of ventricular rate*

The ventricular rate decreased significantly with time in both groups, mainly in the first 6 h ($P<0.002$) (Fig. 2).

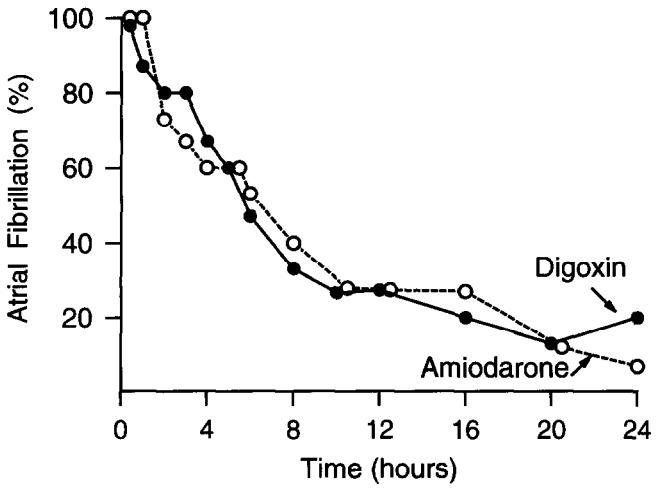


**Fig. 1.** Percentage of patients in atrial fibrillation during first 24 h after commencement of treatment

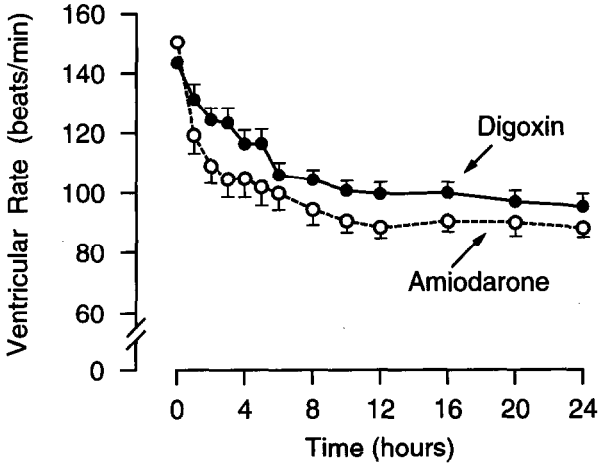


**Fig. 2.** Ventricular rate over the 24-h study period in the amiodarone and digoxin groups (mean ± SEM). There was no significant difference in rate between the two treatments ($P=0.33$)

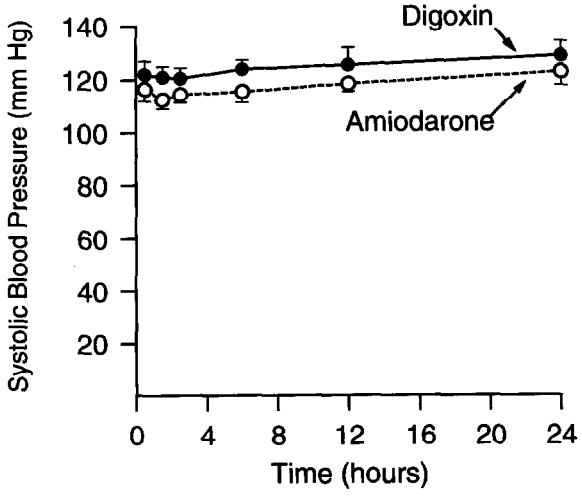


**Fig. 3.** Systolic arterial blood pressure in the two groups over 24 h (mean ± SEM). There was no significant difference between the two groups ($P=0.90$).

Over the 24-h period there was a trend toward lower rates in the amiodarone group, but there was no significant difference between the groups ($P=0.33$).

*Blood pressure and side effects*

Systolic blood pressure was similar in both groups (Fig. 3) ($P=0.90$). No patient in either group developed clinically significant hypotension or cardiac conduction abnormalities. It was not necessary to cease amiodarone treatment in any patient because of hypotension or any other side effects.

## Discussion

This study demonstrates that, in patients without severe impairment of left ventricular function, the use of intravenous amiodarone infusion is safe and at least as effective as digoxin in the rapid control of AF after cardiac surgery.

Ventricular rates decreased over the 24-h study period in both groups. How much of this decrease was spontaneous and how much due to therapy is unknown as no untreated control group was included (for ethical reasons). The slowing in ventricular rate appeared to be more marked in the aminodarone group than in the digoxin group, but the difference was not statistically significant. It is possible that a superior effect of amiodarone in reducing the ventricular rate was missed due to the small numbers of patients in each group (Type II error).

The reported incidence of sustained supraventricular tachyarrhythmias following cardiac surgery varies from 10 to 53% [4, 21]. The incidence of sustained AF in our unit was 28% during the period of the study, ranging from 14% in patients under 40 years of age to 40% in patients over 70 years of age. Atrial arrhythmias occurring in the early period after cardiac surgery are often regarded as benign. However, when the ventricular response is rapid, myocardial performance is compromised and haemodynamics may be impaired.

Arrhythmia prophylaxis has been addressed in recent studies [1], but little attention has been focused on pharmacological strategies for rapid arrhythmia control. Currently, digoxin, calcium channel blockers or quinidine-like agents provide the mainstay of treatment, with cardioversion reserved for patients with significant haemodynamic compromise.

Amiodarone is an iodinated benzofuran derivative which has been used extensively in the management of ventricular and supraventricular arrhythmias. Amiodarone has mainly class 3 antiarrhythmic activity (it prolongs the duration of the action potential in conducting fibres and increases their refractory period) but also has some class 1 (membrane stabilising) action [10].

Few studies have evaluated the role of amiodarone after cardiopulmonary bypass. Installe and colleagues described their experience with parenteral amiodarone in the initial management of 95 patients with a wide vari-

ety of post-operative rhythm disturbances [8]. Using a bolus dose of 2.5–5.0 mg/kg followed by an infusion for 72 h, reversion to sinus rhythm was achieved in 61% of 90 patients with supraventricular tachycardia. Of 18 patients with AF, 10 reverted within 12 h and the remaining patients demonstrated a marked reduction in ventricular rate. Other studies have yielded similar results [12]. Recently McAlister and colleagues compared parenteral amiodarone and oral quinidine, in a study of post-operative patients with supraventricular arrhythmias refractory to initial management with digoxin or atrial pacing [11]. A higher rate of reversion to sinus rhythm was achieved with quinidine than with amiodarone (64% vs 41%), however, side effects were more common with quinidine.

The group of patients occasionally seen in the early post-operative period with a combination of atrial and ventricular arrhythmias presents a therapeutic challenge. In view of the proven efficacy of amiodarone in the treatment of ventricular arrhythmias after cardiac surgery, it may be that amiodarone has a unique role to play in the treatment of these complex arrhythmias [8]. Our own clinical experience favours this conclusion.

Enthusiasm for the use of amiodarone before and after cardiac surgery has been tempered by concern about the development of serious side effects [9]. Parenteral amiodarone is associated with a low incidence of acute adverse reactions. In the absence of left ventricular dysfunction, an infusion of 5 mg/kg, similar to the loading dose employed in the present study, has only a weak negative inotropic effect [16]. With severe left ventricular impairment, profound hypotension may result as the myocardium fails to maintain cardiac output in the face of reduced peripheral resistance and myocardial depression [17].

The precipitation of atrioventricular and intraventricular conduction delays by amiodarone, including complete heart block, is well documented but uncommon [6]. These reactions almost invariably occur after an intravenous bolus injection and appear to be uncommon after intravenous infusions. The side effects of chronic therapy with amiodarone are numerous [7, 16, 19], and therefore its use for long-term therapy for post-operative atrial arrhythmias is difficult to justify. Severe amiodarone-induced pulmonary complications after cardiopulmonary bypass appear to be confined to patients who have had pre-operative amiodarone pulmonary toxicity [13]. To avoid haemodynamic compromise, we excluded patients with poor left ventricular function and administered amiodarone as an intravenous infusion rather than a bolus. Our dosage regimen was similar to those previously described [8, 20].

The rate of arrhythmia recurrence was low in both treatment groups. This may in part reflect the natural history of AF and flutter, which is a trend towards spontaneous reversion. Amiodarone has a long serum and tissue half-life [13] and some antiarrhythmic benefit might be expected to persist beyond the period of infusion. However, to minimise early arrhythmia recurrence, short-term maintenance therapy with an oral antiarrhythmic agent is desirable [11]. Digoxin must be introduced with caution as the interaction of amiodarone and digoxin, resulting in elevated serum digoxin levels, is well recognised. Because of the potential for side effects including pulmonary toxicity and haemodynamic compromise with further cardiopulmonary bypass, long-term oral amiodarone therapy after cardiac surgery appears to be contraindicated.

In view of its known potent action in controlling ventricular arrhythmias [10] amiodarone may be the treatment of choice in post-operative patients with a combination of atrial and ventricular arrhythmias.

## Conclusions

1. Short-term parenteral amiodarone infusion is safe and effective in the management of AF after cardiac surgery in patients wihout severe pre- or post-operative left ventricular dysfunction.
2. Amiodarone is of similar efficacy to digoxin in the management of post-operative AF.

*Acknowledgements*. The authors acknowledge the advice of Dr. M. Rabinov and Dr. J. Federman and the statistical assistance of Mr. Edward Burt and Mr. Antony Ugoni.

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