Clinical Reports

Relationship between preoperative amiodarone treatment and complications observed during anaesthesia for valvular cardiac surgery

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Two groups of ASA physical status class III and IV patients undergoing cardiac surgery were reviewed in an attempt to obtain more conclusive data concerning dangerous interactions between amiodarone and anaesthesia. The amiodarone group (Group 1, ten patients, cumulative dose 10 g) was compared with a control group (nine patients, Group 2). Amiodarone (A) and desethylamiodarone (NA) concentrations in plasma and myocardium were measured and haemodynamic and antiarrhythmic effects were analysed. Throughout anaesthesia haemodynamic status was similar in both groups. No correlation was found between A/NA and cardiac index changes. No patients needed intraaortic blood pressure augmentation or developed low systemic vascular resistances. Pacemaker dependency was similar in both groups and there was no evidence of increased anaesthetic risk. An excellent antiarrhythmic effect was obtained during the postoperative period. We conclude that preoperative treatment with amiodarone is effective against postoperative arrhythmias.

Dans le but d'éclaircir l'interaction dangereuse décrite entre l'amiodarone et l'anesthésie générale, nous avons comparé deux groupes de patients ASA III ou IV subissant une intervention à cœur ouvert soit un groupe amiodarone (Groupe 1: dix patients, dose cumulative 10 g) et un groupe contrôle (Groupe 2: neuf patients). Nous avons mesuré les concentrations myocardiques et plasmatiques d'amiodarone et de déséthylamiodarone ainsi que leurs effets antiarythmiques et hémodynamiques. Les profils hémodynamiques des deux groupes étaient comparables sauf pour une plus faible augmentation de l'index cardiaque dans le Groupe 1. Nous n'avons pas trouvé de corrélation entre A,NA et les variations d'index cardiaque. Aucun patient n'a eu besoin de contre-pulsion aortique ou n'a présenté de résistances vasculaires périphériques trop basses. L'usage de pace-maker etait comparable dans les deux groupes et l'amiodarone n'a pas augmenté le risque anesthésique. L'effet antiarythmique obtenu pendant la période post-opératoire était excellent. Nous concluons donc que l'amiodarone en pré-opératoire prévient efficacement les arythmies post-opératoires.

Key words
ANAESTHESIA: cardiac;
HEART: antiarrhythmics, amiodarone;
INTERACTIONS (DRUG): amiodarone anaesthesia;
SURGERY: cardiac.

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Amiodarone was initially studied as an antianginal agent.[1] Subsequently this drug was found to have pronounced antiarrhythmic effects[2] and is currently used for control of supraventricular and ventricular tachyarrhythmias.[3] Because of these properties, many patients are taking long-term oral amiodarone treatment. Previous studies have suggested an increased risk of general anaesthesia for these patients.[4,5] Amiodarone has been suggested as a cause of atropine-resistant bradycardia, myocardial depression, severe hypotension, and increased perioperative mortality.[4] However, this dangerous interaction between amiodarone and anaesthesia has been disputed in a report in which mortality was not increased by amiodarone.[6]

Postoperative arrhythmias are usual in patients with valvular disease undergoing general anaesthesia with

TABLE I Preoperative clinical and haemodynamic data

	Control group	*Amiodarone group*
Patient population	$n = 9$ F = 2; M = 7	$n = 10$ F = 5; M = 5
Age yr (range)	49 (39–69)	49 (28–68)
Operation		
– mitral valve replacement	8	5
– aortic valve replacement	2	3
– commissurotomy under ECC	1	2
Preoperative rhythm		
– sinus rhythm	5	7
– atrial fibrillation	4	3
Postoperative rhythm		
– sinus rhythm	6	8
– atrial fibrillation	3	2
Pacemaker dependency	3	3
CPB time (min)	50 (28–91)	42 (22–63)
CI ($L \cdot min^{-1} \cdot m^{-2}$)	2.30 ± 0.2L	2.69 ± 0.25
LVSWI ($gm \cdot m \cdot m^{-2}$)	37.5 ± 4.9	49.2 ± 4.7
SVRI ($dynes \cdot sec \cdot cm^{-5} \cdot m^{-2}$)	2966 ± 351	2808 ± 384
HR ($beat \cdot min^{-1}$)	78.6 ± 4.6	73.5 ± 3.3
MAP (mmHg)	87.4 ± 6.6	93.1 ± 3.6

cardiopulmonary bypass (CPB).[7] Previously we reported our experience of arrhythmias in 32 patients, 16 of whom received amiodarone therapy preoperatively.[8] In this study, haemodynamic data were available for 19 patients. In view of the conflicting opinions concerning the interaction between amiodarone and general anaesthesia, the haemodynamic status and perioperative mortality was reviewed in these 19 patients.

Methods

Nineteen patients undergoing mitral or aortic valve replacement constitued the patient population. The protocol was reviewed by the Ethical Board Committee. All patients NYHA status III or IV, were informed about the study, gave their consent to participate, and were randomly divided into two groups. The amiodarone group (Group 1) was given amiodarone (Cardarone*) 600 mg orally every day for one week and then 400 mg every day for two weeks prior to surgery (Total dose 10 g). Patients not receiving amiodarone constituted the control group (Group 2). Table I shows the clinical data. Cardiac catheterization data were available in all patients before amiodarone treatment.

Anaesthesia

After intramuscular premedication with atropine 0.025 mg, diazepam 10 mg, and alimemazine 25 mg, anaesthesia was induced with thiopentone (3–4 $mg \cdot kg^{-1}$), fentanyl (15–20 $\mu g \cdot kg^{-1}$), and droperidol (0.2 $mg \cdot kg^{-1}$).

Tracheal intubation was performed after administration of d-tubocurarine (0.4 $mg \cdot kg^{-1}$). Ventilation was controlled (Servo B-Siemens Elema) and adjusted to maintain $PaCO_2$ and PaO_2 in a normal range (FiO_2 = 0.5). Anaesthesia was maintained with incremental doses of fentanyl. Monitoring was established with a five-lead ECG, a radial arterial cannula and a 7 F thermodilution pulmonary artery catheter (Edwards Laboratories, Santa Ana, CA) introduced via the right internal jugular vein. Haemodynamic status was assessed prior to cardiopulmonary bypass (CPB) which was performed under normothermic condition (35–36° C) in all patients. Further haemodynamic measures were determined 30 min after weaning from CPB. During the 24-hour postoperative period, continuous ECG Holter monitoring was performed. Serum potassium concentration was maintained at normal levels in all patients. Prior to CPB, samples of plasma and myocardium were obtained to measure con-

TABLE II Haemodynamic data (mean ± SEM)

	Amiodarone group		*Control group*	
	Pre-CPB	*Post-CPB*	*Pre-CPB*	*Post-CPB*
HR ($beat \cdot min^{-1}$)	57.5 ± 4.7	66 ± 3.7	69 ± 5.2	75 ± 2.9
MAP (mmHg)	68.6 ± 3.8	69.3 ± 2.5	76.2 ± 6.5	75.8 ± 5.8
CI ($L \cdot min^{-1} \cdot m^{-2}$)	1.73 ± 0.12	2.26 ± 0.5**	1.78 ± 0.17	2.75 ± 0.13**
PVRI ($dynes \cdot sec \cdot cm^{-5} \cdot m^{-2}$)	145 ± 27.5	117 ± 13.7	373 ± 44.5	245 ± 47.9
SVRI ($dynes \cdot sec \cdot cm^{-5} \cdot m^{-2}$)	2958 ± 309	2803 ± 184†	3053 ± 442	1843 ± 319†
CVP (mmHg)	9.9 ± 1	12.8 ± 0.9	11.6 ± 1.4	13.9 ± 1.6
PCWP (mmHg)	16.3 ± 1.6	16.6 ± 2.3	18.3 ± 1.9	16.5 ± 2.1
MPAP (mmHg)	19 ± 1.6	20.8 ± 1.7	26.3 ± 2.4	26.5 ± 2.1
LVSWI ($gm \cdot m \cdot m^{-2}$)	29.9 ± 2.5	34 ± 2.7	27.7 ± 4.3	41.7 ± 4.4*
RVSWI ($gm \cdot m \cdot m^{-2}$)	8.6 ± 1.3	10 ± 0.7	10 ± 1.5	14 ± 1.3*
SI ($ml \cdot beat^{-1} \cdot m^{-2}$)	31.7 ± 3.3	34.6 ± 2.3	27.3 ± 3.2	37.5 ± 2.3

*$P < 0.05$.
†$P < 0.01$.

TABLE III Plasma and myocardial concentrations of amiodarone (A) and desethylamiodarone (NA)

	Plasma concentration $mg \cdot l$		*Myocardial concentration* $mg \cdot kg^{-1}$	
Patients	*A*	*NA*	*A*	*NA*
1	1.03	0.362	7.5	9.1
2*	0.904	1.32	5.6	6.1
3	0.524	0.62	12.5	12
4	0.628	0.68	23.5	18.6
5	0.226	0.48	4.7	9.8
6	0.620	0.22	8.7	13.3
7	0.822	0.458	7.3	15.4
8	0.964	0.398	12	3.6
9*	0.384	0.402	4.5	5.7
10*	0.398	0.184	9.9	9.3
Mean	0.65	0.512	9.62	10.30
±SEM	±0.09	±0.32	±1.78	±1.46

*Pace-maker dependent.

centrations of amiodarone and desethylamiodarone by high-pressure liquid chromatography.

Data analysis

To compare data within a group the Wilcoxon's test was utilized. The values between Group 1 and Group 2 were compared using the Mann-Whitney test. A P value < 0.05 was accepted as statistically significant. Data are given as means ± SEM.

Results

The two groups were not statistically different in age, weight, or severity of heart disease. In both groups, cardiac index (CI), mean arterial pressure (MAP), systolic vascular resistance index (SVRI), left ventricular systolic work index (LVSWI), right ventricular systolic work index (RSWI), mean pulmonary artery pressure (MPAP) were not statiscally different (Table II).

During the post-CPB period, IC increased significantly (1.78 to 2.75 in Group 2, 1.73 to 2.26 in Group 1) and SVRI decreased in both groups. There was no significant change in PCWP, MPAP. Three patients out of ten, and three out of nine were pacemaker-dependent in Group 2, and Group 1 respectively. No patient required intra-aortic balloon pump augmentation (IAPBA) and there were no deaths within one month of surgery.

In both groups no patient developed severe arrhythmia. After surgery, there were 1,507 supraventricular premature beats during the 24 hr in Group 2 and 75 in Group 1 ($P < 0.01$), while 621 ventricular premature beats were found in Group 2 and 53 in group 1 ($P < 0.01$).

Table III summarizes the amiodarone plasma concentrations before CPB. There was no relationship between plasma or tissue amiodarone or desethylamiodarone levels and pacemaker dependency, and changes in cardiac indices (CI, MAP).

Discussion

Amiodarone possesses non-competitive, adrenergic blocking effects[9] which can produce sinus bradycardia, and arterial and venous vasodilatation.[10] In anaesthetized patients after tracheal intubation Elliot *et al.*[6] found no haemodynamic differences between an amiodarone group and a control group. But, in the study of Liberman *et al.*,[4] 50 per cent of amiodarone-treated patients undergoing cardiac surgery required IABPA to be weaned from CPB and 13 per cent developed low SVRI and required alpha adrenergic stimulation.

In the present study after weaning from CPB cardiac index, LVSWI, increased with a concomitant decrease in SVRI in the control group. In the amiodarone group CI increased but this increase was less than in the control group and the MPAP, PCWP remained unchanged. Despite higher PVRI values left ventricular function improved in the control group. These results support the concept that amiodarone could decrease left ventricular function during anaesthesia. They are in contrast with Liberman's results because no patients needed IAPBA or developed low SVRI. These differences may be attributed to type of surgery (no patients underwent coronary grafting), or CPB technique, but could not be due to amiodarone dosage differences. Plasma amiodarone and desethylamiodarone concentrations found in our study were quite similar with those measured by several authors during an initial amiodarone treatment.[11,12] The cumulative dose was low in the present study, 10 g, but 2/3 of Liberman's patients who died had received a cumulative dose less than 12 g (8.4 and 11.2 g). Desethylamiodarone concentrations were not available in Liberman *et al.*'s study. In two patients receiving long-term amiodarone treatment and undergoing general anaesthesia, Nalos *et al.*[13] measured myocardial A and NA concentrations. Although higher myocardial concentrations were found than in the present study, no decrease of cardiac output occurred during surgery. Thus, low cardiac output after anaesthesia can occur over a wide range of amiodarone, desethylamiodarone plasma or myocardium concentrations.

Arrhythmias occur frequently after cardiac surgery.[7] The present data are in agreement with previous studies demonstrating that amiodarone has an excellent antiarrhythmic effect which was obtained in the postoperative period[14] and was achieved with therapeutic plasma concentrations that did not exceed 2.5 $mg \cdot L^{-1}$.[11] Previous studies have reported various arrhythmias in patients taking amiodarone. These included atropine-resistant

sinus bradycardia,[4,5] slow nodal rhythm, heart block and the need for ventricular pacing. Contrary to Lieberman, we did not find a difference in pacemaker dependence after CPB. There was no relationship between pacemaker dependency and plasma or tissue amiodarone concentrations. All patients who developed A-V block or sinus depression had serum amiodarone concentrations below 1 $mg \cdot L^{-1}$. This is in contrast with long-term amiodarone treatment where rhythmic complications have been described at serum amiodarone concentrations ranging from 1.7 to 2.5 $mg \cdot L^{-1}$.[15]

In conclusion, this study confirmed the antiarrhythmic effect of amiodarone during valvular surgery and demonstrated moderate myocardial depression. Unlike previous studies no additional complications nor mortality was observed in the amiodarone group.

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