

Effect of Amiodarone on atrial fibrillation after coronary artery bypass surgery

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ABSTRACT

Objective: Atrial fibrillation occurs in 10%–40% of patients undergoing coronary artery bypass grafting. This study investigates whether prophylactic Amiodarone use reduces the rate of atrial fibrillation post myocardial revascularisation.

Methods: In a prospective study conducted at the Cardiothoracic Center over a 6 month period, 192 patients were randomized to either Amiodarone or placebo. The Amiodarone group received Amiodarone infusion followed by oral Amiodarone on a decreasing dose for a total period of 6 weeks. The placebo group were started on an infusion of dextrose 5% solution and then maintained on a matched regimen of placebo tablets for a corresponding period of time.

Results: Of the 100 patients recruited for the Amiodarone arm of the study, 12 were excluded for a variety of reasons detailed in the discussion with atrial

fibrillation occurring in 28 (a rate of 32%). Of the 92 controls, 32 developed atrial fibrillation (a rate of 35%). There were no significant differences between the groups. The maximum ventricular rate during atrial fibrillation however, was significantly slower in the Amiodarone group (108+/-18) compared to (136+/-22) $P < 0.05$. Moreover, there were no significant differences in the mortality rates between the 2 groups; a rate of 3% (3 of 88) in the Amiodarone group as opposed to 3% (3 of 92) in the controls.

Conclusion: In this study prophylactic Amiodarone did not reduce the rate of atrial fibrillation post coronary artery bypass surgery. However, it reduced the maximum ventricular rate. Amiodarone had no effect on mortality post coronary artery bypass.

Keywords: Atrial fibrillation, Amiodarone, coronary surgery.

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Atrial Fibrillation (AF) is the most common arrhythmia post coronary artery bypass surgery (CABG), occurring in 10%-40% of patients.¹⁻¹¹ It can also lead to hemodynamic instability necessitating emergency treatment including cardioversion. Atrial fibrillation predisposes to embolic phenomenon with the consequent risk of cerebro-vascular accident (CVA) or distal embolization.³ Postoperative arrhythmias, especially AF, can delay recovery and prolong hospitalization.³ There has been anecdotal evidence that the prophylactic use of anti-arrhythmic medications such as Amiodarone can reduce the rate of AF

postoperatively. To test this, a study was designed at the Cardiothoracic Centre to examine whether prophylactic Amiodarone use reduces the rate of AF post CABG.

Methods. Two groups of patients undergoing elective CABG using the Cardiopulmonary Bypass machine who were preoperatively in sinus rhythm were randomized to either Amiodarone infusion followed by oral Amiodarone or dextrose 5% infusion followed by placebo for a period of 6 weeks. The infusions were started in the intensive care unit

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on the day of the operation as soon as the patients were stable and warmed up and continued for 24 hours. On the 2nd day, the first group of patients were started on Amiodarone 200mg orally 3 times a day reduced to 200mg twice daily a week later and 200mg once a day the following week and continued for the following 4 weeks. The 2nd group received a matched regimen of placebo tablets. At 6 weeks, the patients were assessed in the Outpatients Department and an electrocardiogram (ECG) was obtained and data collected. Exclusion criteria was as follows: 1. Preoperative AF. 2. Patients undergoing additional procedures to myocardial revascularisation (for example valvular replacement or aneurysmal repair). 3. Patients planned for beating heart surgery "Off Pump Surgery" were excluded whether they eventually underwent "Off Pump" or "On Pump" surgery. 4. Patients fitted with Permanent Pacemakers. 5. Patients maintained on anti-arrhythmic medications. 6. Patients with abnormal liver function tests (LFTs). 7. Concomitant thyroid disease. 8. History of Amiodarone side effects or use within the last 6 months. 9. Uncontrolled heart failure. Patients were randomized to either "Amiodarone" or "Placebo" using a table of random numbers. All patients received the same postoperative management and potassium (k+) was kept above 4.0mmol/l and magnesium (Mg++) in the normal range. The patients' demographic details are shown in Table 1. There were no significant differences between the 2 groups in all of the parameters.

Results. One hundred patients were recruited into the "Amiodarone" arm of the study of which 88

Table 1 - Patient demographic details.

Variable	Control	Amiodarone	P value
Number	92	88	NS
Age (years)	69.6 +/- 7.6	66.5 +/- 4.9	NS
Sex (M:F)	(72/20), 3.6:1	(70/18), 3.8:1	NS
Preoperative hemoglobin (g/dl)	M - 14.30+/-0.4 F - 12.5+/-0.4	M - 13.7+/-0.7 F - 11.9+/-0.3	NS
Preoperative creatinine (mcg/ml)	105+/-10	98+/-14	NS
Angina class (Canadian class)	65% Class III or above	60% Class III or above	NS
NYHA Class	2.8 +/- 0.6	2.5 +/- 0.7	NS
Number of grafts	3.8 +/- 0.8	3.5 +/- 0.7	NS
M=male, F= female, NYHA=New York Heart Association NS=non significant			

patients continued. The remaining 12 patients were excluded for the following reasons: 1. Intolerance or side effects of Amiodarone - 5 patients. 2. Severe bradycardia (sustained heart rate below 50 beats/min) - 4 patients. The remaining 3 patients who underwent additional cardiac procedures to CABG were excluded (2 patients underwent valvular replacement while the last patient underwent replacement of the ascending aorta). Results were as follows: Control group of 92 had AF in 32 patients (a rate of 35%). The Amiodarone group of 88 had AF in 28 patients (a rate of 32%). There was no significant difference between the groups $P>0.05$. The maximum ventricular rate during AF was significantly slower in the Amiodarone group (108+/-18) compared to (136+/-22) in the controls giving a P value <0.05 . There were no significant differences between the 2 groups in the incidence of AF.

Discussion. Atrial fibrillation is the most common arrhythmia following CABG occurring in 10-40% of patients.¹⁻¹¹ The cause of AF post myocardial revascularisation is debated, but some factors have been suggested, those included increasing age, male gender, hypertension, greater number of grafts, myocardial infarction, previous cardiac procedures and poor left ventricular function.^{3,5,12-14} Other factors that have been implicated are, prolonged duration of the operative ischemic period, poor myocardial preservation of the atria and the need for intraoperative intra-aortic balloon pump.^{3,5,10,12-14} Operative factors that have been suggested in addition to increased operative time are method of cardioplegia delivery being lower in the continuous as opposed to the intermittent one,¹⁵ and the role of atrial ischemia.¹⁶ Post myocardial revascularisation AF seems to require a well defined anatomical and electrical substrate that is generated by increased left atrial dimensions, a greater extension of the coronary lesions and a possible electrical remodelling consequent to prior repetitive episodes of paroxysmal AF.¹⁷

This study did not demonstrate any significant difference with Amiodarone in the rate of AF, however the maximum ventricular rate was reduced. Amiodarone achieves its anti-arrhythmic action by prolongation of the refractory period of the atrioventricular (AV) node, effects of Ca-channel (calcium channel) blocking and non-competitive adrenergic antagonism.² Therefore, it's not surprising that a higher proportion of patients in the Amiodarone arm of the study experienced bradycardias. In this study Amiodarone was well tolerated with no major side effects. This can be explained by the rather short duration that the drug was taken for. However in other studies the side effects have varied with up to 18% of patients experiencing them.¹⁸ In comparison to other studies,

we can find for example that Lee et al¹ selected patients going for CABG used a loading dose followed by a maintenance dose for 3 days before and 5 days after the operation. They found that Amiodarone significantly reduced the incidence, ventricular rate and duration of AF post coronary artery surgery.¹ Dorge et al² similarly, selected patients planned for coronary surgery used 2 different concentrations of Amiodarone (first group - 300mg bolus followed by 20 mg/kg of weight for 3 days, 2nd group - 150mg bolus followed by 10mg/kg of weight for 3 days given after aortic cross-clamping and a 3rd group receiving placebo). They found no benefit of Amiodarone in reducing the rate of AF.² Hohnloser et al¹⁸ performed a placebo controlled study of intravenous Amiodarone as prophylaxis to AF after CABG. They demonstrated a significant reduction in postoperative AF.¹⁸ However, ECG monitoring was only carried out in the first 48 hours after the operation and 18% of the patients had to discontinue the medication due to side effects.¹⁸ Redle et al¹⁹ randomized 127 patients to receive oral Amiodarone at 2 gms/day for 3 days before and 400mg/day for 7 days after coronary artery surgery or placebo. They also found no significant reduction in the incidence of AF.¹⁹ Daoud et al²⁰ conducted a double blind study of oral Amiodarone as prophylaxis to AF after coronary or valvular surgery. Their result showed a reduction in the rate of postoperative AF.²⁰ It should be mentioned that other drugs have been investigated in the literature. In a double blind, placebo-controlled study the administration of Sotalol in dosages ranging from 80 to 120 mg was associated with a significant reduction in postoperative AF in patients undergoing CABG.²¹ The combination of Digoxin and Verapamil to reduce the ventricular rate in AF post CABG was associated with a conversion back into sinus rhythm in over 90% of patients.²² Magnesium (Mg) however did not decrease the incidence of AF post CABG.²³

In conclusion, Amiodarone did not reduce the rate of AF post CABG. It did however reduce the maximum ventricular rate. It also had no effect on mortality post CABG.

References

- Lee S, Chang C, Lu M, Lee R, Cheng J, Hung C, et al. Intravenous amiodarone for prevention of atrial fibrillation after coronary artery bypass grafting. *Ann Thorac Surg* 2000; 70: 157-161.
- Dorge H, Schoendube F, Schoberer M, Stellbrink C, Voss M, Messmer B. Intraoperative amiodarone as prophylaxis against atrial fibrillation after coronary operations. *Ann Thorac Surg* 2000; 69: 1358-1362.
- Groves PH, Hall RJC. Atrial tachyarrhythmias after cardiac surgery. *Eur Heart J* 1991; 12: 458-463.
- Matangi MF, Neutze JM, Graham KJ, Hill DG, Kerr AR, Barratt-Boyes BG. Arrhythmia prophylaxis after aorta-coronary bypass. The effect of minidose propranolol. *J Thorac Cardiovasc Surg* 1985; 89: 439-443.
- Mohr R, Smolinsky A, Goor DA. Prevention of supraventricular tachyarrhythmia with low-dose propranolol after coronary bypass. *J Thorac Cardiovasc Surg* 1981; 81: 840-845.
- Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, VanderVilet M. Predictors of atrial fibrillation after coronary artery surgery. *Circulation* 1996; 94: 390-397.
- Mathew JP, Parks R, Savino JS, Freidman AS, Koch C, Mangano DT et al. Atrial fibrillation following coronary artery bypass graft surgery. *JAMA* 1996; 276: 300-306.
- Leitch JW, Thomson D, Baird DK, Harris PJ. The importance of age as a predictor of atrial fibrillation and flutter after coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 1990; 100: 338-342.
- Fuller JA, Adams GG, Buxton B. Atrial fibrillation after coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 1989; 97: 821-825.
- Rubin DA, Nieminski KE, Reed GE, Herman MV. Predictors, prevention and long term prognosis of atrial fibrillation after coronary artery bypass graft operations. *J Thorac Cardiovasc Surg* 1987; 94: 331-335.
- Siebert J, Rogowski J, Jagielak D, Anissimowicz L, Lango R, Narkiewicz M. Atrial Fibrillation after coronary artery bypass grafting without cardiopulmonary bypass. *Eur J Cardiothorac Surg* 2000; 17: 520-523.
- Menasche P, Maisonblanche P, Bousseau D, Lorente P, Piwnicka A. Decreased incidence of supraventricular arrhythmias achieved by selective atrial cooling. *Eur J Cardiothorac Surg* 1987; 1: 33-36.
- Tchervenkov CI, Wynands JE, Symes JF, Malcolm ID, Dobell ARC, Morin JE. Persistent atrial activity during cardioplegic arrest. *Ann Thorac Surg* 1983; 36: 437-443.
- Edwards FH, Clark RE, Schwartz M. Coronary artery bypass grafting. *Ann Thorac Surg* 1994; 57: 12-19.
- Paull DL, Tidwell SL, Guyton SW, Harvey E, Woolf RA, Holmes JR et al. Beta blockade to prevent atrial dysrhythmias following coronary bypass surgery. *Am J Surg* 1997; 173: 419-421.
- Kolvekar S, D'Souza A, Akhtar P, Reek C, Garratt C, Spyt T. Role of atrial ischaemia in development of atrial fibrillation following coronary artery bypass surgery. *Eur J Cardiothorac Surg* 1997; 11: 70-75.
- Ducceschi V, D'Andrea A, Liccardo B, Alfieri A, Sarubbi B, De Feo M et al. Perioperative clinical predictors of atrial fibrillation occurrence following coronary artery surgery. *Eur J Cardiothorac Surg* 1999; 16: 435-439.
- Hohnloser SH, Meinertz T, Dammbacher T, Steiert K, Jahnchen E, Zehender M et al. Electrocardiographic and antiarrhythmic effects of intravenous amiodarone: results of a prospective, placebo-controlled study. *Am Heart J* 1991; 121: 89-95.
- Redle JD, Khurana S, Marzan R. Prophylactic low dose Amiodarone versus placebo to prevent atrial fibrillation in patients undergoing coronary artery bypass graft surgery. *J Am Coll Cardiol* 1997; 29: 289-289A.
- Daoud EG, Strickberger SA, Man KC, Goyal R, Deeb GM, Bolling SF et al. Preoperative Amiodarone as prophylaxis against atrial fibrillation after heart surgery. *N Engl J Med* 1997; 337: 1785-1791.
- Gomes JA, Ip J, Santoni-Rugiu F, Mehta D, Ergin A, Lansman S et al. Oral d'I sotalol reduces the incidence of postoperative atrial fibrillation in coronary artery bypass surgery patients: a randomized, double-blind, placebo-controlled study. *J Am Coll Cardiol* 1999; 34: 334-339.
- Myers MG, Alnemri K. Rate control therapy for atrial fibrillation following coronary artery bypass surgery. *Can J Cardiol* 1998; 14: 1363-1366.
- Parikka H, Toivonen L, Pellinen T, Verkkala K, Jarvinen A, Nieminen MS. The influence of intravenous magnesium sulphate on the occurrence of atrial fibrillation after coronary artery by pass operations. *Eur Heart J* 1993; 14: 251-258.