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Case Series:

A Comparative Study of Preoperative Oral Amiodarone with Intraoperative Intravenous Diltiazem in Prophylaxis of Atrial Fibrillation after Off-pump Coronary Artery Bypass Grafting

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Abstract:

The prophylactic effect of preoperative oral amiodarone was compared with intraoperative intravenous diltiazem in reducing incidence of atrial fibrillation after off-pump coronary artery bypass grafting in two groups of 30 patients each. Patients were monitored continuously for 5 days after surgery. The incidence of postoperative atrial fibrillation was not significantly different between the diltiazem group (10%) and amiodarone group (13.3%). Thus the prophylactic use of both diltiazem and amiodarone is feasible for patients undergoing off-pump coronary artery bypass grafting, with similar rates of atrial fibrillation.

Keywords: Oral Amiodarone , Diltiazem

Introduction

Atrial fibrillation (AF) is a common complication of cardiac surgery, ranging in incidence from 10% to 65%. It is associated with increased morbidity, mortality, and extended hospitalization, and usually occurs between the second and fifth postoperative day [1]. Prophylaxis and atrial overdrive pacing remain the options for patients at risk of developing postoperative AF. In such cases, management strategies are directed towards restoration of sinus rhythm or control of ventricular rate [2]. Beta blockers and amiodarone are considered as standard and effective prophylactic agents in decreasing AF and sudden cardiac death after cardiovascular surgery, with minimal adverse effects [3,4].

Diltiazem is also considered an effective prophylactic agent for AF [5]. This study evaluated the comparative role of preoperative oral amiodarone and intraoperative intravenous diltiazem in reducing incidence of AF after off-pump CABG.

Material and Methods

The present study was conducted at Department of Cardiothoracic and Vascular Surgery at a tertiary level super specialty institute of Northern India from August 2019 to November 2019. The study included 60 patients undergoing OPCABG who gave informed consent, were >18 years old, had at least one week before surgery

was scheduled, and had normal sinus rhythm. Patients were excluded if they were allergic to amiodarone or diltiazem, had used amiodarone or diltiazem within 6 months of enrolment, had a history of amiodarone toxicity, had AST or ALT levels > 4 times the upper limit of normal, required the use of antiarrhythmic therapy other than beta-receptor antagonists, had untreated thyroid disease, were pregnant females, had a resting heart rate of <50 beats per minute in the absence of medical therapy known to slow the sinus rate or had any associated valvular pathology along with CAD.

All patients were admitted and underwent detailed history taking, routine blood investigations, chest radiography, ECG and 2D echocardiography. These patients were divided in to 2 groups of 30 patients each by using random allocation through coin toss method – group 'A' and group 'D'. The patients in group 'A' in preoperative period received oral amiodarone tablet of 100 mg TDS for 3 days, then BD for 3 days and then OD to be continued till the day of surgery. The patients in group 'D' did receive identical placebo without any additional anti-arrhythmic therapy preoperatively but intraoperative diltiazem infusion at dose of 0.5 mcg/kg/min.

All patients underwent off-pump coronary artery bypass grafting. After surgery, patients were shifted to an intensive care unit and invasive BP, ECG, saturation and CVP monitoring was continuously done for at least 5 days after surgery. Incidence of any postoperative arrhythmias was noted along with presence of hemodynamic instability. Patients in group 'D' were continuously given diltiazem infusion in postoperative period at dose of 0.5 mcg/kg/min for 48 hours and later shifted to oral diltiazem 15 mg TDS. Any incidence of AF in all patients was treated according to ventricular rate. In case of AF with FVR (ventricular rate >120 bpm), patient was started on intravenous amiodarone with loading dose of 150 mg over 10 minutes followed by infusion at dose of 7.5 mcg/kg/min to be titrated according to heart rate.

Any patient who developed bradycardia during intraoperative or postoperative period was excluded from study due to need for discontinuation or modification of therapy.

All data was tabulated using Microsoft Excel and analysed using chi-square test in SPSS version 20. All qualitative variables were analysed using chi-square test and continuous variables were analysed using unpaired student 't' test. Any difference between the two groups was considered to be significant if p-value was obtained to be <0.05. Accordingly results were compiled.

Results

Analysis of the preoperative demographic and clinical characteristics as well as intraoperative parameters of the patients eligible for this study showed that the two groups were well matched (table 1). No statistically significant differences were observed for the parameters recorded.

Characteristic	Group 'A'	Group 'D'	p-value
Mean Age	64.2 (±9.8) Years	63.7 (±7.9) Years	0.62
Male:female ratio	25:5	26:4	0.79
Mean Left ventricular ejection fraction	44.3 (±2.7)%	47.1 (±2.3)%	0.14
Number of patients having left main CAD	8	9	0.48
Mean NYHA functional class	2.5 (±0.8)	2.6 (±0.7)	0.63
Mean number of vessels involved in CAD per patient	2.4 (±0.6)	2.5 (±0.7)	0.41
Previous myocardial infarction	18	16	0.39
Systemic hypertension	19	17	0.53
Diabetes mellitus	16	17	0.62
Chronic renal insufficiency	2	2	1.00
Chronic obstructive pulmonary disease	3	2	0.37
Mean duration of surgery	211.1 (±31.3) mins	202.3 (±35.2) mins	0.21
Mean number of grafts implanted per patient	2.6 (±0.4)	2.7 (±0.3)	0.12
Number of patients requiring epicardial defibrillation to restore sinus rhythm during surgery	1	2	0.09
Number of patients needing CPB support during surgery	1	1	1.00
Mean duration of intubation after surgery	20.2 (±0.7) hours	18.7 (±1.2) hours	0.13
Number of patients requiring temporary epicardial pacing after surgery	0	0	-

There was one death in group 'A' due to sepsis caused by deep sternal wound infection. No deaths were reported in group 'D'. Two patients in group 'A' and one patient in group 'D' were excluded from study due to developing bradycardia and undergoing discontinuation of therapy. No other serious morbidity was observed.

When episodes of atrial fibrillation that occurred during first 5 postoperative days were considered, the incidence of atrial fibrillation was 13.3% (4 of 30 patients) in the group 'A' and 10.0% (3 of 30 patients) in the group 'D' (p=0.14). There was no statistically significant difference between the two groups in this regard.

Atrial fibrillation occurred a mean of 1.8 (±1.1) days after surgery in the patients of group 'A' and 2.2 (±1.2) days after surgery in the patients of group 'D' (p=0.60). The mean maximal ventricular rate during atrial fibrillation was significantly lower in the group 'A' than in the group 'D' [112.1 (±23.2) vs. 126.1 (±23.2) beats per minute, p=0.03]. Symptoms attributable to atrial fibrillation were reported by 3 of 4 patients (75.0%) in the group 'A' and 2 of 3 patients (66.7%) in the group 'D' (p=0.81). Atrial fibrillation required management by amiodarone infusion in 1 patient (25%) in group 'A' and in 2 patients (50%) of group 'D' (p=0.12). There were no cases of ventricular fibrillation or ventricular tachycardia (more than 10 consecutive premature ventricular complexes). One instance of second-degree atrioventricular block was recorded in group 'A' which was transient and no therapeutic intervention was required. No significant difference in length of hospitalization was noted between group 'A' and group 'D' [11.2 (±2.9) vs. 11.9 (±5.1) days, p=0.24].

Discussion

Atrial fibrillation is one of the most common complications after open heart surgery and prophylaxis still remains the main modality and a point of controversy [6]. Amiodarone has been used as an antiarrhythmic and antianginal drug since the 1970s. It is a structural analog of thyroid hormone and some of its antiarrhythmic properties and toxicity may be attributable to interactions with nuclear thyroid hormone receptors [7]. The lipid solubility of amiodarone gives it an exceptionally long half-life and it has a wide antiarrhythmic profile. Amiodarone is as effective in reducing the incidence of AF and atrial flutter following heart surgery [8]. Amiodarone also demonstrated efficacy in suppressing ventricular arrhythmias [3,9,10]. In general, amiodarone is considered one of the first choices of drugs to reduce the incidence of postoperative AF in cardiac patients [11].

On the other hand, diltiazem is a calcium channel blocker known to be effective in the treatment of angina pectoris, postoperative hypertension, and supraventricular arrhythmias.8 Diltiazem is metabolized to desacetyl diltiazem, both having no effect on renal function. Also, myocardial injury during open heart surgery is mediated in part by intracellular calcium overload, a possible reason for postoperative AF. Therefore, improved myocardial protection is expected from agents that block transmembrane calcium movements. This suggests a possible role for diltiazem, especially during the early postoperative hours. In the prophylactic perioperative setting, diltiazem displays no adverse effect on hemodynamics and systolic myocardial function, and provides potent anti-ischemic and antiarrhythmic protection by lowering the incidence of AF following CABG [5,12]. Preoperative oral treatment with diltiazem also ameliorates left ventricular diastolic dysfunction in patients after CABG [13]. Colson and colleagues [14] reported that heart rate, MAP, and inotropy were decreased during coronary artery surgery with diltiazem. In this context, diltiazem reduces myocardial oxygen demand through decreases in heart rate, inotropy, and systolic function, while increasing myocardial oxygen delivery through coronary vasodilatation.

Both diltiazem and amiodarone have a well-established role in clinical management of cardiac arrhythmias in the nonsurgical environment and have been assessed as prophylaxis in the postoperative period also. A recent comparative study of these two drugs in the treatment of atrial tachyarrhythmias in a nonsurgical intensive care unit showed that diltiazem afforded significantly better 24 hour heart rate control but with a significant incidence of hypotension; the authors suggested that amiodarone may be an alternative in patients

with severe hemodynamic compromise [15]. However in our study no incidences of hypotension were reported in group 'D'.

Amiodarone is associated with several side effects, the most common being pulmonary and thyroid. These are presumed to be due to the fact that amiodarone is an iodinated benzofuran derivative that is a structural analogue of thyroid hormone. Diltiazem lacks the side-effect profile of amiodarone, and can thus be considered for protection against AF after CABG. It was concluded from this study that treatment with diltiazem or amiodarone in the perioperative period of CABG is feasible and safe and reduces the rate of AF postoperatively. Diltiazem should be considered for postoperative prophylaxis as it demonstrates a generally lower toxicity profile than amiodarone. However, amiodarone remains the superior choice for patients with a low heart rate and low arterial pressure. Additional studies are needed to determine the optimal dose scheduling and the possible combination of these two antiarrhythmic agents with other drugs in the prevention of post-surgical AF after CABG.

References:

1. Maisel WH, Rawn JD, Stevenson WG. Atrial fibrillation after cardiac surgery. Ann Intern Med 2001;135:1061–73.

2. Olshansky B. Management of atrial fi brillation after coronary artery bypass graft. Am J Cardiol 1996;78:27–34.

3. Solomon AJ, Greenberg MD, Kilborn MJ, Katz NM. Amiodarone versus a beta-blocker to prevent atrial fibrillation after cardiovascular surgery. Am Heart J 2001;142:811–5.

4. McAlister FA, Teo KK. Antiarrhythmic therapies for the prevention of sudden cardiac death. Drugs 1997;54:235–52.

5. Seitelberger R, Hannes W, Gleichauf M, Keilich M, Christoph M, Fasol R. Effects of diltiazem on perioperative ischemia, arrhythmias, and myocardial function in patients undergoing elective coronary bypass grafting. J Thorac Cardiovasc Surg 1994;107:811–21.

6. Patel AN, Hamman BL, Patel AN, Hebeler RF, Wood RE, Cockerham CA, et al. Epicardial atrial defi brillation: successful treatment of postoperative atrial fibrillation. Ann Thorac Surg 2004;77:831–7.

7. Doggrell SA. Amiodarone – waxed and waned and waxed again. Expert Opin Pharmacother 2001;2:1877–90.

8. Wurdeman RL, Mooss AN, Mohiuddin SM, Lenz TL. Amiodarone vs. sotalol as prophylaxis against atrial fi brillation/fl utter after heart surgery: a meta-analysis. Chest 2002;121:1203–10.

9. 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.

10. Tisdale JE, Padhi ID, Goldberg AD, Silverman NA, Webb CR, Higgins RS, et al. A randomized, double-blind comparison of intravenous diltiazem and digoxin for atrial fi brillation after coronary artery bypass surgery. Am Heart J 1998;135:739–47.

11. Haan CK, Geraci SA. Role of amiodarone in reducing atrial fi brillation after cardiac surgery in adults. Ann Thorac Surg 2002;73:1665–9.

12. Hannes W, Fasol R, Zajonc H, Schindler M, Schumacher B, Schlosser V, et al. Diltiazem provides anti-ischemic and anti-arrhythmic protection in patients undergoing coronary bypass grafting. Eur J Cardiothorac Surg 1993;7:239–45.

13. van der Maaten JM, de Vries AJ, Henning RH, Epema AH, van den Berg MP, Lip H. Effects of preoperative treatment with diltiazem on diastolic ventricular function after coronary artery bypass graft surgery. J Cardiothorac Vasc Anesth 2001;15:710–6.

14. Colson P, Medioni P, Saussine M, Seguin JR, Cuchet D, Grolleau D, et al. Hemodynamic effect of calcium channel blockade during anesthesia for coronary artery surgery. J Cardiothorac Vasc Anesth 1992;6:424–8.
15. Delle Karth G, Geppert A, Neunteufl T, Priglinger U, Haumer M, Gschwandtner M, et al. Amiodarone versus diltiazem for rate control in critically ill patients with atrial tachyarrhythmias. Crit Care Med 2001;29:1149–53.

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