

<http://www.pjbs.org>

PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSI*net*

Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Biatrial Pacing vs. Intravenous Amiodarone in Prevention of Atrial Fibrillation after Coronary Artery Bypass Surgery

F. Akbarzadeh, B. Kazemi-Arbat, A. Golmohammadi and L. Pourafkari
Department of Cardiology, Shahid Madani Cardiovascular Research Center,
Tabriz University of Medical Sciences, Tabriz, Iran

Abstract: This study was aimed to compare the results of post operative biatrial pacing and IV amiodarone in prevention of AF. In a single blind randomized clinical trial, 210 patients scheduled for elective CABG surgery were randomized either to receive overdrive biatrial pacing, IV amiodarone or no intervention. Incidence of AF postoperatively evaluated. Pacing was successful in 83% of patients and 80% of patients in amiodarone group could receive their drug. Twenty and one patients developed AF. Incidence of AF in pace, amiodarone and control group was 10.7, 5.3 and 17.9%, respectively ($p = 0.08$). Comparing incidence of AF between pacing and control group, the difference was not significant ($p = 0.2$), but the difference between amiodarone and control groups was significant statistically ($p = 0.03$). Patients who developed AF were older but their left ventricular ejection fraction was not different with patients without AF. The ICU stay was higher in patients with AF. Use of IV amiodarone was more effective than biatrial pacing in prevention of post operative AF and we recommend use of this drug in high risk patients.

Key words: Atrial fibrillation, biatrial pacing, amiodarone

INTRODUCTION

Atrial Fibrillation (AF) is one of the most important complications of coronary artery bypass grafting (CABG) surgery which occurs in 15-45% of patients (Koplan, 2007; Magee *et al.*, 2007). Its incidence was not decreased despite of more improvements in surgical techniques, may be due to increasing age of patients who undergoing CABG (Magee *et al.*, 2007). Post operation AF may result in significant morbidity like as congestive heart failure, renal insufficiency, prolonged ventilation, readmission to the intensive care unit and a threefold to fourfold increased risk of early postoperative stroke (Magee *et al.*, 2007). Lot of studies showed that post operation AF resulted in long ICU and hospital stay and increased hospital costs (Koplan, 2007; Magee *et al.*, 2007; Ott and Marcus, 2006; Zebis *et al.*, 2008).

Mechanisms of post CABG atrial fibrillation are different and inflammatory mediators, adrenergic tone, fluid and electrolyte shifts and atrial ischemia likely play a larger role (Koplan, 2007; Kolvekar *et al.*, 1997; Cosgrave *et al.*, 2005). It has been suggested that low serum and atrial magnesium (Mg^{++}) levels are related to a high risk for developing atrial fibrillation (Piper *et al.*, 2007).

In attempt for decreasing incidence of post operative AF, multiple studies used drugs like as amiodarone (Redle *et al.*, 1999), atorvastatin (Song *et al.*, 2008), betablockers (Sleilaty *et al.*, 2008; Acikel *et al.*, 2008), sotalol (Aerra *et al.*, 2006), omega3 products (Calò *et al.*, 2005) magnesium (Shepherd *et al.*, 2008; Rostron *et al.*, 2005) and steroids (Prasongsukarn *et al.*, 2005). Some other studies used single atrial (Blommaert *et al.*, 2000; Fan *et al.*, 2000; Avila *et al.*, 2007), biatrial (Gerstenfeld *et al.*, 2001; Eslami *et al.*, 2005; Hakala *et al.*, 2005) and three atrial site pacing (Ozin *et al.*, 2005) to prevent incidence of AF after CABG. The results were variable. Further studies needed to clarify the role of atrial pacing in prevention of post operative AF (Vora, 2005).

The purpose of this study was to verify the results of biatrial pacing versus intravenous amiodarone in the incidence of AF after CABG surgery.

MATERIAL AND METHODS

With an interventional prospective and single blind randomized clinical trial from December 2006 to February 2008 two hundred and ten of 237 consecutive patients scheduled for elective on pump CABG surgery, were randomized (www.randomizer.org) into three groups either

to receive IV amiodarone or biatrial pacing after entering to ICU as therapy groups and one group without any intervention as control group. Patients with (1) significant valvular disease, (2) rhythm of AF at admission, (3) taking antiarrhythmic drugs other than beta blockers, (4) patients with implanted pacemakers and (5) development of cardiogenic shock and significant ventricular arrhythmias or AV blocks after surgery and 6- redo CABGS were excluded from the study. The cardiac surgeons of study were unaware of grouping of patients and cardiologists of study had no role in randomization of patients. Study was approved by cardiovascular research center of university and written informed consent was obtained from all patients.

Demographic, drug history and echocardiographic data including diastolic M-mode left atrial size were collected before surgery. Data about left ventricular ejection fraction and number of vessel diseased were obtained by angiography. All medications, including beta blockers, were continued until surgery.

Patients underwent on pump CABGS on standard cardiopulmonary bypass with myocardial protection provided by blood cardioplegia. Epicardial pacing wires were placed at the epicardium of the right atrial appendage and at the roof of the left atrium at the end of surgery. On arrival in the surgical ICU, the sensing and pacing thresholds of the pacing wires were measured. The configuration of atrial pacing for biatrial pacing was as follows: the LA pacing wire was connected to the negative pole of the pulse generator and the RA pacing wire was connected to the positive pole. Patients with a capture threshold >3 volt or a sensing threshold <1 mV and diaphragmatic stimulation were excluded from the study. In patient who randomized to be in pacing group overdrive atrial inhibited pacing was initiated, with output programmed at 3 times the capture thresholds. Sensitivity was set at 1 mV. The lowest rate was 80 beats per minute (b/m) or 10 beats above the intrinsic heart rate. The maximum pacing rate allowed was 110 b/m. Overdrive pacing was continued during ICU stay. In patients in amiodarone group, IV amiodarone started at ICU with 150 mg over 30 min and 1 mg h⁻¹ for 6 h and 0.5 mg min⁻¹ for the resting of ICU stay and stopped after discharge. Patients in control group had no intervention. Continuous

telemetry monitoring was done during ICU stay and recorded digitally for evaluation. The 12-lead ECG was performed daily during ICU stay for all patients. The pacing and sensing thresholds were checked daily and the output was adjusted accordingly. Electronic records and ECGs were reviewed daily by a cardiologist who was unaware of patient group. The pacing wires were removed by simple transcutaneous retraction at the day of discharge from ICU in the absence of a clinical end point. In determining of AF during ICU stay, atrial pacing and infusion of amiodarone stopped and proper therapy started if needed.

The primary end point of the study was the occurrence of significant new-onset atrial fibrillation after coronary artery bypass surgery. Significant atrial fibrillation episodes were defined as those lasting more than 1 h or the episodes associated with hemodynamic compromise. ECG and echocardiography were performed at the discharge time from hospital.

Statistical analysis: Continuous variables were expressed as Mean±SD and analyzed using unpaired 2-tailed Student's t-test. Categorical variables were summarized as percentage and compared by chi-square analysis. The 95% CI was reported where appropriate. P values less than or equal 0.05 considered as significant difference. Data entry and analysis were done by SPSS 11.5 software for windows.

RESULTS

Two hundred and ten patients were eligible to enter the study. Demographic, echocardiographic and angiographic data of patients are listed in Table 1. Twenty and six patients withdrew from the study between randomization and first booked intervention; four patients died during follow up.

Fourteen patients died in pacing group: Three had failure to capture of pacemaker, two had diaphragmatic stimulation, seven had epicardial lead displacement and two patients died in ICU stay (one because of pump failure and another due to complications of extensive anterolateral myocardial infarction).

Table 1: Demographic and angiographic data of patients

Characteristics	Pace (n = 70)	Amiodarone (n = 70)	Control (n = 70)	Total (n = 210)	p-value
Male (%)	64	80	84	76	0.01
Age (y)	59±10	56±10	61±10	59±10	0.03
Admission LVEF (%)	51±5	48±9	45±9	48±3	0.4
Left atrial size (cm)	3.4±0.5	3.4±0.6	3.5±0.5	3.5±0.5	0.5
Admission ð blocker (%)	77	87	82	82	0.3
3 vessel disease (%)	50	54	73	60	0.01
2 vessel disease (%)	34	23	25	27	0.3
1 vessel disease (%)	16	23	2	13	<0.001
Discharge LVEF in completed cases (%)	46±9	47±8	45±7	46±8	0.3



Fig. 1: Incidence of atrial fibrillation in randomized groups

Thirteen patients died in amiodarone group: Eight had systolic blood pressure <100 mmHg (Libby and Braunwald, 2008), four had HR less than 50 b/m (Maras *et al.*, 2001) and one had AV block.

Three patients died in control group: One underwent unpredicted mitral valve surgery and two died in ICU (one due to severe pump failure and another due to ventricular fibrillation).

In the first day of ICU stay when patients received their booked intervention, all patients had sinus rhythm. Incidence of AF in 2nd, 3rd and 4th day of ICU was 4.4, 5 and 2.2%, respectively (P value for 4 days follow up = 0.01). Incidence of AF in our patients was 11.6% totally.

As shown in Fig. 1, the incidence of AF in pace, amiodarone and control group was 10.7, 5.3 and 17.9%, respectively ($p = 0.08$). Comparing incidence of AF between pacing and control groups, the difference was not significant ($p = 0.2$) but the difference between amiodarone and control groups was significant statistically ($p = 0.03$). Considering AF patients, 28.6% of patients were in pace group, 14.3% in amiodarone and 57.1% in control group. This difference was statistically significant ($p = 0.01$).

Thirty patients were withdrawn from study because of above mentioned causes. By adding these patients to control group we had 97 patients without any intervention. The incidence of AF in this group of patients was 22.6% which may be our real incidence of post operative AF. With this assumption the difference between incidence of AF in patients of pace group and patients who didn't receive any intervention was significant statistically ($p = 0.05$).

Mean ICU stay of patients with and without AF was 6 and 4 days respectively ($p < 0.001$). Admission left ventricular ejection fraction (LVEF) was not different between patients with (45%) and without AF (48%), $p = 0.2$.

Incidence of AF in patients with three, two and one vessel disease was 14.8, 8.2 and 4.3%, respectively. This

difference was not significant statistically ($p = 0.2$). Prevalence of three, two and one vessel disease in patients with AF was 76.2, 19 and 4.8%, respectively. This difference was statistically significant ($p < 0.001$). Mean age of patients in patients with AF was 67 ± 7 and without AF was 57 ± 10 ($p < 0.001$).

Data analysis of patients withdrawn from study showed some differences. Admission LVEF ($44 \pm 10\%$) was lower and prevalence of three vessel coronary artery disease was higher (80%) in this group of patients. Other characteristics were equal. Incidence of AF was 33.3% which was different statistically with incidence of AF in patients who completed their follow up (11.6%) ($p = 0.004$).

DISCUSSION

More decrease in incidence of AF after CABG in amiodarone group (5.3%) than pacing (10.7%) and control group (17.9%) again confirmed the efficacy of this drug in prevention of post operative AF. This finding is compatible with findings of Zebis *et al.* (2008) and Kerstein *et al.* (2004) that showed decrease in incidence of post operative AF after CABG with intravenous amiodarone. Maras *et al.* couldn't show beneficial effect of pre operation single dose of oral amiodarone in this regard (Maras *et al.*, 2001).

Although, the difference in incidence of post operative AF between pace and control group was not significant, by adding withdrawn cases to control group and calculating incidence of AF in this new group of patients the difference will be significant. Blommaert *et al.* (2000) in their study showed beneficial effects of atrial overdrive pacing in reducing of AF in the second day of ICU stay after CABG.

The number of patients with AF in each group was low so analysis of some data like as LVEF and number of vessel disease between groups was not significant statistically. Although LVEF was not different between patients with and without AF, prevalence of 3VD was high in patients with AF. This finding is in contrast with findings of Dogan *et al.* (2007). Haghjoo *et al.* (2008) couldn't show any difference between of LVEF between two groups Although difference between ages of patients between randomized groups was not significant, this difference was significant statistically between patients with and without AF. Some studies considered age as strong predictor of post operative AF (Dogan *et al.*, 2007; Haghjoo *et al.*, 2008; Hakala and Hedman, 2003).

Use of betablocker was not different between randomized groups and patients with and without AF

also. Post operative management of patients in randomized groups was similar.

Administration of amiodarone is simple and cost effective (Zebis *et al.*, 2008), on the other hand pacing of patients is slightly sophisticated. The surgeon should implant temporary pacing wires which may be time consuming sometimes. In our center surgeons usually implant one ventricular lead routinely. Successful working of atrial pacing wires is an important issue. In our study pacing was technically successful in 83% of patients which was compatible with results of Hakala *et al.* (2005) they showed 80% success in their study. The cost effectiveness of pacing is not evaluated before.

ICU stay of patients with AF was two days longer than other patients. Aranki *et al.* (1996) showed the same results before. Although other studies didn't show longer stays of patients with post operative AF but costs of these patients were higher (Zebis *et al.*, 2008).

CONCLUSION AND LIMITATION

Use of IV amiodarone was more effective than biatrial pacing in prevention of post operative AF and we recommend use of this drug in high risk patients.

Low sample size is one of our limitations. Although, the cardiologist who evaluated AF incidence was blind to grouping of patients but study was not double blinded.

REFERENCES

- Acikel, S., H. Bozbas, B. Gultekin, A. Aydinalp, B. Saritas and U. Bal *et al.*, 2008. Comparison of the efficacy of metoprolol and carvedilol for preventing atrial fibrillation after coronary bypass surgery. *Int. J. Cardiol.*, 126: 108-113.
- Aerra, V., M. Kuduvalli, A.N. Moloto, A.K. Srinivasan, A.D. Grayson and B.M. Fabri *et al.*, 2006. Does prophylactic sotalol and magnesium decrease the incidence of atrial fibrillation following coronary artery bypass surgery: a propensity-matched analysis. *J. Cardiothoracic Surg.*, 25: 1-6.
- Aranki, S.F., D.P. Shaw, D.H. Adams, R.J. Rizzo, G.S. Couper and M.V. Vliet *et al.*, 1996. Predictors of atrial fibrillation after coronary artery surgery, Current trends and impact on hospital resources. *Circulation*, 94: 390-397.
- Avila, Neto V., R. Costa, K.R. Silva, A.L. Martins, L.F. Moreira, L.B. Santos and R.F. Melo, 2007. Effect of temporary right atrial pacing in prevention of atrial fibrillation after coronary artery bypass graft surgery. *Rev. Bras. Cir. Cardiovasc.*, 22: 332-340.
- Blommaert, D., M. Gonzalez, J. Mucumbitsi, O. Gurné, P. Evrard and M. Buche *et al.*, 2000. Effective prevention of atrial fibrillation by continuous atrial overdrive pacing after coronary artery bypass surgery. *J. Am. Coll. Cardiol.*, 35: 1411-1415.
- Calò, L., L. Bianconi, F. Colivicchi, F. Lamberti, M.L. Loricchio and E. de Ruvo *et al.*, 2005. N-3 fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery a randomized, controlled trial. *J. Am. Coll. Cardiol.*, 45: 1723-1728.
- Cosgrave, J., J.B. Foley, R. Kelly, E. McGovern, K. Bennett and V. Young *et al.*, 2005. Perioperative serum inflammatory response and the development of atrial fibrillation after coronary artery bypass surgery. *Heart*, 91: 1475-1476.
- Dogan, S.M., M. Buyukates, O. Kandemir, M. Aydin, M. Gursurer and S. Acikgoz *et al.*, 2007. Predictors of atrial fibrillation after coronary artery bypass surgery. *Coronary Artery Dis.*, 18: 327-331.
- Eslami, M., H.S. Mirkhani, M. Sanatkar, H. Bayat, R. Sattarzadeh and M. Mirhoseini, 2005. Role of biatrial pacing in prevention of atrial fibrillation after coronary artery bypass surgery. *Indian Pacing Electrophysiol. J.*, 5: 5-11.
- Fan, K., K.L. Lee, C.S. Chiu, J.W. Lee, G.W. He and D. Cheung *et al.*, 2000. Effects of biatrial pacing in prevention of postoperative atrial fibrillation after coronary artery bypass surgery. *Circulation*, 102: 755-760.
- Gerstenfeld, E.P., M. Khoo, R.C. Martin, J.R. Cook, R. Lancey and K. Rofino *et al.*, 2001. Effectiveness of Bi – atrial pacing for reducing atrial fibrillation after coronary artery bypass graft surgery. *J. Interv. Card. Electrophysiol.*, 5: 275-283.
- Haghjoo, M., H. Basiri, M. Salek, M.A. Sadr-Ameli, F. Kargar and K. Raissi *et al.*, 2008. Predictors of postoperative atrial fibrillation after coronary artery bypass graft surgery. *Indian Pacing Electrophysiol. J.*, 8: 94-101.
- Hakala, T. and A. Hedman, 2003. Predicting the risk of atrial fibrillation after coronary artery bypass surgery. *Scandinavian Cardiovascular J.*, 37: 309-315.
- Hakala, T., A.J.M. Valtola, A.K. Turpeinen, A.E. Hedman, R.E.U. Vuorenniemi and J.M. Karjalainen *et al.*, 2005. Right atrial overdrive pacing does not prevent atrial fibrillation after coronary artery bypass surgery. *Europace*, 7: 170-174.
- Kerstein, J., A. Soodan, M. Qamar, M. Majid, E. Lichstein, G. Hollander and J. Shani, 2004. Giving IV and oral amiodarone perioperatively for the prevention of postoperative atrial fibrillation in patients undergoing coronary artery bypass surgery, The GAP study. *Chest*, 126: 716-724.

- Kolvekar, S., A. D'Souza, P. Akhtar, C. Reek, C. Garratt and T. Spyt, 1997. Role of atrial ischaemia in development of atrial fibrillation following coronary artery bypass surgery. *Eur. J. Cardiothorac Surg.*, 11: 70-75.
- Koplan, B.A., 2007. Adrenergic blockade for management of atrial fibrillation after coronary artery bypass surgery: Is it important to go beyond the α 1-receptor? *Heart Rhythm*, 4: 1175-1176.
- Libby, P. and E. Braunwald, 2008. Braunwalds Heart Disease: A Textbook of Cardiovascular Medicine. 8th Edn., Saunders/Elsevier, New York, ISBN: 9781416041047.
- Magee, M.J., M.A. Herbert, T.M. Dewey, J.R. Edgerton, W.H. Ryan, S. Prince and M.J. Mack, 2007. Atrial fibrillation after coronary artery bypass grafting surgery: development of a predictive risk algorithm. *Ann. Thorac. Surg.*, 83: 1707-1712.
- Maras, D., S.D. Boskoviæ, Z. Popoviæ, A.N. Neskoviæ, S. Kovaceviæ and P. Otaseviæ *et al.*, 2001. Single-day loading dose of oral amiodarone for the prevention of new-onset atrial fibrillation after coronary artery bypass surgery. *Am. Heart J.*, 141: E8-E8.
- Ott, P. and F.I. Marcus, 2006. Atrial fibrillations after coronary artery bypass surgery. *J. Electrocardiol.*, 39: 55-56.
- Ozin, B., A. Sezgin, I. Atar, O. Gülmez and B. Sarita^o *et al.*, 2005. Effectiveness of triple-site triggered atrial pacing for prevention of atrial fibrillation after coronary artery bypass graft surgery. *Clin. Cardiol.*, 28: 479-482.
- Piper, S.N., A.H. Kiessling, S.W. Suttner, M. Ducke, J. Boldt and K.D. Röhm, 2007. Prevention of atrial fibrillation after coronary artery bypass graft surgery using a potassium-magnesium-aspartate solution (Inzolen). *Thorac. Cardiovasc. Surg.*, 55: 418-423.
- Prasongsukarn, K., J.G. Abel, W.R. Jamieson, A. Cheung, J.A. Russell, K.R. Walley and S.V. Lichtenstein, 2005. The effects of steroids on the occurrence of postoperative atrial fibrillation after coronary artery bypass grafting surgery: A prospective randomized trial. *J. Thorac. Cardiovasc. Surg.*, 130: 93-98.
- Redle, J.D., S. Khurana, R. Marzan, P.A. McCullough and J.R. Stewart *et al.*, 1999. Prophylactic oral amiodarone compared with placebo for prevention of atrial fibrillation after coronary artery bypass surgery. *Am. Heart J.*, 138: 144-150.
- Rostron, A., A. Sanni and J. Dunning, 2005. Does magnesium prophylaxis reduce the incidence of atrial fibrillation following coronary bypass surgery? *Interact. Cardiovasc. Thorac. Surg.*, 4: 52-58.
- Shepherd, J., J. Jones, G.K. Frampton, L. Tanajewski, D. Turner and A. Price, 2008. Intravenous magnesium sulphate and sotalol for prevention of atrial fibrillation after coronary artery bypass surgery: a systematic review and economic evaluation. *Health Technol. Assess.*, 12: 1-118.
- Sleilaty, G., S. Madi-Jebara, A. Yazigi, F. Haddad and G. Hayeck *et al.*, 2008. Postoperative oral amiodarone versus oral bisoprolol as prophylaxis against atrial fibrillation after coronary artery bypass graft surgery: A prospective andomized trial. *Int. J. Cardiol.*, 137: 116-122.
- Song, Y.B., Y.K. On, J.H. Kim, D.H. Shin and J.S. Kim *et al.*, 2008. The effects of atorvastatin on the occurrence of postoperative atrial fibrillation after off-pump coronary artery bypass grafting surgery. *Am. Heart J.*, 156: 373-316.
- Vora, A., 2005. To pace or not to pace—Prevention of atrial fibrillation after coronary artery bypass surgery. *Indian Pacing Electrophysiol. J.*, 5: 1-4.
- Zebis, L.R., T.D. Christensen, I.S. Kristiansen and V.E. Hjortdal, 2008. Amiodarone cost effectiveness in preventing atrial fibrillation after coronary artery bypass graft surgery. *Ann. Thorac. Surg.*, 85: 28-32.