USE OF PROPRANOLOL AND DILTIAZEM IN THE PROPHYLAXIS OF SUPRAVENTRICULAR TACHYARRHYTHMIA FOLLOWING CORONARY ARTERY BYPASS GRAFTING

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Supraventricular tachyarrhytmia (SVT) is considered as one of the bening complications that can be seen early after coronary artery bypass grafting (CABG) in 15-40 % of all patients. Various prophylactic treatments has been concerned for SVT. In this study, our aim was to point out safety and efficacy of oral propranolol used postoperatively, and intravenous infusion of diltiazem started with the beginning of anesthesia. A total number of 92 patients were studied prospectively in three groups. First group was administrated intravenous infusion of diltiazem (0.1 mg/kg/h), second group was administrated oral (or via nasogastric tube) propranolol 10 mg every eight hours and the third group was designed as a control group. all groups had a comparable incidence of risk factors concerning age, extent of coronary disease, preoperative medication. SVT occured in 8/21 (38%) patients in group 1, and 11/31 (35%) in group 3 (control), that was significantly different when compared with 2/25 (8%) patients in group 2 (p<0.05).

As a result; low dose oral propanolol perioperatively can be used in all patients undergoing coronary artery bypass grafting safely and effectively in the prophylaxis of supraventricular tachyarrhythmias.

Key words: Coronary artery bypass grafting, arrhythmias, diltiazem, propranolol

Supraventricular tachyarrhythmia (SVT), in the early postoperative period following coronary artery bypass grafting (CABG) has been proved to be a major rhythm disturbance seen quite frequently (15-40 % of all patients) [2-11]. Although SVT seems to be a relatively bening

complication, there were many studies investigating anti-arrhythmic drug prophylaxis in the past concerning digitalis, β -blocking agents, and recently Ca^{++} channel antagonists. It is suggested by many aothors that maintenance of propranolol administration has been associated with greater hemodynamic stability during anesthetic induction before cardiopulmonary bypass [1,9,10,13,14]. Furthermore, it has been claimed that hypersensitivity to adrenergic stimulation due to propranolol withdrawal might be the main factor precipitating myocardial ischemia, and causing a high incidence of SVT following CABG [6,10,15,16]. It has been also shown that perioperative infision of calcium channel antagonists such as nifedipine [17,18,20] and diltiazem [19,20] up to 24 hours after the operation, substantially decreases the prevalence and extent of postoperative myocardial ischemia. Additionally, diltiazem has been also proven effective prevention of postoperative supraventricular and infraventricular arrythmias.

This investigation was designed to compare which prophylactic drug therapy is more effective in preventing SVT following CABG.

MATERIALS AND METHODS

This study was performed on 92 patients undergoing elective CABG. The patients were randomized prospectively into three groups. Patients with unstable angina (NYHA IV), additional surgical or redo procedures, chronic obstructive lung disease, preoperative ejection fraction less than 40%, or reoperation because of excessive postoperative bleeding were excluded from the study.

Patients in Group 1. were administered continious intravenous infusion of diltiazem (0.1 mg/kg/h) from the beginning of anesthesia until 48 hours postoperatively. Patients in Group II. were administred 10 mg propranolol orally (or via nasogastric tube) every 8 hours postoperatively, and Group III was accepted as the control group.

Saphenous vein grafts and/or internal mammary artery grafts were used for myocardial revascularization, and all surgical procedures were performed under moderate hypothermia with a membrane oxygenator. For myocardial protection during cardiac arrest, cold potassium cardioplegic solution (Plegisol ® Abbott) was given via aortic root in addition to topical cooling by cold saline. Partial occlusion clamp was used for proximal anastomosis.

Hemodynamic parameters (heart rate, mean arterial pressure and central venous pressure) were interpretted for 48 hours. Continious three channel electrocardiographic (ECG) monitoring was performed during that period by an experienced nurse and physician. In all patients, serum levels of creatine kinase - MB (CK-MB), SGOT, SGPT and LDH were measured before and after operation, 12, 24, 48 hours thereafter. Myocardial infaction was defined as persistent ST segment elevation of 2 mm or more in ECG, new Q wave development, or postoperative elevation of CK-MB level exceeding 32 U/I 8 hours after the operation.

As statistical analysis, mean values ± standart deviations were given for continious variables, and were analyzed by means of student's t test for unpaired variables. Where appropriate, x^2 test or Fisher's exact test was used to compare discontinious variables.

RESULTS

Preoperative and postoperative, clinical and surgical data about 92 patients are summarized in Table I. and Table II. There were no significant differences between three groups concerning age, sex, previous risk factors such as hypertension, history of myocardial infarction (MI), diabetes mellitus (DM), smoking, NYHA and also extent of coronary artery disease. Preoperative medication with nitrates, Ca^{++} channel blockers, β-blockers and digitalis was evenly distributed in all patient groups. There was also no siginificant difference between groups when we look at the operative variables such as number of grafts per patient, IMA grafts, total bypass time and also cross clemp time.

During the postoperative period, significant difference was not found between groups concerning hemodynamic parameters such as

Table I. Clinical data of 92 patients

	Diltiazem	Propranolol	Control
No.of Patients	30	31	31
Age (years)	61.2±7.9	60.4±9.1	63.7±8.3
Sex (m/f)	24/6	25/6	23/8
Risk Factors (%)			
Hypertension	53	58	48
History of MI	57	48	45
Diabetes mellitus	13	16	13
Smoking	40	32	42
NYHA Class II	40	42	39
NYHA Class III	60	58	61
Preoperative Drugs (%)			
Nitrates	93	84	94
Diltiazem	73	65	68
Verapamil	10	16	7
β-blockers	53	45	54
Digitalis	7	3	7
Angiography			
LVEDP (mmHg)	12±6	13±7	12±5
EF (%)	61±7	63±9	59±10
LMC (n)	211		
LAD (n)	29	27	29
CX (n)	26	27	28
RCA (n)	28	29	29
Operative variables			
No.of grafts / patient	2.6	2.9	2.7
IMA grafts (%)	40	48	45
Total bypass time (min)	85±17	89±22	93±21
Cross clamp time (min)	45±11	48±17	50±16

Table II. Results of 92 patients who underwent CABG; while receiving diltiazem, propranolol and plasebo.

	Diltiazem	Propranolol	Control
Heart rate (/min)	89±12.3	82±9.7	90±10.2
Mean arterial P.(mmHg)	80.7±12.4	84.9±13.8	80.3±1.9
Central venous P (mmHg)	9.7±3.2	8.9±2.9	9.2±3.3
CK (U/l)	549±329	564±402	591±382
CK-MB(U/l)	17.8±12.8	18.3±10.9	21.4±11.8
SGOT(U/l)	42.7±13.7	40.9±14.3	38.8±15.2
SGPT(U/l)	36.7±18.5	39.4±17.5	41.3±21.8
LDH (U/l)	382±253	409±312	375±274
Withdrawals in catecholamine treatment	9 (30%)	5 (16 %)	4 (13%)
- hypotension	8	3	3
- bradycardia	-	1	-
- Perioperative MI	1	1	1
SVT	8/21 (38%)	2/25 (8%)	11/31 (35%)

heart rate, mean arterial pressure and central venous pressure. Also serum levels of cardiac enzymes (CK, CK-MB, SGOT, SGPT and LDH) did not differ significantlly.

9 out of 30 patients (30%) treated with diltiazem needed positive inotropic medication during early hours after operation, and they had to be withdrawn from study because of hypotension in 8 patients and perioperative MI in one patient. In the second group treated with propranolol 5 out of 31 patients (16%) needed catecholamines at the early hours and were discarded from the study. In the control group 4 out of 31 patients (13%) received catecholamines but they were not withdrawen, because the study was not designed as double-blind. The difference was significant for diltiazem vs. control group ($p<0.05$). One patient in every group had perioperative MI.

8 patients in the diltiazem group out of the remaining 21 patients (38%) developed SVT. This was not significantly different from the control group as 11 out of 31 patients (35%). But only 2 patients out of the remaining 25 (8%) treated with propranolol developed SVT that was significantly different ($p<0.05$).

DISCUSSION

SVT can be considered as a relatively bening complication; it is one of the common complications (15-40 % of all patients) that can be seen in early postoperative period after CABG [2-11].Many studies demonstrate that nearly 90% of SVT occur within a few days following coronary revascularization. Although these rhythm disturbances are not usually life treatening, they do increase morbidity as they reduce cardiac output, prolong monitorization hospitalization and increase cost effect [3,21].

There are several predisposing factors thought to increase postoperative SVT; including older age (>60 years old), cardiomegaly, dilated left atrium, preexisting cardiac damage, prolonged bypass time, sudden withdrawal of β-adrenergic blocking agents, and also inadequate protection of atrial myocardium [5,12,21-24]. Perioperative infusion of antiischemic and antiarrhythmic substances appears to be remarkably effective in improving myocardial protection during and early after CABG [17-19,25]. In the ischemic myocardial cell, a depletion of ATP stores, and an increased cytoplasmic Ca^{++} concentration are found [26,27]. Ca^{++} channel blockers decrease the inward flow and, therefore, intracellular Ca accumulation. Thus, during ischemia, Ca^{++} channel blockers protect mitochondrial ATP production. So, prophylactic diltiazem has been suggested by some authors that it may reduce postoperative SVT, perioperative ischemic episodes, and postoperative cardiac enzyme levels[20,28]. Since catecholamines have positive chronotropic and inotropic actions, β-adrenergic antagonists decrease the heart rate and reduce myocardial oxygen consumption. Many studies have shown that administration of β-adrenergic receptor blockers during the early phases of acute myocardial infarction may decrease mortality and morbidity[2,23]. β-blockers are also a common treatment in coronary artery disease, and their withdrawal is supposed to be a risk factor for the development of postoperative SVT [2,23].

Hence, both β-blockers and Ca^{++} channel blockers could be beneficial for the prevention of postoperative myocardial protection.

In contrast to other investigators we could not prove any effect of diltiazem on the occurence of SVT. SVT incidence in the diltiazem group was very similar to the control group. This result leads us to conclude that diltiazem does not reduce clinically relevant SVT in the dose applied in this study. A higher dose does not seems appropriate because of possible negative hemodynamic effects like prolonged hypontension, or an increased need for catecholamine application. Also the effect of diltiazem infusion in reducing cardiac enzyme levels could not be significant in this study [2-11,20,28]. Several studies with propranolol have been shown to be effective in reducing the incidence of SVT [2-8,10,13]. Results found in this study, support these findings that postoperative use of low dose oral propranolol enables a prophylaxis close to optimum.

As a conclusion; we can say that the oral use of low dose oral propranolol seems safer and more effective than intravenous infusion of diltiazem in the applied doses.

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