Efficacy of Low-dose Propranolol in Preventing Postoperative Supraventricular Tachyarrhythmias

A Prospective, Randomized Study

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A prospective, randomized study was performed in 100 consecutive patients undergoing coronary artery bypass surgery to assess the efficacy of the early reinstitution of propranolol in reducing the incidence of postoperative supraventricular tachyarrhythmias (SVT). Patients were randomized to receive propranolol 10 mg every 6 hours enterally starting the morning after surgery (Group I, 50 patients) or to serve as controls (Group II, 50 patients). No patient was excluded because of poor ventricular function, need for urgent revascularization, or transient necessity for ionotropic support. Both groups had a comparable incidence of risk factors, previous infarction, unstable angina, and abnormal ventricular function. The extent of coronary disease, preoperative propranolol dose, and number of grafts performed were also similar. SVT occurred in 3/50 (6%) patients in Group I compared with 14/50 (28%) in Group II ($p < 0.01$). There were no preoperative or intraoperative discriminators to predict the occurrence of SVT. In addition, perioperative infarction and the need for mechanical or pharmacologic circulatory support did not predispose to SVT. The data indicate that early readministration of propranolol should be given to all patients after myocardial revascularization to decrease the incidence of these postoperative rhythm disturbances.

PROPRANOLOL, OR OTHER beta-recepter antagonists, in conjunction with nitrate preparations, comprise the standard medical treatment for symptomatic ischemic heart disease. The discontinuance of propranolol before coronary bypass surgery was advocated initially because of the possible negative ionotropic effect in the early postoperative period of beta-adrenergic blockade. However, recent evidence indicates that maintenance of propranolol administration until the time of surgery has been associated with greater hemodynamic stability during anesthetic induction before cardiopulmonary bypass is instituted without necessitating an inordinate need for postoperative ionotropic support.[1-3] Furthermore, the abrupt cessation of propranolol administration has been associated with acute ischemic events.[4,5] Hypersensitivity to adrenergic stimulation after withdrawal has been postulated as etiologic not only in precipitating myocardial ischemia, but also as causative for the 8% to 30% incidence of significant supraventricular tachyarrhythmias (SVT) following myocardial revascularization procedures.[6]

Because of the proven efficacy of propranolol in the treatment and prophylaxis of a variety of tachyarrythmias[7,8] and the theoretically deleterious sequelae of its abrupt withdrawal, a prospective, randomized study was performed to determine the effectiveness of the early reinstitution of propranolol in low dosage to patients following coronary artery bypass grafting in reducing the incidence of postoperative SVT.

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Patients and Methods

One hundred consecutive patients undergoing coronary artery bypass grafting without additional cardiac surgical procedures at the University of Illinois Hospital and Westside Veterans Administration Hospital were prospectively entered in the study regardless of ventricular performance or need for urgent revascularization. All patients were receiving propranolol before surgery. Preoperatively, patients with stable angina had their propranolol dose tapered to 40 mg every 6 hours by the day before surgery, or, if receiving a lower dose, continued at that level. Patients with previously unstable angina or significant left main stenosis were maintained on the drug dose they were taking upon entering the hospital. In all patients, the last dose was given

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orally on call to the operating room. Patients receiving digoxin, diuretics, procainamide, or quinidine had these medications discontinued 24 hours before surgery.

Surgical and anesthetic techniques were uniform. All anastamoses were performed on cardiopulmonary bypass using a total crystalloid prime, bicaval venous cannulation, aortic arch perfusion, and selective left ventricular venting only to facilitate exposure of circumflex vessels or if ventricular distention occurred. Distal anastamoses were performed first during a single period of aortic cross-clamping with myocardial protection effected by intermittent, hypothermic, hyperkalemic potassium cardioplegia. Proximal anastamoses were performed after aortic unclamping during rewarming. Temporary pacing wires were sutured to the right ventricle for removal on the fifth postoperative day.

Postoperatively, patients were randomized to receive propranolol 10 mg orally or via nasagastric tube starting at 6:00 A.M. of the first postoperative day and continuing until discharge (Group I, 50 patients) or to serve as controls (Group II, 50 patients). Randomization was by birthdate. Those born on an even day received propranolol, and those born on an odd day served as controls. Group I and II did not differ in regard to age, incidence of hypertension, diabetes mellitus, previous myocardial infarction, impaired ventricular function, and unstable angina, preoperative inderol dosage, extent of coronary disease, number of grafts performed, total cardiopulmonary bypass time, and duration of aortic cross-clamping (Table 1). After surgery, all patients were continuously electrocardiographically monitored in the surgical intensive care unit for at least 48 hours. When transferred to the ward, daily 12-lead electrocardiograms and rhythm strips were obtained. When supraventricular tachycardias occurred, they were controlled with intravenous digoxin and propranolol.

Perioperative myocardial infarction was judged to occur if two of the three following indicators were present: new Q waves, elevation of cardiac isoenzymes, and positive radionuclide scanning. The incidence of phenomenon were statistically compared by chi square analysis with a p value of <0.05 considered significant.

TABLE 1. *Clinical Characteristics of Study Population*

	Group I (50 patients)	Group II (50 patients)	P
Age	55.2 ± 1.7	58.2 ± 1.5	N.S.
Male/female	48/2	45/5	N.S.
Hypertensive	44%	54%	N.S.
Diabetes mellitus	24%	20%	N.S.
Previous infarction	56%	64%	N.S.
Unstable angina	42%	48%	N.S.
Abnormal LV function*	52%	58%	N.S.
Preop propranolol dosage (mg/24 hours)	182 ± 14	210 ± 22	N.S.
Extent coronary disease			N.S.
1 Vessel	2%	4%	
2 Vessel	18%	14%	
3 Vessel	62%	64%	
Left main	18%	18%	
Grafts/patient	3.2 ± 0.1	3.5 ± 0.1	N.S.
Bypass time (min.)	106.5 ± 4.6	117.9 ± 5.1	N.S.
Cross-clamp time (min.)	34.5 ± 1.5	38.3 ± 1.8	N.S.
Perioperative infarction (#pts.)	5	6	N.S.
Incidence SVT†	6%	28%	<.01

* Localized wall motion abnormality, ejection fraction <50%.
† Supraventricular tachycardia.
Left ventricular end diastolic pressure >15 mm Hg.
Selected data presented as mean ± standard error of mean.

Results

Three of 50 patients (6%) in Group I developed supraventricular arrhythmias. Each rhythm disturbance was atrial fibrillation. Fourteen of 50 patients (28%) in Group II developed supraventricular arrhythmias. Eight arrhythmias were atrial fibrillation, and six were atrial flutter. All arrhythmias occurred between the second and twelfth postoperative day. The time of initial occurrence of each arrhythmia is charted in Table 2. The incidence of tachyarrhythmias in Group I was significantly less than the incidence in Group II ($p < 0.01$). The mean time after surgery that the arrhythmia occurred was not different. The rapid ventricular response in each instance was initially controlled by pharmacologic therapy irrespective of the early reinstitution of propranolol, and no one required emergency electrical cardioversion for hemodynamic embarrassment. All patients except one in group II converted to sinus rhythm within 48 hours. This patient was electively cardioverted before discharge.

There were no preoperative discriminators that would predict which patients would subsequently develop SVT. The mean age (58.2 ± 1.2 SEM), incidence of hypertension (57%), previous infarction (62%) and abnormal ventricular function (50%), preoperative daily inderal dosage (208 mg ± 22) and extent of coronary disease (71% left main or 3-vessel) of the 17 patients who developed arrhythmias did not differ from either

TABLE 2. *Time and Frequency of Arrhythmia Occurrence*

	Postoperative Day										
	2	3	4	5	6	7	8	9	10	11	12
Group I.											
Atrial flutter	0	0	0	0	0	0	0	0	0	0	0
Atrial fibrillation	1	1	0	0	0	1	0	0	0	0	0
Group II.											
Atrial flutter	3	1	0	1	0	0	0	0	0	0	1
Atrial fibrillation	3	2	0	1	1	0	0	0	1	0	0

Group I, Group II, or the combined group who had no rhythm disturbances. Similarly, the number of grafts performed (3.5 ± 0.1) total pump time (111.8 ± 8.0 min.), and ischemic time (38.3 ± 2.7 min.) were not different. Five patients (10%) in Group I and 6 patients (12%) in Group II had perioperative infarctions as determined by the criteria previously defined. None of the three patients receiving postoperative propranolol and 2 of 14 of the control patients who developed arrhythmias also sustained a perioperative infarction. Therefore, in this series, perioperative infarction was not associated with an increased incidence of supraventricular arrhythmias. In addition, none of the nine patients who had preanesthetic insertion of an intraaortic balloon pump for stabilizing severe angina pectoris or because of critical left main occlusive disease developed arrhythmias. Finally, no correlation could be made between the transient necessity for ionotropic support (12%) in the first 24 hours and the occurrence of atrial tachyarrythmias. Of the seven patients in group I requiring ionotropic agents, one developed SVT compared with no SVT occurring in the five patients in group II requiring postoperative ionotropic agents.

Propranolol in the dosage administered was well tolerated. No patient developed significant bradycardia, bronchospasm or difficulty in controlling diabetes mellitus necessitating discontinuance of the medication.

Discussion

Previous studies have endeavored to find an efficacious, safe drug that can be given prophylactically to prevent the significant incidence of supraventricular tachyarrhythmias (SVT) following coronary artery bypass surgery.[9,10] Based on the favorable experience gleaned following pulmonary resections,[11,12] digitalis preparations have been given both before and after operation to patients undergoing coronary revascularization. O'Kane et al. gave ouabain immediately after surgery and prevented SVT from occurring in a small group of patients.[13] Using a different regimen, Johnson and coworkers showed that preoperative digitalization with maintenance doses restarted on the first postoperative day decreased the incidence of these rhythm disturbances from 26% to 6%.[14] In a nonrandomized study in patients whose beta-blockers were discontinued at least 1 week before operation, Csicsko et al. showed that digitalization within 4 hours after operation decreased the incidence of SVT from 15% to 2%.[15] However, in a well-controlled, randomized study of the effect of prophylactic digitalization, Tyras et al. showed that the drug had no benefit in the prevention of SVT following coronary artery surgery and, in fact, predisposed patients to these arrhythmias.[16] Given the known vulnerability of ischemic myocardium to digitalis intoxication,[17] the shifts in digoxin stores between serum and myocardium during extracorporeal circulation,[18] and the metabolic alkalosis and hypokalemia following perfusion, digitalis preparations would theoretically be a hazardous medication to administer prophylactically to patients undergoing coronary revascularization.

The appropriate perioperative administration of propranolol has been the subject of a continuing controversy. Initial reports of mortality following coronary revascularization in patients receiving long-term propranolol therapy were attributed to the negative ionotropic effect of persistent beta-adrenergic blockade.[19] However, further clinical studies suggested that abrupt withdrawal of propranolol from patients with symptomatic coronary artery disease may result in serious arrhythmias and acute myocardial infarction.[4,5] The salutary effects of maintaining propranolol therapy up until 2 hours before operation were shown in reports by Wechsler,[1] Kirsch et al.,[2] and Jones et al.[3] Continuing propranolol resulted in a more stable hemodynamic course during anesthetic induction, intubation and sternotomy without the potentially deleterious increases in the rate-pressure product and myocardial oxygen consumption. Moreover, an increased necessity for temporary ionotropic support was manifested primarily in patients receiving 320 to 480 mg of propranolol just before surgery.

Further evidence suggested that propranolol administration be reinstituted in the postoperative period. In normal subjects given the drug for 2 to 3 months, abrupt withdrawal was accompanied by a shortening of platelet survival and enhancement of sympathetically mediated reflex tachycardia.[20] Thus a mechanism whereby arrhythmias and ischemic events could be precipitated was postulated. Boudoulas restarted propranolol within 24 hours following myocardial revascularization in 21 patients and only one patient developed SVT.[21] However, the dosage and length of administration were not noted. Oka et al. gave 19 patients one mg of propranolol intravenously every 4 hours for 36 to 48 hours following surgery.[22] They noted no postoperative myocardial depression, a diminished myocardial oxygen need, and a minimal incidence of SVT. However, they monitored their patients for arrhythmias only during the first 24 hours following surgery.

Several previous studies have suggested the efficacy of propranolol in the prevention of cardiac arrhythmias following coronary artery bypass grafting. Stephenson and coworkers randomized patients to receive propranolol 10 mg orally every 6 hours following discharge from the intensive care unit or to serve as controls.[23] The drug group had an 8% incidence of SVT compared to 18% in untreated patients. However, the groups were

of unequal size, the initiation of therapy was not uniform as to time following surgery, modes of myocardial protection were by present standards inadequate, and patients requiring transient ionotropic support were excluded. The postoperative regimen of Mohr and coworkers involved restarted low-lose propranolol 6 hours following bypass surgery.[6] They showed that the incidence of SVT was decreased by reinstituting propranolol only in patients who were receiving beta-blockers after operation. They included patients having concomitant ventricular aneurysmectomy and 60% of their patients had prophylactic or therapeutic catecholamine support. Unlike the present study, they found that antecedent hypertension predisposed to postoperative SVT. Roffman and Fieldman, in a nonrandomized study, showed that the combination of postoperative digitalization in conjunction with orally administered propranolol beginning 48 hours after surgery decreased the incidence of SVT occurring after the 3rd postoperative day when compared with groups receiving digitalization alone or receiving no medication.[24] Arrhythmias occurring in the first 48 hours were not prevented. Interestingly, they found patients with arrhythmia were older, had more grafts performed, and had longer ischemic times.

The present study was performed in a prospective, randomized fashion in a homogenous patient population where anesthetic and surgical technique and modes of myocardial protection were uniform. Patients were not excluded because of severity of ventricular dysfunction, necessity for urgent revascularization, or need for pharmacologic or mechanical circulatory support. These data clearly indicate that there were no preoperative discriminators that could predict a patient subgroup predisposed to the postoperative development of SVT. Similarly, intraoperative events such as the number of grafts performed, the total bypass time, and aortic cross-clamp time also did not correlate with SVT occurrence. Moreover, perioperative infarction and the need for transient ionotropic support were not arrhythmogenic. Finally, the dosage of propranolol administered caused no significant morbidity, yet significantly decreased the incidence of postoperative SVT. Therefore, the authors feel all patients undergoing coronary artery bypass grafting should have the early postoperative reinstitution of low-dose propranolol therapy.

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