COMPARISON OF HEMODYNAMIC EFFECTS OF DILTIAZEM AND METOPROLOL IN CORONARY ARTERY BYPASS WITHOUT CARDIOPULMONARY BYPASS

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Coronary artery bypass grafting (CABG) operation is the standard and the most effective treatment in atherosclerotic coronary artery disease.

Physiologic and pathologic side effects of performing coronary artery bypass operation by means of extracorporeal circulation, aortic cross-clamping and arresting heart chemically all have limiting effects on indication especially in high risk patients. Coronary artery bypass grafting on the beating heart, eliminates these side effects. A number of mechanical devices and pharmacological agents are available to decrease mobility of the heart in order to perform effective and safe coronary anastomosis on the beating heart.

In a prospective study in Koşuyolu Heart and Research Hospital, hemodynamic effects of diltiazem and metoprolol, administrated for decreasing heart rate during CABG on the beating heart, were compared.

20 patients were present both in diltiazem (group D) and metoprolol groups (group M) . In group D, 18 patients were male and 2 were female, while there were 17 male and 3 female in group M. Mean ages were 54.4±11.8 in group D and 54.7±12.0 in group M. Preoperative left ventricular performance scores were 11.25±1.65 in group D and 10.95±1.76 in group M. Number of revascularized coronary arteries was 2.15±0.98 in group D and 1.9±0.96 in group M.

Mean parenteral dose given during the operation was 34.00±8.67 mg for diltiazem and 21.73±8.74 mg for metoprolol. There was no hospital mortality and perioperative myocardial infarction. The two groups were compared with respect to hemodynamic data.

Heart rate, mean arterial pressure and pulmonary capillary wedge pressure values were significantly lower in group M than group D. Within physiologic ranges, cardiac index values were also lower in group M ($p<0.05$).

Myocardial creatine kinase (CPK-MB) values were significantly higher in group D than in group M ($p<0.05$). Five patients had transient electrocardiographic changes, three patients had atrial fibrillation and one patient had ventricular fibrillation in group D (9/20, 45%). In group M, one patient had transient electrocardiographic changes and another one had ventricular extrasystoles (2/20, 10%). In our opinion, metoprolol can be effectively and safely used in CABG on the beating heart to ensure decreased heart mobility.

Key words: CABG on the beating heart, diltiazem, metoprolol

Coronary artery bypass grafting operation is the standard treatment method in atherosclerotic coronary artery disease (1). Atherosclerotic coronary artery disease is a leading reason of mortality and morbidity in developed countries. The aim of the therapy is to eliminate the symptoms that decrease quality of life and increase survival rate by means of medical and invasive cardiologic interventions or revascularization procedures (2).

Despite the fact that using extra-corporeal circulation and arresting the heart chemically is the conventional method in coronary artery bypass grafting, morbidity and mortality of CABG operation mainly results from extracorporeal circulation, global cardiac arrest, hypothermia and median sternotomy (3).

In order to avoid the side effects of extracorporeal circulation, aortic cross-clamping and cardiac arrest, CABG on the beating heart has been updated in the past 10 years (4).

CABG on the beating heart means performing revascularization on epicardial coronary arteries while heart is beating at its own rhythm, without using ECC, aortic cross-clamping and cardiac arrest (5-7).

CABG on the beating heart ensures lower morbidity rates in high risk patients including the aged that suffer from disturbances in left ventricular, hepatic, renal, pulmonary, hematological and immune system functions.

In order to decrease the coronary mobilization while performing the anastomosis, a number of methods like using traction sutures (8-11), horseshoe metallic device or Octopus tissue stabilizer (12), have been used. In line with this, pharmacological agents like beta-blockers, adenosine, calcium canal blockers or vagal discharge producers have been used not only to reduce cardiac chronotropism but also to ensure optimal hemodynamic conditions (13,14).

MATERIAL AND METHODS

40 patients with indication of coronary artery bypass operation on the beating heart were selected for the present prospective study. 20 of them were in group D and remaining 20 were in group M. There was no statistically significant difference in preoperative features of the two groups. Mean age in group D was 54.4±11.8, while it was 54.7±13.0 in group M. In group D, 18 patients (%90) were male and two (%10) were female, while in group M 17 were male (%85) and three (%15) were female. Left ventricular performance score was 11.25±1.65 in group D and 10.95±1.76 in group M. There was no statistically significant difference between the two groups in number of diseased coronary arteries (Table 1).

Mean revascularized coronary artery number was 1.35±0.48 in group D and 1.45±0.68 in group M ($p>0.05$). Mean coronary artery occlusion time was 10.37±2.06 min for the patients of group D and 10.90±0.96 min for group M ($p>0.05$). Patients in group D, were given 180 mg diltiazem per day orally, while patients in group M received 200 mg metoprolol per day orally for at least 7 days before the operation.

OPERATIVE TECHNIQUE

After performing median sternotomy, pericardiotomy and harvesting the left internal

Table 1. Preoperative characteristics of patients.

	Group D	Group M
Mean age(year)	54.4±11.8	54.7±12.0
Sex		
Male	18(%90)	17(%85)
Female	2(%10)	3(%15)
DCAN	2.15±0.98	1.90±0.96
LVPS	11.25±1.65	10.95±1.76

DCAN: Number of diseased coronary arteries,
LVPS: Left ventricular performance score.

thoracic artery (LITA), patients were heparinized to obtain an ACT ≥ 200 sec. In both groups, after harvesting LITA, either diltiazem 2 mg or metoprolol 2.5 mg was administered parentally as a bolus. Parenteral drug administration was ceased when distal anastomosis was completed. Total parental diltiazem and metoprolol doses were 34.00±8.67 mg and 21.73±8.74 mg, respectively. Right internal jugular vein was cannulated via a 7.5 F thermodilution catheter, inserted to the pulmonary artery. Hemodynamic parameters were measured via Gould Cardiac Output Computer in 6 different phases: Before induction (A), at the beginning of the anastomosis (B), at the end of anastomosis (C), at the end of the operation (D), postoperative 2nd hour (E) and postoperative 4th hour (F).

RESULTS

Electrocardiography: Five patients had transient electrocardiographic changes, three had atrial fibrillation and one had ventricular fibrillation in group D (9/20, 45%). In group M, transient electrocardiographic changes occurred in one patient, while another patient had ventricular extrasystoles (2/20, 10%).
Cardiac enzymatic changes: CPK values and especially CPK-MB values specific for myocardial cell injury were significantly higher in Group D compared to group M ($p<0.001$)(Table 2).

Table 2. Enzymatic changes.

	Grup D	Grup M
Early Postoperative		
CPK	505.1±354.1	406±336.1
CPK-MB	35.6±17.6	34.6±13.9
Postoperative 1st .day		
CPK	1861.5±102.8	516.3±98.5
CPK-MB	76.0±56.2	25.0±9.1

Heart Rate: Heart rate did not change significantly during intravenous diltiazem administration in group D. On the other hand, heart rate decreased significantly in group M during parenteral drug administration ($p<0.05$). Heart rate values were at lowest

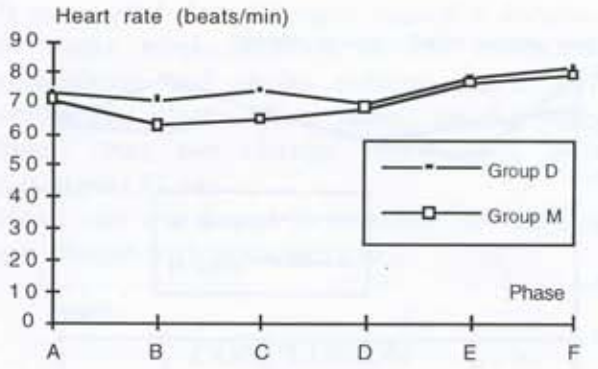


Figure 1. Changes in heart rate.

level during coronary anastomosis. It was shown that heart rate was significantly decreased in Group M compared to group D, especially during the anastomosis (Figure 1).
Pulmonary Vascular Resistance (PVR): After drug administration, pulmonary vascular resistance values decreased during the first phase. But, after the first phase, PVR values increased even during the drug administration in both groups (Figure 2).

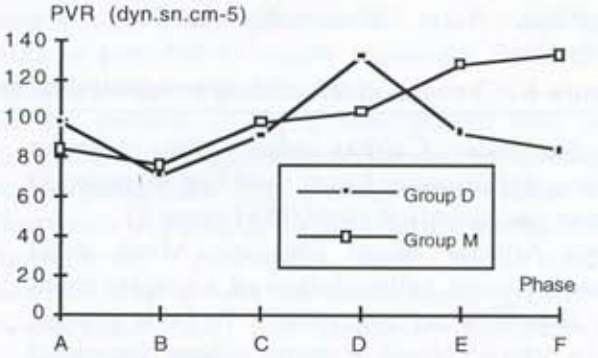


Figure 2. Changes in pulmonary vascular resistance.

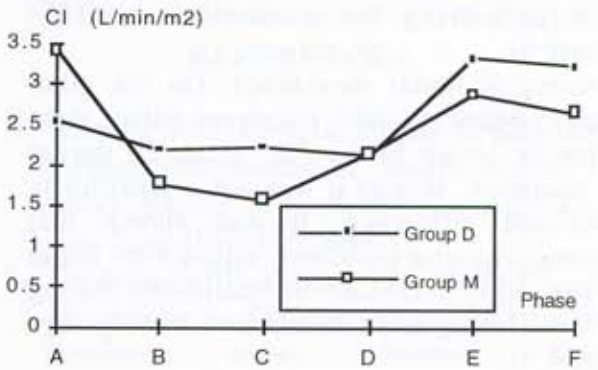


Figure 3. Changes in cardiac index.

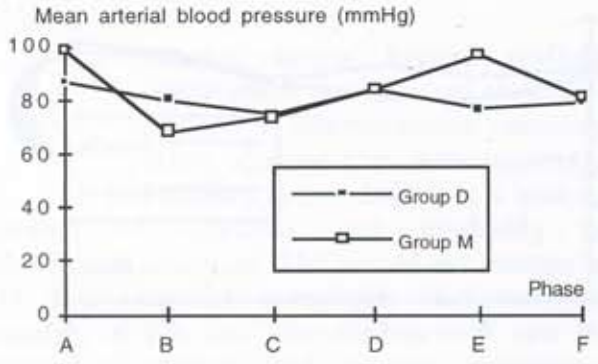


Figure 4. Changes in mean arterial pressure.

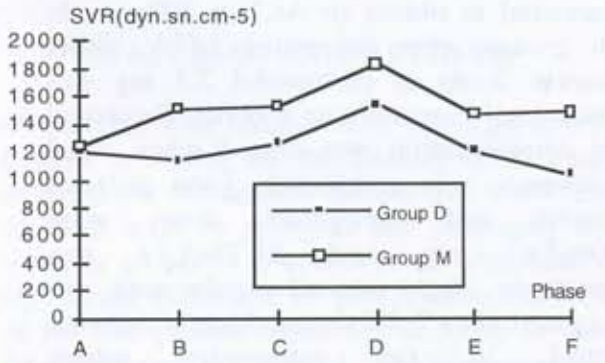
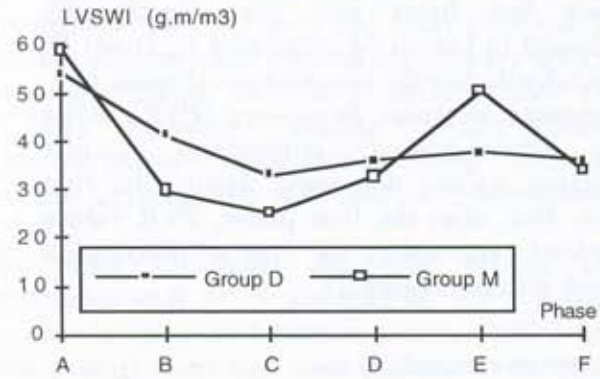


Figure 5. Changes in systemic vasculary resistance.



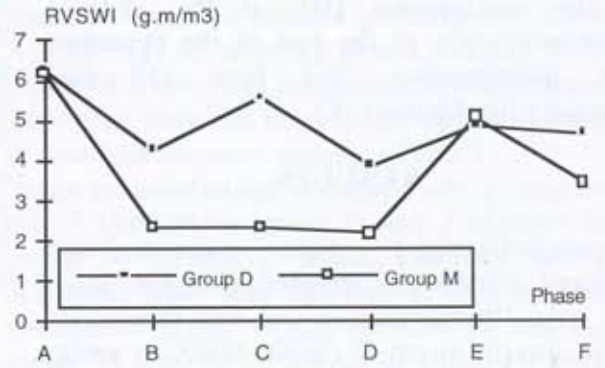


Figure 6. Changes in left and right ventricular stroke work indexes.

Cardiac Index: Cardiac index values of group M was significantly lower than that of group D during the operation ($p<0.05$)(Figure 3).

Mean Arterial Blood Pressure: Mean atrial blood pressure values followed a similar trend like that of heart rate values. In both groups, mean arterial blood pressure values decreased during drug administration and increased after cessation of the drug. But in group M, values were significantly lower than group D while performing the anastomosis ($p<0.05$) (Figure 4).

Systemic Vascular Resistance: On the other hand, systemic vascular resistance values were higher in group M than in group D during the operation, though it was not a statistically significant difference. It was shown that systemic vascular resistance values were either unchanged or increased insignificantly during parenteral drug administration in both groups (Figure 5).

Left Ventricular Stroke Work Index and Right Ventricular Stroke Work Index: In both groups, left ventricular stroke work index decreased significantly after drug administration, but was significantly lower in group M than that of group D, especially during the anastomosis. On the other hand, while right ventricular stroke work index significantly decreased during drug administration in group M, there was not a significant change in values of group D (Figure 6).

DISCUSSION

When coronary artery bypass grafting was newly introduced the pioneering operations were performed on the beating heart. Later on, extracorporeal circulation and myocardial protection methods became prominent. But disadvantages and indication limiting effects of extracorporeal circulation and myocardial protection, made coronary artery bypass grafting on the beating heart become current once again.

Four main determinants of left ventricular myocardial oxygen demand are myocardial

contractility, arterial blood pressure, left ventricular volume and heart rate. Heart rate and systolic arterial blood pressure are considered as the most important determinants (15).In line with this, postoperative myocardial ischemia might directly be associated with tachycardia, in case other hemodynamic parameters were stable (16-18). Beta-blocker administration causes coronary blood flow to shunt towards ischemic areas, to subendocardial areas in particular (19). It was reported that preoperative beta-blocker administration prevented the myocardial ischemia due to tachycardia (20). Metoprolol was reported to increase collateral blood flow to ischemic myocardial areas, limit infarct area, decrease both symptomatic and silent ischemic attacks (21,22). Beta-blockers decrease oxygen demand in ischemic and non-ischemic myocardium (23).

Beta-blocker administration in coronary artery bypass grafting on the beating heart was reported previously (24,25). Intravenous b-blocker administration causes a transient increase in total peripheral resistance in the acute phase (26).

Cristakis et al. reported that diltiazem was useful in patients with postoperative hypertension, tachycardia, coronary spasm and ischemia risk, but its usage was controversial in patients with left ventricular dysfunction (27). Seitelberger et al. also reported that diltiazem had anti-ischemic and antiarrhythmic effects in patients who underwent a CABG operation (28).

Donegani et al. stated that ischemic changes in electrocardiography, arrhythmia, conduction disturbances and perioperative hypertension incidence decreased, but severe contraction disturbances could develop with diltiazem (29). Diltiazem decreases total peripheral resistance (30). Intravenous diltiazem was reported to decrease afterload. It also decreases preload by increasing left atrial diastolic pressure and/or increasing ventricular relaxation (31).

Diltiazem has the least negative inotropic but the most antidiamotrophic effects compared to the other calcium canal blockers. Also its vasodilator effect on coronary arteries is more prominent than its effect on systemic arteries (32).

It was stated that diltiazem caused a decrease in stroke work, increase in left ventricular compliance and stroke volume index. Left ventricular stroke work index, on the other hand, does not change significantly with diltiazem (33,34).

Heart rate was found to increase, decrease or not change with diltiazem (35).

CONCLUSION

Medication in coronary artery bypass grafting on the beating heart has to ensure optimal myocardial protection against ischemia and surgical comfort for performing a coronary anastomosis as effective and safe as obtained using ECC.

In order to use this procedure without myocardial damage, heart rate and LVEDH should not increase, coronary perfusion pressure should not decrease and hemodynamic stability should be ensured. Above all, cardiac chronotropic activity should be in balance at a rate as low as possible to perform coronary anastomosis safely, and as high as possible to supply metabolic demands of both the heart and the body.

In the present study, it was shown that in coronary artery bypass grafting on the beating heart, metoprolol both provided a decrease in heart rate within physiologic limits during the anastomosis procedure and had more sophisticated results on electrocardiographic, biochemical and hemodynamic parameters compared to diltiazem.

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