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Original Article

Effects of Six Beta Blocking Agents on Cardiovascular Responses during Exercise

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Abstract: The cardiovascular effects of six beta blocking agents; atenolol (50 mg), carteolol (5 mg), propranolol (10 mg), nipradilol (3 mg), dilevalol (100 mg) and metoprolol (40 mg) during Master's test exercise were assessed in 85 healthy young adults. All drugs significantly reduced the increments in pressure-rate product during exercise at 1 hr as well as 2 hr after the drug administration, which might reflect myocardial oxygen consumption. Therefore, after administration of these beta blockers, an equivalent workload can be achieved with less myocardial oxygen consumption. The potency of 6 drugs at 1 hr after drug administration was: metoprolol>nipradilol>atenolol>propranolol>dilevalol>carteolol, and that at 2 hr after administration was: atenolol>carteolol>metoprolol>propranolol>dilevalol>nipradilol.

Key words: Beta Blockers, Master's Test, Nipradilol, Dilevalol, Healthy Young Adults

INTRODUCTION

Beta blocking agents are used for the prevention of anginal attacks by virtue of an increase in the level of exercise performance mainly by reducing two principal determinants of the myocardial oxygen requirement: heart rate and contractility[1,2]. The effects are predictable from the role of adrenoceptors in regulating these functions. A number of beta blocking agents have now been developed and used clinically on many patients, however comparative data are lacking on the effects of the drugs on the cardiovascular responses during exercise under the same experimental condition.

The purpose of this study was to estimate the exercise-induced hemodynamic responses to six beta blockers in healthy young adults. We selected the protocol for the Master's test, which was the well established method to assess the exercise tolerance[3], and we measured arterial blood pressure (BP) and pulse rate (PR) to obtain the pressure-rate product (PRP).

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SUBJECTS AND METHODS

Eighty-five healthy young volunteers; systolic blood pressure (SBP) 117±2 mmHg, diastolic blood pressure (DBP) 68±1 mmHg, PR 79±1 beats/min, age 22.6±0.2 years old, male 70, female 15, participated in this double-blind, placebo-controlled study. The over-all purpose and the design of the study were explained to the subjects as a group, and the subjects were free to drop out of the study at any point.

The double protocol of the Master's test was used for exercise[4]. SBP and DBP were measured in a sitting position using automatic pneumatic cuff manometers (MB-304H, SHARP K.K.). PR was also examined by palpation of the pulses in the radial artery.

First, these parameters were measured before and after exercise to obtain the control values, and drugs were p.o. given, and then the parameters were measured again before and after exercise at 1 hr and 2 hr after drug administration.

The drugs used in this study were atenolol (50 mg), carteolol hydrochloride (5 mg), propranolol hydrochloride (10 mg), nipradilol (3 mg), dilevalol hydrochloride (100 mg) and metoprolol tartrate (40 mg), which were given in single doses recommended for clinical use. The data was presented as mean±SEM, and statistical differences were analyzed using paired *t*-test. P values less than 0.05 were considered significant.

Results

There were no volunteers who were unable to tolerate the protocol of the present study. Fig. 1A shows the effects of beta blockers on the changes in SBP during exercise. Atenolol, carteolol, propranolol, dilevalol and metoprolol significantly reduced the increments in SBP at 1 hr and 2 hr from respective control values. Nipradilol also showed a similar trend ($p<0.1$) at 1 hr and 2 hr.

Fig. 1B shows the effects of beta blockers on

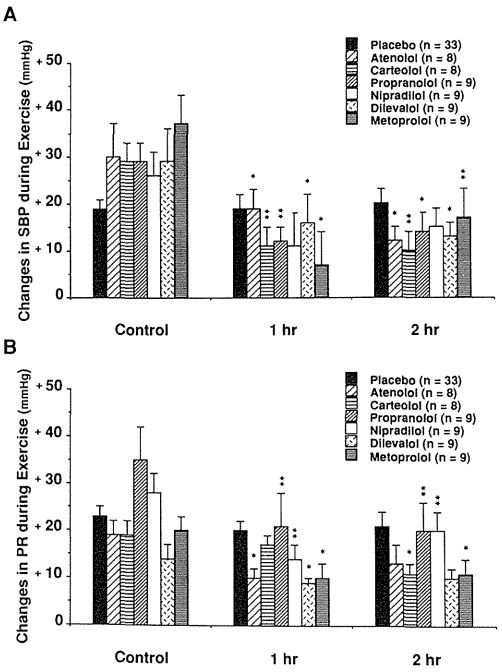

Fig. 1. Time courses of systolic blood pressure (SBP) and pulse rate (PR). (A) Changes in SBP during exercise load at control, 1 hr and 2 hr after drug administration. (B) Changes in PR during exercise load at control, 1 hr and 2 hr after drug administration. *Difference between control data and drug administered data in each drug. $P<0.05$, $**P<0.01$.

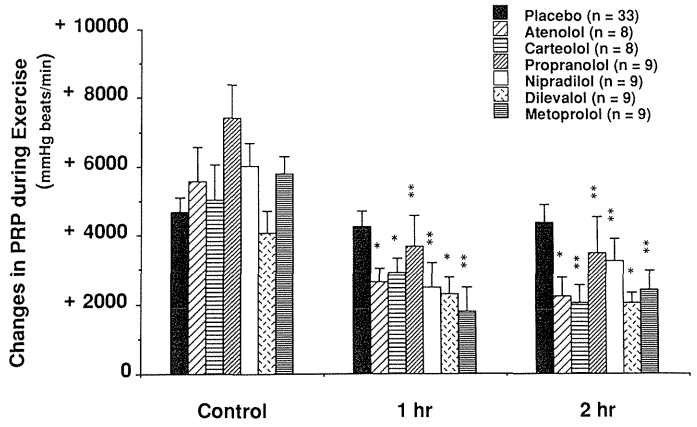

Fig. 2. Time courses of change in pressure-rate product (PRP) during exercise at control, 1 hr and 2 hr after drug administration. *Difference between control data and drug administered data in each drug. $P<0.05$, $**P<0.01$.

the changes in PR during exercise. Atenolol, propranolol, nipradilol, dilevalol and metoprolol significantly reduced the increments in PR during exercise at 1 hr from respective control value, and carteolol, propranolol, nipradiolol and metoprolol also caused a significant reduction at 2 hr.

Fig. 2 shows the effects of beta blockers on the changes in PRP during exercise. All the drugs except placebo significantly reduced the increments in PRP during exercise at 1 hr and 2 hr from respective control values. The percent changes in the increments in PRP during exercise of atenolol, carteolol, propranolol, nipradilol, dilevalol and metoprolol from respective control values were −9%, −52%, −42%, −50%, −59%, −44% and −69% at 1 hr, and −6%, −60%, −59%, −53%, −45%, −50% and −58% at 2 hr, respectively.

Fig. 3 shows the effects of beta blockers on DBP before exercise. At 1 hr after the drug administration, propranolol significantly increased the DBP from its control value. At 2 hr, nipradilol significantly decreased the DBP and dilevalol showed a similar trend ($p<0.1$). The other drugs had no significant effect on DBP at 1 hr or 2 hr ($p>0.1$).

Discussion

It is well established that physical exercise causes an increase in sympathetic activity, as has been shown by rises in the levels of plasma catecholamines[5] and also as increase in the BP and PR in the present study. The beta blocking action in the 6 medicated groups in this study was demonstrated by the attenuation in exercise induced SBP and PR responses.

PRP is an index of myocardial oxygen consumption and is a good parameter for comparison of various cardiac intervention[2,3]. In our study, the increments in PRP during exercise after beta blockade were significantly decreased from those at control, while there was no significant decrease in the increments in PRP during exercise of placebo group, when the same exercise was repeated. The percent changes in the increments in PRP during exercise from those of control values were larger in beta blocker groups than in placebo group. Therefore, an equivalent workload can be achieved with less myocardial oxygen consumption after these beta blockers have been administered.

Only nipradiolol and dilevalol decreased the DBP in the resting condition. These findings suggest that these two drugs possess some

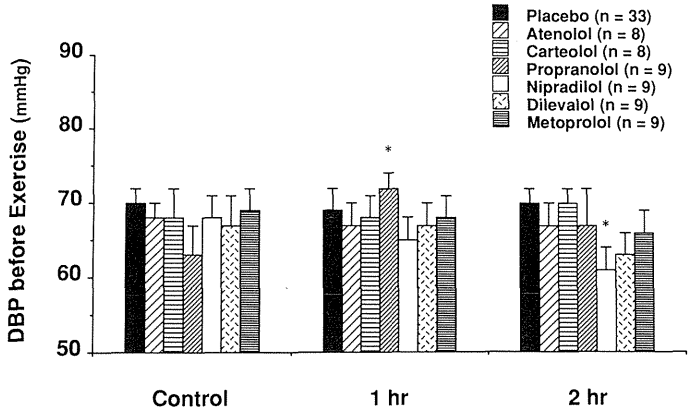

Fig. 3. Time courses of diastolic blood pressure (DBP) before exercise at control, 1 hr and 2 hr after drug administration. *Difference between control data and drug administered data in each drug. $P<0.05$.

types of vasodilator actions, which are consistent with the previous reports that nipradilol has a nitroglycerin-like action[6], and dilevalol has partial beta-2 agonism[7]. As the vasodilator beta-2 receptors are blocked, propranolol increased DBP in the resting condition, which was consistent with the previous report that propranolol blocks the vasodilator response to beta adrenergic stimulation[1].

In conclusion, the 6 beta blockers significantly reduced the increments in myocardial oxygen consumptions during exercise as estimated by the PRP, and their potency 1 hr after administration was: metoprolol > nipradilol > atenolol > propranolol > dilevalol > carteolol, and that at 2 hr after administration was: atenolol > carteolol > metoprolol > propranolol > dilevalol > nipradilol.

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