Regression of Left Ventricular Hypertrophy in Hypertensive Patients: 
Responses to Exercise by Antihypertensive Treatment

Mikio Arita, M.D., Setsuko Fujiwara, M.D., Yuji Ueno, M.D.
Masahiko Shiotani, M.D., Yoshinari Nakamura, M.D., Chigusa Nakatsu, M.D.
Ichiro Nishio, M.D., and Yoshiaki Masuyama, M.D.

The effects of various antihypertensive treatments on the echocardiographic and electrocardiographic findings of left ventricular (LV) hypertrophy were studied in 75 patients with essential hypertension. The hemodynamic effects of the therapy during exercise were also compared.

LV mass by echocardiogram was significantly reduced by β-blockade and angiotensin converting enzyme inhibition (ACEI), but only slightly reduced by Ca channel blockade. QRS high voltage criteria of LV hypertrophy by electrocardiogram were reduced by all 3 of these antihypertensive treatments.

At submaximal exercise, the pressor responses were attenuated by captopril, but not influenced by metoprolol or nifedipine. The increase in plasma norepinephrine by exercise was significantly suppressed after captopril, but was somewhat augmented after metoprolol or nifedipine.

These observations indicate that the responses of hemodynamics and sympathetic nervous activity to exercise are different after the treatment by β-blocker, Ca channel blocker or ACEI, in spite of the equal antihypertensive effect. However, it is suggested that the regression of LV hypertrophy might be induced by antihypertensive therapy, though the different grade by the individual drug.

The regression of left ventricular (LV) hypertrophy in hypertensive patients has been detected recently by the measurement of LV dimensions with echocardiography. Earlier studies have suggested that combination therapy with various antihypertensive drugs could lead to a reduction in LV mass. However, some controversy remains about the regression of cardiac hypertrophy during antihypertensive therapy. Sympatholytic drugs and β-blockers were reported to induce regression of LV hypertrophy, but some other antihypertensive agents, such as vasodilators and diuretic drugs, have been reported ineffective.

In this study, we investigated the regression of LV hypertrophy associated with long-term antihypertensive treatments and compared the hemodynamic effects of various antihypertensive therapy during exercise.

SUBJECTS AND METHODS

Two studies were performed involving a total of 75 patients, aged 33 to 68 years, with mild to moderate essential hypertension. Resting blood pressure for all patients was over 150/90 mmHg at several initial visits to the clinic. Secondary hypertension was excluded by individual examination in the hypertension clinic.

Study [I]: Regression of LV hypertrophy

---

Key words:
Regression of left ventricular hypertrophy
Hypertensive heart
Antihypertensive treatment
Response to exercise

Division of Cardiology, Department of Medicine, Wakayama Medical College, Wakayama, Japan
Mailing address: Mikio Arita, M.D., Division of Cardiology, Department of Medicine, Wakayama Medical College, 27, 7-Bancho, Wakayama 640, Japan

Japanese Circulation Journal Vol. 54, May 1990 575
caused by long-term antihypertensive drug therapy.

Forty-five hypertensive patients were included in this study, with ages ranging from 36 to 68 years old. Antihypertensive monotherapy, including β-receptor blocking drugs, calcium channel blockers, and converting enzyme inhibitors was continued for more than 2 years. Mean duration of antihypertensive drug therapy in this study was 31.5 months. Seventeen patients were treated with β-blockers, 20 patients with Ca channel blockers, and 8 patients with angiotensin converting enzyme (ACE) inhibitors. There were no significant age differences among these 3 groups.

Antihypertensive treatment was initiated after a control electrocardiogram and two-dimensional guided M-mode echocardiogram were obtained. From the two-dimensional guided M-mode echocardiogram, LV mass was calculated by the method of Devereux and Reichek using the Penn measurement conventions.8

Study [II]: Changes of response to exercise associated with antihypertensive drug therapy

Thirty patients aged from 33 to 56 years and

Japanese Circulation Journal Vol. 54, May 1990
Heart Rate

Metoprolol  Nifedipine  Captopril

Cardiac Output

Metoprolol  Nifedipine  Captopril

Fig. 2. Changes in heart rate and cardiac output during exercise before and after antihypertensive treatments. Submax.: submaximal exercise

with essential hypertension were studied. After blood pressure and heart rate had reached a steady state, the exercise test was performed in a supine position on a bicycle ergometer (Siemens). A graded exercise test was started at a work load of 50W, and the load was increased by 25W up to a maximum of 100W, every 3 min. Blood pressure, heart rate and cardiac output were recorded at each step. Cardiac output was determined by two dimensional guided M-mode echocardiogram. All medications were discontinued for at least 2 weeks before the treatment was begun. Patients were randomly selected for antihypertensive therapy using metoprolol, captopril, or nifedipine.

After the first hemodynamic study with exercise test, 10 patients received daily doses of 60 mg of metoprolol, 10 patients 30 mg of nifedipine, and 10 patients 37.5 to 75 mg of captopril, in 3 divided doses. The aim was to achieve a casual sitting blood pressure of less than 140/90 mmHg. After a 4 week treatment period, the exercise test was again conducted.

The significance of differences was statisti-
cally analyzed using the Student’s t-test for paired observations. Values are expressed as means ± SEM, and p < 0.05 was considered to be significant.

RESULTS

I. Regression of LV hypertrophy associated with long-term antihypertensive drug therapy

The effects of monotherapy with β-blockade, Ca-channel blockade or ACE-inhibition alone on the blood pressure, and electrocardiographic QRS voltage (SV1 + RV5) and LV mass in echocardiogram are summarized in Table I. Anti-hypertensive treatment with β-blocker, Ca channel blocker or ACE inhibitor alone significantly reduced mean blood pressure (p < 0.01).

The voltage of SV1 + RV5 decreased significantly after each antihypertensive treatment. There was a significant reduction of LV mass as assessed by echocardiogram after treatment with β-blocker or ACE inhibitor alone. However, the reduction of LV mass was not significant by Ca channel blocker alone.

II. Changes of response to exercise with antihypertensive drug therapy

Changes in blood pressure during exercise before and after antihypertensive treatments are shown in Fig. 1. Systolic and diastolic blood pressure elevated progressively during exercise. Metoprolol significantly reduced systolic blood pressure, but did not affect the blood pressure responses to exercise. Nifedipine significantly reduced the blood pressure at rest, but the peak response of blood pressure with exercise was no different from the control. Captopril significantly reduced systolic blood pressure before and after exercise, while the peak value of diastolic blood pressure after exercise was unchanged in spite of its significant reduction before and 10 min after exercise. As shown in Fig. 2, the heart rate was decreased at rest by metoprolol, but not significantly. The peak increase in heart rate with exercise was significantly suppressed by metoprolol. The increase in heart rate after exercise was significantly augmented by nifedipine. Baseline heart rate and increase in heart rate after exercise were not affected by captopril.

Cardiac output was increased with exercise as shown in Fig. 2. Metoprolol significantly decreased cardiac output, both at rest and at peak response to exercise. On the other hand, nifedipine and captopril did not affect cardiac output at rest and the peak response of exercise. Plasma norepinephrine significantly increased with exercise as shown in Fig. 3 (p < 0.05). At rest, the plasma norepinephrine level was slightly, but not significantly, higher than the control after nifedipine or captopril treatment. The exercise-induced increase in plasma norepinephrine was significantly suppressed by cap-
topril, but was slightly augmented by metoprolol or nifedipine.

DISCUSSION

This study showed regression of LV hypertrophy with antihypertensive monotherapy with β-blockade, Ca channel blockade or ACE inhibition for more than 2 years. High voltage criteria in electrocardiograms show the regression of LV hypertrophy with all these antihypertensive treatments. LV mass as measured by echocardiogram, was significantly reduced with β-blocker and ACE inhibitor treatment; Ca channel blocker treatment produced on insignificant reduction. Previous studies have documented a reduction in LV mass with antihypertensive treatment. Sympatholytics, including methyldopa and reserpine, have been associated with significant regression of LV hypertrophy. ACE inhibitors and Ca channel blockers have also led to significant regression of hypertrophy. Foud et al. suggested that the reduction in sympathetic activity associated with therapy with methyldopa can play a permissive role in helping to reverse cardiac hypertrophy. However, the exact mechanisms for the reversal of hypertrophy in hypertensive patients cannot be fully explained. Further studies are needed to assess the effects of regression in LV hypertrophy.

We examined changes in hemodynamics and sympathetic nerve activity in response to exercise. Recently, it has been proposed that the choice of antihypertensive therapy may be important because different antihypertensive medications may have different pharmacodynamic effects at rest and during exercise. Exercise systolic blood pressure is reported as a good predictor of LV mass, and antihypertensive treatment should be aimed at controlling blood pressure not only at rest, but also during exercise.

In this study, exercise produced a significant increase in blood pressure, heart rate, and cardiac output associated with increased plasma norepinephrine levels. The exercise-induced increase in blood pressure was significantly suppressed by captopril, but not significant suppressed by metoprolol or nifedipine.

The hemodynamic mechanism underlying the hypotensive effects of metoprolol appears to be represented by a decrease in cardiac output. This phenomenon appears to be exclusively mediated by a reduction in the heart rate. With β-blockers, there is an associated chronic reduction in the cardiac index at rest and during exercise.

The exercise induced increase in blood pressure was augmented rather than suppressed by nifedipine. However, different hemodynamic effects of Ca-channel blockers were seen during exercise, indicating that Ca channel blockers induced a reduction in blood pressure without reduction in the cardiac index. It is well known that reflex tachycardia is caused by blood pressure fall with nifedipine. In our study, an increase in heart rate with exercise was somewhat augmented by nifedipine.

Fagard et al. indicated that the action of captopril was characterized by arteriolar and possibly venous dilatation both at rest and during exercise. In this study, captopril affected neither cardiac output nor heart rate. This absence of overt tachycardia in the face of a decreased total peripheral resistance has intrigued several investigators and angiotensin II may be required for normal functioning of the baroreceptor reflexes. The exercise-induced increase in blood pressure and in plasma norepinephrine was suppressed by captopril administration.

These results suggest that angiotensin II might partially contribute to blood pressure regulation during exercise through the augmentation of the sympathetic nervous system.

These observations indicate that the effects of β-blockade, Ca channel blockade or ACE inhibition on the responses of hemodynamics and sympathetic nervous activity to exercise are different, even if the antihypertensive effects are similar. Therefore, it is suggested that these antihypertensive drugs should be selected individually, on the basis of their hemodynamic effects during the patient’s daily life and their influence on the regression of LV hypertrophy.

REFERENCES

2. ROWLANDS DB, GLOVER DR, IRELAND MA, McLEAY RAB, STALLARD TJ, WATSON RDS, LITTLEWELL WA: Assessment of left ventricular mass and its response to antihypertensive treatment. Lancet 1: 467, 1982
4. COREA L, BENTIVOLIO M, VERDECCHIA P:
8. REICHEK N: Standardization in the measurement of left ventricular wall mass: M-mode echocardiography. Hypertension 9 (Suppl II): 27, 1987