Effect of Acute Blood Pressure Reduction on Oxygen Uptake Kinetics at the Onset of Exercise in Hypertensive Patients

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SUMMARY

The aim of the present study was to investigate the adverse effects of hypertension on the cardiovascular system in daily activities and the effect of acute blood pressure reduction on oxygen (O₂) uptake kinetics.

Twenty hypertensive patients were included in the study group. Patients performed treadmill exercise tests (2.5 km/hour and 5 inclines) twice, before and after blood pressure reduction with sublingual captopril. In the control group, ten hypertensive patients underwent two tests one hour apart without blood pressure reduction brought about by drug therapy. The changes in O₂ kinetic values (O₂ deficit and mean response time [MRT]) between the two tests were investigated.

In the study group, the O₂ deficit and MRT values measured during the first exercise testing were found to be 547 ± 183 mL and 40 ± 9 seconds, while those in the second exercise testing were 401 ± 127 mL and 34 ± 7 seconds, respectively. In the control group, the O₂ deficit and MRT values measured during the first exercise test were 491 ± 217 mL and 42 ± 16 seconds and 515 ± 159 mL and 41 ± 13 seconds in the second exercise test. The differences in O₂ deficit and MRT in the study group were considered to be statistically significant (P = 0.008 and P = 0.004, respectively).

Based on our findings, there was a significant improvement in O₂ kinetic values with an acute reduction in blood pressure in hypertensive patients, most likely as a result of an improved response in cardiac output. (Jpn Heart J 2004; 45: 799-805)

Key words: Oxygen kinetic values, O₂ deficit, Mean response time

FATIGUE is a common complaint of most patients with hypertension during their daily life activities. Although patients with high blood pressure remain asymptomatic in the beginning, some adverse effects could be observed in the cardiovascular system after some years. Most are not aware of their high blood pressure and some use their medication irregularly. By means of symptom-lim-
itted exercise testing we can measure peak oxygen (O$_2$) uptake and anaerobic threshold (AT). This test is also helpful for objective evaluation of functional capacity and for the follow-up of several cardiovascular diseases.$^{1,2)}$ It was shown that the O$_2$ kinetic values (O$_2$ deficit and mean response time [MRT]) measured with a constant workload test under the anaerobic threshold, are inversely related with maximal oxygen uptake (VO$_{2\text{max}}$).$^{3,4)}$ In this study, we investigated the effects of acute blood pressure reduction on the cardiovascular system in hypertensive patients on O$_2$ uptake kinetics.

**METHODS**

Low-level constant-load exercise testing was performed in 30 patients with hypertension. Patients were not included in the study if there was any evidence of myocardial ischemia during exercise (angina pectoris, electrocardiographic abnormalities, abnormal thallium scintigraphy or stress echocardiography, abnormal coronary angiography), abnormal pulmonary function tests, peripheral vascular disease, anemia, or orthopedic and neurological problems making them not suitable for the exercise treadmill test. The test was not applied to those with a systolic blood pressure greater than 200 mmHg or a diastolic blood pressure greater 115 mmHg at rest. All patients had normal left ventricular systolic functions and were in sinus rhythm. A Quinton 5000 treadmill and Cortex Metalyser 3B were used for exercise testing. Gas and volume calibrations were done before every measurement. Prior to a test, at least three blood pressure measurements at 5 minute intervals were obtained for each patient. All patients performed 6 minutes of treadmill exercise test at 2.5 km/hour and with 5 inclines, which is similar to the workload in the second stage of the modified Bruce protocol. The first test was conducted when the patient was not receiving any drugs and the second test was performed after administering 25 or 50 mg sublingual captopril in the study group. In the control group, the patients performed two tests one hour apart without blood pressure reduction using any drug. Both tests were performed on the same day. After collecting 1 minute of resting gas exchange, constant workload exercise was performed by walking on the treadmill at a speed of 2.5 km/hour and 5 inclines for 6 minutes without a warm-up period. During the study, O$_2$ uptake and minute ventilation were recorded. A standard 12 lead ECG was recorded and blood pressure was measured at rest, during exercise, and in the recovery period. O$_2$ deficit measurements and MRT were calculated from O$_2$ uptake diagrams using a computerized Metalyzer 3B cardiopulmonary exercise test system. Oxygen deficit was determined by measuring the area between the ideal square curve of O$_2$ uptake at the onset of the constant work rate exercise and the actual exponentially shaped curve. MRT described the rapidity of VO$_2$ of a subject to
respond to the constant workload$^5$ and was calculated using the following formula: 
$$
\text{MRT} = \frac{\text{O}_2 \text{ deficit}}{\Delta \text{VO}_2}
$$
All data are given as the mean ± standard deviation. Student’s paired $t$ test was used to compare variables between the study and control groups. Differences were considered statistically significant at a $P$ value < 0.05.

**RESULTS**

Twenty patients (8 women and 12 men, median age, 55 ± 9 years) were included in the study group. Ten patients (5 women and 5 men, median age, 61 ± 9 years) were included in the control group. All of them completed the study uneventfully and the workload was under the anaerobic threshold because O$_2$ uptake reached a steady-state by 3 minutes in all patients. A comparison of the mean O$_2$ uptake kinetics is displayed in Table I. In the study group at the beginning of the test, the mean systolic and diastolic blood pressures were 187 ± 14 mmHg and 94 ± 8.8 mmHg, respectively. In the control group the mean O$_2$ deficit was 547 ± 183 mL and MRT was 40 ± 9 seconds at the first exercise test. After 25 or 50 (in three patients) mg captopril had been used sublingually, mean systolic blood pressure was 133 ± 8 mmHg and diastolic blood pressure was 84 ± 6 mmHg before the second submaximal exercise test. At the second test, the mean O$_2$ deficit values and MRT were 401 ± 127 mL and 34 ± 7 seconds, respectively. In the control group at the beginning of the first test, the mean systolic and diastolic blood pressures were 175 ± 19 mmHg and 94 ± 8.8 mmHg, respectively. At the beginning of the second exercise, the mean systolic and diastolic blood pressures were 180 ± 20 mmHg and 94 ± 8.8 mmHg. In the control group during the first constant exercise test, the mean O$_2$ deficit was 491 ± 217 mL and the MRT was 42 ± 16 seconds. At the second exercise, the mean O$_2$ deficit values and MRT were 515 ± 159 mL and 41 ± 3 seconds, respectively. When blood pressure decreased, there was a statistically significant decline in O$_2$ deficit and MRT in the study group ($P = 0.008$ and $P = 0.004$, respectively) (Figure 1). There was no statistical difference in these parameters in the control group ($P = 0.082$ and $P = 0.068$, respectively).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study group 1st exercise</th>
<th>Study group 2nd exercise</th>
<th>Control group 1st exercise</th>
<th>Control group 2nd exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BP</td>
<td>187 ± 14/94 ± 8</td>
<td>133 ± 8/84 ± 6$^{**}$</td>
<td>175 ± 19/94 ± 8</td>
<td>180 ± 20/94 ± 8</td>
</tr>
<tr>
<td>O$_2$ Deficit</td>
<td>547 ± 183</td>
<td>401 ± 127$^{*}$</td>
<td>491 ± 217</td>
<td>515 ± 159</td>
</tr>
<tr>
<td>MRT</td>
<td>40 ± 9</td>
<td>34 ± 7$^{**}$</td>
<td>42 ± 16</td>
<td>41 ± 13</td>
</tr>
</tbody>
</table>

BP = blood pressure; O$_2$ = oxygen; MRT = mean response time, $^*P < 0.05$, $^{**}P < 0.005$. 

Table I. Comparison of Oxygen Uptake Kinetics
DISCUSSION

The aim of this study was to evaluate the effect of high blood pressure on cardiac function during daily activities and the effects of O\textsubscript{2} uptake kinetics at the onset of exercise with decreased blood pressure. We examined whether cardiac function at the onset of exercise was different before and after a reduction in high blood pressure. Functional capacity in cardiovascular diseases is generally determined by the measurements of VO\textsubscript{2} at maximal exercise testing. Nevertheless, it is more convenient to use parameters obtained during submaximal exercise testing for evaluation of complaints during daily activities. Characteristic findings of the hypertensive heart are increased left ventricular mass, impairment of diast-
tolic functions, congestive heart failure, and abnormal coronary reserve.\(^7\) In most hypertensive patients, shortness of breath and fatigue occur even at low exercise levels. Leg fatigue is defined a failure by both heart and lung at increasing O\(_2\) levels that supply the metabolic demands of muscles.\(^8\)

Cardiopulmonary alterations and O\(_2\) uptake kinetics curves at a constant exercise level are used in the diagnosis and follow-up of several diseases.\(^4,9\) When a constant submaximal exercise is performed at a level below the AT, the O\(_2\) uptake value increases rapidly to a stable level in 3 minutes and remains there until the end of the 6th minute.\(^10\) There are three phases of O\(_2\) uptake at submaximal exercise test below the AT.\(^11\) The first is the cardiodynamic phase, which reflects O\(_2\) uptake related to the sudden increase in cardiac output without any increase in arteriovenous oxygen difference. The second phase is the adjustment to the metabolic adaptation or the widening of the arteriovenous O\(_2\) difference. In the third phase, O\(_2\) uptake reaches a steady-state. Therefore, O\(_2\) deficit could be defined as the adaptation of the heart to the constant workload exercise.\(^12\) The O\(_2\) deficit is the difference between the O\(_2\) demand and O\(_2\) uptake measured.\(^13\) In a healthy heart, O\(_2\) uptake rapidly reaches a steady-state at a fixed velocity exercise level. In these cases, aerobic metabolism plays the most important role, lactic acid increases in the blood, and the O\(_2\) deficit decreases.\(^14\)

In left ventricular systolic dysfunction, O\(_2\) uptake reaches a steady-state level slowly. In these cases, anaerobic metabolism occurs early at the lower level of exercise, which causes shortness of breath.\(^15\) Lund-Johnsen\(^16\) found that hypertensive patients had a smaller increase in cardiac output and higher peripheral vascular resistance than that in normals during exercise. In a healthy person, peripheral vascular resistance decreases during exercise, but its decrease is smaller in hypertensive individuals compared to that in normotensive subjects.\(^17\) Oxygen deficit is calculated by the subtraction of total actual the O\(_2\) uptake value from the product of steady-state O\(_2\) uptake. The oxygen deficit is calculated as the difference between the total O\(_2\) uptake and the product of the steady-state VO\(_2\) and the exercise duration.\(^10\) The fixed speed walking test is simple and could be easily performed in almost all patients in this study. VO\(_2\) max is the best parameter to determine functional capacity in individuals with normal left ventricular systolic function. Such patients are able to do much longer aerobic exercise and have a much lower O\(_2\) deficit than others with impaired systolic function.\(^14\) Lim, \textit{et al} pointed out that exercise capacity is 30% lower in hypertensive patients than those in normotensives.\(^18\) Cuocolo, \textit{et al} observed abnormal ejection fraction during exercise due to impaired diastolic functions in individuals with hypertrophied left ventricle.\(^19\)

We planned to evaluate the effects of high blood pressure on cardiac function in submaximal exercise and the effects of O\(_2\) kinetics in the early phase of
We examined whether cardiac adaptation is different between patients with high and reduced blood pressure at the same speed walking. The variability in the MRT at the same speed walking was noted also. We preferred to use sublingual captopril because it is easy to use and does not have any effect on heart rate. We noted a significant decrease in blood pressure after captopril use. The present study has demonstrated that decreases in blood pressures to normal levels cause decreases in O2 deficit and MRT in hypertensive cases. The cause of these changes could be attributed to a faster increase in cardiac output at the onset of exercise because the O2 uptake is equal to the multiplication of cardiac output and arteriovenous O2 difference. Koike, et al investigated the acute effects of nicorandil on the kinetics of O2 uptake at the onset of constant mild intensity cycle exercise in patients with ischemic heart disease and found that oral administration of nicorandil shortens the time constant of O2 uptake. They thought this could be attributed to a faster increase in cardiac output or a more rapidly increasing arteriovenous oxygen difference at the onset of exercise.20) Matsumoto, et al found the kinetics of VO2 are closely related to cardiac output in patients with chronic heart failure.21) Our results show that hypertensive patients had a prolonged increase in O2 uptake at the onset of exercise during high blood pressure, and in the same patients an acute reduction of blood pressure improved the kinetics of O2 uptake.

As a result, high blood pressure causes a reduction in cardiovascular performance even during daily activities. According to our findings, there was a significant improvement in O2 uptake kinetics with an acute reduction in blood pressure in hypertensive patients, most likely as a result of an improved response in cardiac output. Heart can more quickly adapt to its workload and can perform the same workload with a lower energy requirement, even in the early phase of blood pressure control.

REFERENCES


