Beneficial Effects on Blood Pressure and Lipid Profile of Programmed Exercise Training in Subjects With White Coat Hypertension

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Background: Patients with white coat hypertension comprise a substantial portion of the hypertensive population. Previous reports have shown that moderate-intensity regular exercise training in patients with mild hypertension usually reduces blood pressure (BP), but there is a lack of data regarding individuals with white coat hypertension. This study was performed to evaluate whether programmed exercise was effective in reducing BP in patients with white coat hypertension and whether it also had beneficial effects on other biochemical parameters.

Methods: A total of 42 patients (23 men and 19 women) with white coat hypertension (mean 24-h ambulatory BP 119.2/78.3 mm Hg) were divided randomly into two groups: control (n = 20) (no exercise), and moderate-intensity exercise (n = 22). The training group exercised three times per week at the prescribed exercise intensity using a treadmill exercise program. Blood pressure, heart rate, and biochemical parameters were monitored every 4 weeks for 12 weeks.

Results: Significant reductions in clinic and ambulatory BPs were seen in the exercise group after only 4 weeks regular exercise training and these persisted over the 12-week study. The mean maximal reductions in clinic BP were 11 mm Hg for systolic and 5 mm Hg for diastolic pressure. Significant reductions were found in plasma total cholesterol (−6.1%), low-density lipoprotein cholesterol (LDL-C) (−14.1%), and triglyceride (−11.4%). Elevation of high-density lipoprotein cholesterol (HDL-C) (+11.2%) was also noted.

Conclusions: These data, which are clinically significant, suggest that 12 weeks of exercise training can result in successful reduction of BP and favorable changes in the lipid profile that would be beneficial to patients with white coat hypertension. Am J Hypertens 2002;15:571–576 © 2002 American Journal of Hypertension, Ltd.

Key Words: Exercise, lipid, treadmill, white coat hypertension.
compared with physically fit patients, those who were less fit had a relative risk of 1.5 for the development of hypertension. 9

Regular exercise has also been found to lower BP. In mildly hypertensive men, short-term physical activity decreased BP for 8 to 12 h after exercise, and average BP was lower on exercise than on nonexercise days. 10 Mild-to-moderate exercise was shown to have greater effects in lowering BP than high-intensity exercise. 11

However, the beneficial effect of exercise training in white coat hypertension has not been studied. The chief aim of this study was to evaluate whether programmed regular exercise training in patients with white coat hypertension could have a beneficial effect on BP. As regular exercise has also been recommended to improve abnormal lipid profiles, as mentioned in the latest report of the National Cholesterol Education Program, we also monitored the plasma lipids in these patients. 12

Patients and Methods

Subjects

Hypertensive patients were recruited from hospital outpatient clinics. Patients were eligible if they were between 20 and 60 years old, weighed <120% of their ideal weight according to Metropolitan Life tables, had a history of essential hypertension, were not currently performing regular aerobic exercise, and had not taken antihypertensive medications within 6 weeks of being screened for the study. Patients were excluded if they had coronary artery disease or other organic heart disease, asthma, chronic obstructive pulmonary disease, or secondary hypertension. Informed consent was obtained from all subjects. This study was approved by the Local Investigation and Research Committee.

Baseline Blood Pressure

All patients had three BP measurements taken in a clinic setting by a nurse or research assistant, 5 min apart on three separate occasions with a random zero sphygmomanometer. Patients were included if either their mean systolic BP was between 140 and 180 mm Hg or their mean diastolic BP was between 80 and 105 mm Hg. All patients underwent a physical examination by a physician to rule out obvious secondary causes of hypertension and contraindications to exercise. Then, on separate days, ambulatory BP monitoring and exercise testing were performed.

Ambulatory Monitoring

Ambulatory BP monitoring was performed using an AccuTracker monitor (Suntech Medical Instruments, Raleigh, NC). Monitoring was done on a typical workday and subjects were encouraged to pursue a variety of routine activities. Ambulatory monitors were placed on subjects at approximately 8 AM and were removed by a research assistant the following day. Blood pressures were recorded on a fixed schedule every 60 min. At each cuff inflation, subjects used a diary to record their posture (standing, sitting, lying), location (home, work, other), activities (physical activity, talking, eating, sleeping), and use of caffeine, alcohol, or medications.

To test the calibration of the monitor, seven auscultatory and ambulatory monitor BP measurements were performed simultaneously on a subset of subjects (n = 25) using a Y-adapter. Ambulatory monitor BP readings were, on average, 0.2/3.0 mm Hg below auscultatory BPs. When mean ambulatory BP readings were adjusted for this calibration difference, classification as white coat or persistent hypertension remained unchanged for 90% of subjects. In view of this high degree of agreement, unadjusted ambulatory BPs were used to classify subjects as having white coat or persistent hypertension. Subjects were defined as having white coat hypertension if both their mean ambulatory systolic BP was ≤135 mm Hg and diastolic BP was ≤85 mm Hg, values regarded as within the normotensive range in previous studies. 1

Blood Lipid Measurement

Biochemical blood tests were performed for each subject every 4 weeks during the study period. Plasma cholesterol and triglycerides were measured by conventional assays, and high-density lipoprotein (HDL) cholesterol was determined after sodium phosphotungstate-magnesium chloride precipitation. 13 Low-density lipoprotein (LDL) cholesterol was calculated by a modified version of the Friedewald formula: LDL cholesterol = total cholesterol − (0.16 × triglycerides + HDL cholesterol). 14 Serum plasma renin activity and aldosterone levels were also examined at each visit. Plasma renin activity was determined by a commercial radioimmunoassay kit (Squibb, Princeton, NJ), using a buffer to maintain pH at approximately 6.0. 15 Aldosterone was measured with a commercial coated-tube radioimmunoassay (Diagnostic Products Corp., Los Angeles, CA). 16

Exercise Tests

One week before the experimental study began, blood biochemical examination was performed for each subject after an 8-h fast. Subjects then reported for a graded exercise test using the Balke protocol on a Schiller Treadmill (Cardiovit CS-100) fitted with a Schiller electrocardiogram monitor and controller (Schiller AG, Basel, Switzerland). The Balke protocol was selected because of its moderate intensity increases per stage. 17 Briefly, during the Balke/Ware protocol the subjects start to exercise at 4.8 km/h, 0% gradient with the percentage gradient increasing by 2.5% every 2 min. Each subject was fitted with a 12-lead electrocardiography system. A licensed physician was present during all tests. Blood pressure and rate of perceived exertion were measured every 2 min. Heart rate and 12-lead electrocardiogram strips were printed every 2 min. The exercise test was terminated if any
subject exhibited ≥1 mm ST-segment change, significant arrhythmias, an inappropriate BP response to increasing workloads, angina pectoris, or exercise-induced bundle branch block. Data for all subjects was collected at baseline and at 4, 8, and 12 weeks during the 12-week exercise program.

### Experimental Groups and Trials

Before initial exercise testing, subjects were assigned randomly to one of two experimental groups: a nonexercising control group and a moderate-intensity aerobic exercise training group (60% to 70% maximal heart rate: average about 6 to 7 metabolic equivalents [MET]; 1 MET = 3.5 Kcal/kg body weight/min). The exercise-training program consisted of 10 min of warm-up, 30 min of treadmill walking/jogging, and 10 min of cool-down three times per week. Resting BP was calculated by averaging the BP measurements after ≥10 min of seated rest by the subject before each of the exercise training sessions. The heart rate during exercise of each subject in the exercise group was continuously monitored by staff members to ensure compliance with the prescribed exercise regimen. In addition, BP was measured every 10 min during exercise to ensure the safety of the subject.

### Statistical Analysis

Values are expressed as mean ± SD. Pre- versus posttraining and between-group differences in heart rate, BP, body weight, maximal MET, and heart rate and BP values at 4-week intervals were examined using analysis of variance for repeated measures and the least square means post hoc test. All other comparisons were examined using one-way analysis of variance and Dunnett’s post hoc test. A value of *P* < .05 was considered to be statistically significant.

### Results

A total of 52 subjects were recruited for this study. Of these, only 42 subjects (23 men and 19 women) completed the 36 exercise sessions within 12 weeks. The mean age of the subjects was 41 years. The baseline characteristics for the exercise and control groups are shown in Table 1. Ten of the 52 subjects (six in the exercise and four in the control group) were not able to complete the study for nonmedical reasons, and they were not included in the data analysis. The subjects’ body mass index (BMI) did not show any significant changes in either the exercise or control group during the 12-week period (*P* = .40 and .96, respectively).

The data show significant findings that through this moderate-intensity aerobic exercise training, the exercise group experienced a dramatic reduction of BP, especially systolic pressure. Blood pressure was significantly reduced even at the first follow-up visit. The mean reduction in systolic BP reached a maximum of 11 mm Hg (8% reduction), whereas the maximal reduction in diastolic BP was 5 mm Hg (6% reduction). The mean reduction in diastolic

### Table 1. Baseline characteristics of subjects with white coat hypertension in control and exercise groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (N = 20)</th>
<th>Exercise (N = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>36.6 ± 7.4</td>
<td>45.5 ± 9.5</td>
</tr>
<tr>
<td>Male/female</td>
<td>11/9</td>
<td>12/10</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.1 ± 2.6</td>
<td>23.3 ± 1.0</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>103.6 ± 12.0</td>
<td>99.3 ± 5.0</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>132.2 ± 60.5</td>
<td>111.8 ± 28.8</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>197.0 ± 15.0</td>
<td>190.5 ± 17.6</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>48.0 ± 10.1</td>
<td>53.3 ± 20.1</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>130.7 ± 24.7</td>
<td>125.5 ± 27.7</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>24.6 ± 17.6</td>
<td>22.0 ± 10.5</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>13.0 ± 6.3</td>
<td>14.7 ± 4.0</td>
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<tr>
<td>BUN (mg/dL)</td>
<td>11.2 ± 3.8</td>
<td>13.7 ± 1.4</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.8 ± 1.6</td>
<td>0.8 ± 0.2</td>
</tr>
<tr>
<td>PRA (pg/mL/min)</td>
<td>18.5 ± 6.3</td>
<td>15.1 ± 3.0</td>
</tr>
<tr>
<td>Aldosterone (pg/mL)</td>
<td>200 ± 55.6</td>
<td>185.8 ± 28.8</td>
</tr>
<tr>
<td>Mean clinic SBP (mm Hg)</td>
<td>137.6 ± 7.9</td>
<td>134.3 ± 12.2</td>
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<tr>
<td>Mean clinic DBP (mm Hg)</td>
<td>91.6 ± 7.9</td>
<td>85.3 ± 10.2</td>
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<tr>
<td>Mean clinic resting HR (beats/min)</td>
<td>84.8 ± 13.2</td>
<td>79.0 ± 16.1</td>
</tr>
<tr>
<td>Mean 24-h SBP (mm Hg)</td>
<td>122.4 ± 7.7</td>
<td>126.0 ± 5.5</td>
</tr>
<tr>
<td>Mean 24-h DBP (mm Hg)</td>
<td>78.8 ± 6.4</td>
<td>80.2 ± 7.6</td>
</tr>
<tr>
<td>Exercise capacity (MET)</td>
<td>9.7 ± 1.3</td>
<td>8.9 ± 1.8</td>
</tr>
</tbody>
</table>

BMI = body mass index [(weight)/(height)]²; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; PRA = plasma renin activity; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate/min; MET = metabolic equivalent.

*P* = not significant for all variables.

Values are mean ± SD.
pressure was also 5 mm Hg, whereas that for ambulatory systolic BP was 8 mm Hg (Table 2).

Exercise training also resulted in favorable changes in the plasma lipid profile of these subjects. There were significant reductions of plasma total cholesterol, LDL cholesterol, and triglyceride, as well as elevations of HDL cholesterol. The most dramatic change was the mean reduction of LDL cholesterol of up to 14.1% with a value of 17.8 mg/dL. As for HDL cholesterol, the maximum elevation was 11.2% with a value 6.0 mg/dL (Table 2). The control group did not show any significant changes in their BP and lipid profile (Table 2). No significant changes were observed in other biochemical data such as aspartate aminotransferase, alanine aminotransferase, plasma renin activity, and aldosterone levels.

**Discussion**

Previous studies have shown that clinic BPs tend to be higher than ambulatory BPs, and that clinic BPs taken by a physician tend to be higher than those taken by a nurse. A possible explanation for this phenomenon is that having BP taken in a clinic setting is a stressful event for patients. Patients with a pronounced BP response to clinic BP measurement might appear to be hypertensive in the clinic but may be normotensive during daily life. It has been suggested that white coat hypertension may simply be a precursor of persistent hypertension. Although there will undoubtedly be some true hypertensive individuals who are misclassified as having white coat hypertension on initial assessment, the literature on this is inconsistent at present. In the Northwick Park study, no attempt was made to repeat ambulatory BP monitoring during follow-up, but a substantial proportion of patients had a comprehensive assessment of target organ damage after an interval of 9 years. The assessment showed that only 11% of individuals with white coat hypertension who left ventricular hypertrophy compared with 38% of patients with persistent hypertension, and there were similar differences in carotid artery intimal thickening. Verdecchia et al studied 1187 patients with newly diagnosed essential hypertension and 205 healthy normotensive subjects and then, after a mean of 3.2 years, retrospectively obtained cardiovascular end points. They defined the white coat hypertension cut off as daytime ambulatory BP <136/87 mm Hg for men and <131/86 mm Hg for women.
women. The present study used this criteria to define white coat hypertension.

In the study by Verdecchia et al, the morbidity differences between patients with white coat or persistent hypertension were more pronounced than in the Northwick Park study: Verdecchia et al reported an event rate of 0.49 per 100 patient-years in individuals with white coat hypertension (similar to the rate of 0.47 in the normotensive individuals), a rate of 1.79 in hypertensive dippers, who constituted the majority of the study population, and a rate of 4.99 in nondippers. The Northwick Park study event rate in individuals with white coat hypertension was 1.32 per 100 patient-years.

Chrysant further suggested that pharmacologic treatment could be withheld in persons with white coat hypertension. Instead, treatment should consist of lifestyle modification, regular exercise, weight reduction, and control of the plasma lipid profile. The finding that regular exercise can reduce cardiovascular mortality and morbidity has been well established. Besides BP reduction, favorable changes in the lipid profile could probably play a role. A meta-analysis of 95 studies, most of which were not randomized controlled trials, concluded that exercise leads to a reduction of 6.3% in total cholesterol, 10.1% in LDL cholesterol, and 13.4% in the cholesterol/HDL cholesterol ratio, and 5% increase in HDL cholesterol. Similar results were observed in our subjects with white coat hypertension. Although the sample size may be too small to reach a definitive conclusion, the present data from this controlled study support these findings of previous investigations. The mechanisms by which exercise may improve the lipid profile remain uncertain. Exercise-induced lipolytic enzyme activity, which promotes the degradation of triglyceride-rich lipoproteins, appears to be a factor.

Sasaki et al also proposed that exercise may activate muscle lipase and decrease serum triglyceride and increase HDL cholesterol levels. Although the exercise group showed a reduction of BP without any change of BMI, the possibilities that changes in the proportion of body fat or insulin resistance might influence BP and lipid profile should be considered.

Previous studies have consistently shown that regularly performed aerobic exercise of mild-to-moderate intensity lowers BP in patients with essential hypertension. A reduction in resting BP among normal healthy subjects was also observed at the end of 1-month exercise training. Several mechanisms accounting for the antihypertensive effects of exercise training have been proposed. It may arise from a decrease of plasma norepinephrine, a decrease of endogenous ouabain-like substance, or an increase of prostaglandin E.

A decrease of plasma renin activity was also proposed to play a role. However, plasma renin activity and aldosterone levels remained unchanged in the subjects during our study period. Other factors such as decreased sympathetic nervous system activity and increased sensitivity of the baroreceptor reflex after exercise training may exert a beneficial influence on BP reduction.

In conclusion, our study shows significant reductions in both clinic BPs and mean 24-h ambulatory BPs among subjects with white coat hypertension, even at the first follow-up visit. These results suggest that exercise could have antihypertensive effects in the short-term period. To the best of our knowledge, this is the first study to find significant BP reduction using programmed exercise training in individuals with white coat hypertension, and also favorable changes in the lipid profile as noted in these subjects who were receiving exercise training. Exercise training also increased exercise capacity in persons with white coat hypertension. These findings may shed further light on the possibility that regular exercise could reduce cardiovascular events and mortality, even in so-called benign white coat hypertension.

References


