Prolonged Isometric Exercise
Part 1: Effect on Circulation and on Renal Excretion of Sodium and Potassium in Mild Essential Hypertension

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SUMMARY The effect of stress, in the form of prolonged isometric exercise, on the circulation and on the renal excretion of sodium and potassium was studied in 18 patients with mild essential hypertension. Thirteen men and five women, aged 20 to 50 years with basal diastolic blood pressures (BP) between 90 and 110 mm Hg were matched by age, sex, and race with 18 controls who had basal diastolic BPs less than 85 mm Hg. After the subjects rested for 90 minutes, basal measurements of pulse rate, BP, and rates of sodium and potassium excretion were made. The subjects then underwent a 1-hour period of isometric exercise involving all four limbs in rotation, followed by 5 hours of rest during which the measurements were repeated at half-hourly intervals for the first 2 hours and at hourly intervals for the last 3 hours. On another day, the subjects were again studied after 1 hour of resting instead of exercise. Responses of each subject were then expressed as ratios of changes from the basal values observed on the exercise and rest days.

Changes in systolic and diastolic BP and heart rate were not significantly different in the hypertensive and control groups. In hypertensive subjects, the rate of sodium and potassium excretion was decreased after isometric exercise compared with the rest day, whereas in normal subjects this response was reversed. For the first 3 hours after exercise, the cation excretion rate of the hypertensive group was significantly less than that of the control group. These results indicate that isometric exercise in mild hypertension induces prolonged renal retention of both sodium and potassium. (Hypertension 3: 182-187, 1981)

KEY WORDS • exercise stress • blood pressure • renal sodium excretion • renal potassium excretion • essential hypertension

BORST AND BORST1 have suggested that deficient sodium excretion could have a primary role in the pathogenesis of all forms of hypertension, a postulate receiving further support from the systems analysis approach of Guyton et al.2 In the Dahl strain of spontaneous hypertensive rat (SHR), Tobian et al.3 have shown that the pressure-natriuresis curve of the isolated kidney of the prehypertensive salt-sensitive rat was shifted to the right, indicating a reduction in the natriuretic capacity of the kidneys. In the Okamoto strain of SHR, a similar observation was made on the kidneys of 12-week-old rats.4 Increased sympathetic stimulation of the kidney may modify the relationship between renal perfusion pressure and sodium and water excretion by renal vasoconstriction or by direct action on the proximal tubule.5 In the Okamoto strain of SHR, there is evidence for an important neurogenic mechanism, as shown by increased renal nerve activity6 and a delay in the development of hypertension following renal denervation,7 the delay being partly due to a decrease in sodium retention observed in sham-operated rats.8

In essential hypertension, an early neurogenic phase may be pathogenetic, at least in some patients.9-14 The pattern of hemodynamic disturbance is very similar to that following emotional stress in normal subjects.14 Patients with high blood pressure (BP) may respond to mental stress with greater renal vasoconstriction than normotensive patients.15 Also, mental stress can induce increased and sustained circulatory changes in labile hypertensive patients and in some normotensive patients with a genetic risk of hypertension.16 Isometric exercise is associated with an impressive increase in both systolic and diastolic pressure and pulse rate, a response similar to, but of greater magnitude than the response to mental stress.18 Some patients with high BP may have a more reactive pressor response during isometric exercise than normal people.19, 20

The relationship of this increased pressor response to stress to the genesis of hypertension, and the part that this transient response plays in leading to further BP elevation, is uncertain. For this reason, we in-
vestigated whether such stress could lead to prolonged sodium retention, which might have a protracted effect in maintaining a raised BP.

Methods

We studied 18 patients with mild hypertension, aged 20 to 50 years (mean age, 33.3 years); there were 11 white and two black men, and three white and two black women. All were untreated, newly-diagnosed hypertensive patients without organ damage and no identifiable cause for the hypertension. Eighteen age, sex, and color-matched control subjects were also studied. The controls were individually age-matched within 2 years of each patient (mean age, 32.6 years). There was no significant difference between the weights of patients (mean, 74.1 ± 2.3 kg) and controls (72.9 ± 2.1 kg). In each subject, the average of eight resting diastolic BP readings, measured on the 2 days of the experiment following 1 ½ hours of supine rest, was calculated. In each hypertensive patient, mean diastolic BP was greater than 90 mm Hg and less than 110 mm Hg; in each control subject, mean diastolic BP was less than 85 mm Hg. No control subject had a family history of high BP. Eight control subjects were recruited from the same working environment as the hypertensive patients, and the remainder were hospital-based volunteers. Blood pressure was measured by the Arteriosonde automatic BP monitor in half the hypertensive and half the control subjects chosen at random, and by cuff sphygmomanometry in the other half. Heart rate was counted from the radial pulse over 30 seconds. Urinary sodium and potassium concentrations were determined by flame photometry.

Patients had been advised to abstain from tea, coffee, and cigarette smoking from midnight. After their usual breakfast, they began the medical investigation at 0900 by voiding. Urine volume was maintained thereafter by ingesting 500 ml of water each hour for the duration of the experiment. A lunch of meat, salad, and trifle was eaten at 1245 hours. Each subject rested supine until 1030 h. The blood pressure (X4) and heart rate (X2) were measured between 1015 and 1030 h, and the urine was collected by voluntary voiding to define the basal rate of sodium and potassium excretion. Subsequently, BP (X2), heart rate, and rate of salt excretion were measured at 1130, 1200, 1230, 1300, 1330, 1430, 1530, and 1630 hours. Subjects were asked to empty their bladders completely on each occasion.

Between 1030 and 1130 hours, patients performed isometric exercises involving each limb in rotation. Using a rolled BP cuff attached to a sphygmomanometer, they sustained a right-hand grip at 50% of maximal voluntary contraction for 1 minute, then rested for 30 seconds, then sustained a left-hand grip at 50% maximal contraction for 1 minute. After another 30-second rest, they outstretched the right leg to 45° above the horizontal for 1 minute, then rested for 30 seconds, and raised the left leg to 45° for 1 minute. A rest of 2 minutes followed, and the entire sequence was repeated six times for 1 hour. Studies were repeated on another day with the subjects resting instead of exercising for 1 hour. The sequence of rest and control days was at random. The BP was measured between 40 and 50 seconds and pulse rate for the last 15 seconds of the final minute of leg exercise of each cycle. The BP was again measured between 15 and 25 seconds and pulse rate between 30 and 45 seconds after the exercise. The salt excretion response was expressed as the ratio of the changes from the basal levels observed on the exercise and rest days. Student's two-tailed t test was used for statistical analysis.

Results

Resting Values

Mean resting systolic BP, using basal results from both days, was 144 mm Hg ± 3.9 se in the hypertensive group and 109 ± 3.2 mm Hg in the control group. Respective values for diastolic BP were 99 ± 2.2 and 72 ± 1.8 mm Hg; for pulse rate 72 ± 2.8/min and 64 ± 1.8/min; for sodium excretion rate 13.8 ± 2.0 and 12.2 ± 1.5 mmoles/hr; for potassium excretion rate 5.1 ± 0.7 and 4.4 ± 0.6 mmoles/hr.

Cardiovascular Responses During and After Exercise

During leg isometric exercise, systolic BP increased an average of 19 mm Hg, diastolic BP 18 mm Hg, and pulse rate 22 beats/min, but the changes in these values were not significantly different comparing the hypertensive to the control group (table 1). Immediately after exercise, BP and pulse rate fell toward baseline, the changes being similar in both groups. No significant adaptation of the circulatory responses to isometric exercise during the seven exercise cycles occurred in either group. The circulatory changes for the first 5 hours following exercise were similar in both hypertensive and control groups, no difference in the changes from basal on exercise and rest days being observed.

The method used for BP measurement did not alter the conclusions, as comparable changes in BP were observed in subjects whose BP was measured by cuff sphygmomanometry or by an automatic BP monitor. There was no difference in circulatory response to exercise in the largest uniform subgroup (11 white hypertensive men) when compared to their controls or to the hypertensive group as a whole.

Sodium Excretion Response to Exercise

Figure 1 illustrates the sodium excretion rates on rest and exercise days for both the hypertensive and control groups. The pattern of sodium excretion on the rest day was similar in both groups, but on the exercise day the patterns were different, the hypertensive group retaining proportionately more sodium relative to the basal level following isometric exercise. As the amount of sodium excreted varies from day to day (and consequently the basal level also varies) and
TABLE 1. Increase in Blood Pressure and Heart Rate (mean ± se) During and Immediately After Isometric Exercise in Hypertensive and Normal Subjects*

<table>
<thead>
<tr>
<th></th>
<th>During exercise</th>
<th></th>
<th>After exercise</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>HT</td>
<td>NT</td>
<td>sig of diff</td>
<td>HT</td>
</tr>
<tr>
<td>Δ Systolic BP</td>
<td>20.1 ± 3.8</td>
<td>18.4 ± 3.2</td>
<td>ns</td>
<td>10.1 ± 3.0</td>
</tr>
<tr>
<td>Δ Diastolic BP</td>
<td>17.7 ± 2.1</td>
<td>17.5 ± 2.1</td>
<td>ns</td>
<td>8.4 ± 2.0</td>
</tr>
<tr>
<td>Δ Heart rate</td>
<td>20.5 ± 3.3</td>
<td>24.3 ± 2.9</td>
<td>ns</td>
<td>9.8 ± 2.4</td>
</tr>
</tbody>
</table>

*The changes are calculated from the mean of the four basal measurements preceding exercise and the mean of the seven measurements made during and immediately after each phase of leg isometric exercise. HT = hypertensive; NT = normotensive; ns = not significant.

as the pattern of sodium excretion on the rest day should be taken into account, the salt excretion response to exercise was expressed as the ratio of the changes from the basal levels observed on the exercise and rest days (fig. 2). The difference between the hypertensive and control groups was significant for the first 3 hours after exercise. This finding was also observed when the 11 white hypertensive men were compared to their controls.

The mean basal sodium excretion in the hypertensive group was greater on the exercise day than on the rest day, however, whereas the opposite occurred in the control group, neither difference being significant. This was due to particularly high basal values in two hypertensive women on the exercise day. When the salt excretion response was expressed as the ratio of the sodium excretion rate at time t on the exercise day to that rate on the rest day, with no correction made for basal rates, the response was significantly different between both groups of men for the first hour after exercise. When the response was expressed as the ratio of the changes from mean basal sodium excretion rate (using basal values from both days), the salt excretion response to exercise was significantly different between both groups of males for the first half hour after exercise.

Potassium Excretion Response to Exercise

The potassium excretion rate during the rest and exercise days in both hypertensive and control groups is shown in figure 3. The pattern of potassium excretion on the rest day was similar in both groups, but on exercise day it was different; the hypertensive group retained proportionately more potassium, relative to the basal levels, than the control group. When the

![Figure 1. Mean ± se sodium excretion rate (mmole/hr) during rest and exercise days in control and hypertensive groups](http://hyper.ahajournals.org/Downloadedfrom)
EXERCISE STRESS, HEREDITY AND ELECTROLYTE EXCRETION IN HYPERTENSION/Parfrey et al

FIGURE 4. Mean ± SE potassium excretion response, expressed as the ratio of changes from basal observed on rest and exercise days, after prolonged isometric exercise in hypertensive (HT) and control (C) groups. Asterisk (*) indicates a significant difference (p < 0.05) between HT and C.

Discussion

This study was designed to investigate whether stress, in the form of isometric exercise, had a more substantial effect, both during and after stress, on the circulation of patients with mild essential hypertension compared to matched control subjects, and whether the control of electrolyte excretion following stress was normal in these patients.

It has been suggested that some patients with high BP tend to have a more reactive pressor response during isometric exercise whereas other workers show no such difference. Our results support the latter observations in that the BP changes were similar in the hypertensive and control groups during and immediately after isometric exercise. These findings were similar to those of McAllister and Sannerstedt and Julius.

Falkner et al. reported a sustained increase in systolic and diastolic pressures for 5 minutes after a 10-minute period of mental arithmetic in young labile

FIGURE 3. Mean ± SE potassium excretion rate (mmole/hr) during rest and exercise days in control and hypertensive groups.
hypertensive patients, a finding not observed in normal subjects. However, Nyberg\(^\text{16}\) did not observe any difference in the circulatory response to mental arithmetic in hypertensive and control subjects. A sustained pressor response to mental stress in hypertensive patients has been observed\(^\text{16}\) but we have not observed any sustained circulatory changes to isometric exercise in our hypertensive patients, although the cardiovascular responses to isometric exercise are similar to, but greater in magnitude, than those to mental stress.\(^\text{19}\)

The effect of exercise on the renal excretion of electrolytes has been little explored. After dynamic exercise in normal subjects, retention of sodium and chloride persists for around 40 minutes after the end of exercise.\(^\text{16,19}\) We have found that isometric exercise in normal subjects has the opposite effect, with a natriuresis and kaliuresis lasting some hours following exercise. The mechanisms underlying both these sequences to exercise are complex and likely to involve both systemic arterial pressure and, more specifically, the level of sympathetic nerve stimulation of the kidney. Sympathetically induced renal vasoconstriction results in a reduced renal blood flow and little change in glomerular filtration rate. Filtration fraction is increased, and sodium clearance falls. In addition, there is evidence in the dog for direct neurogenic control of proximal tubular sodium reabsorption at low levels of renal sympathetic nerve stimulation.\(^\text{5}\)

Immediately after dynamic exercise, the level of plasma norepinephrine is raised,\(^\text{20,21}\) but falls to the resting level within 30 minutes.\(^\text{22}\) If this increase in plasma norepinephrine reflects an increase in renal sympathetic nerve activity, the transient retention of sodium after dynamic exercise could be explained. The rise in plasma norepinephrine is considerably greater immediately after dynamic than isometric (handgrip) exercise,\(^\text{23}\) and it is possible that after the latter, the decline in renal sympathetic nerve activity may permit the sodium and potassium diuresis that has been observed. It is also possible that the rise in diastolic pressure during isometric exercise, rather than the fall observed during dynamic exercise,\(^\text{24}\) might be an additional factor determining the different pattern of sodium excretion after the two forms of exercise.

In contrast to the normal subjects, the hypertensive patients retained sodium and potassium for several hours after exercise. This could have been due either to excessive renal sympathetic nerve activity or to an abnormally large and maintained response of the kidney to the normal sympathetic activity associated with exercise. It could not have been due to a difference between the two groups in regard to the relationship between the basal BP and the postexercise BP on the exercise day, since this relationship was the same in both groups.

The observation that, during mental stress, the percentage rise in renal vascular resistance in hypertensives is greater than in normotensives, whereas the percentage rise in BP is the same,\(^\text{18,16}\) suggests that sympathetically mediated renal vasoconstriction is selectively enhanced in hypertension. Furthermore, the renal vasoconstriction persisted for longer after the stress in the hypertensives. These findings support the hypothesis that the protracted sodium and potassium retention after isometric exercise could be due to excessive renal sympathetic nerve activity in hypertension.

The observed excessive salt retention following isometric exercise in the hypertensive patients may be a consequence of the hypertension or part of a pathogenetic mechanism relevant to the development of hypertension. In its early stages, essential hypertension has features suggesting autonomic nervous overactivity which may influence renal vascular resistance, but other etiological factors, such as dietary sodium, may also play a role. With more marked hypertension, the autonomic element diminishes\(^\text{25}\) but renal vascular resistance rises.\(^\text{31}\) Normal kidneys exposed to increased arterial pressure become abnormal and able to maintain the hypertension when its original cause is removed.\(^\text{32}\) Thus, the renal vasoconstriction following mental stress\(^\text{5}\) and the relative increase in sodium and potassium excretion following isometric exercise seen in the present study may be the
result of hypertension. If this were true, one would expect to find some relationship between electrolyte excretion response to exercise stress and the level of BP or duration of hypertension. The BPs of the patients we studied were in a narrow range (diastolic BP, >90 and <110 mm Hg), and therefore it is not surprising that no significant correlation was observed between the electrolyte excretion response and level of BP. It is also possible that the abnormal electrolyte excretion response to exercise stress is due to some change in the kidney, which is not itself correlated with the level of BP, and then no correlation would be observed between the electrolyte excretion response and the level of BP. It is impossible to assess the duration of hypertension in newly diagnosed hypertensive patients, but patient's age may be related to the duration of hypertension. However, we did not obtain a significant correlation between the electrolyte excretion response and age, perhaps because the subjects were too diverse in sex and race, and the duration of hypertension was unrelated to age.

Protracted sodium retention following stress could augment hypertensive processes. On the other hand, the abnormality of electrolyte excretion uncovered in this study could be relevant to the development of hypertension, as has been demonstrated in the SHR. Part 2 of our report, which follows, summarizes the results of similar studies in young normotensive subjects with a genetic predisposition to hypertension, in an endeavor to solve this problem.

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