Effect of Weight-Reducing Diet on the Blood Pressure of Spontaneously Hypertensive Rats (41223)

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Abstract. Spontaneously hypertensive rats were placed on weight-reducing diets either by limiting regular feedings to twice weekly or by providing half the normal ration daily. Significant reductions in body weight and blood pressure were observed at 2, 4, and 6 weeks after beginning the diet. Blood pressure fell despite maintenance of a normal or elevated sodium intake indicating that the reduction was not secondary to decreased sodium intake. Reinstitution of a normal food intake resulted in a return of body weight and blood pressure within 3 weeks.

A fall in blood pressure usually accompanies a reduction in body weight. This observation has been documented in obese patients on weight-reducing diets (1, 2) and from populations enduring severe caloric restriction such as during the siege of Leningrad in World War II (3). Although a relationship between reduced food intake and lowering of blood pressure is generally accepted, a controversy exists as to whether it is secondary to a reduction in calories or in sodium (4, 5). The present study was designed to examine the effect of weight reduction on the blood pressure of the Kyoto strain of spontaneously hypertensive rat (SHR). To our knowledge there have been no previous studies of the effects of weight reduction on the hypertension of the SHR. In the present investigation, salt intake was maintained at or above control levels during the period of caloric restriction.

Methods. Both male and female 4- to 5-month-old SHR were included. The diet of the rats consisted of a commercial feed (Wayne Lab-Blox) which contained 14.5% protein and 4.1% fat. The normal average daily consumption of this diet was approximately 21 g in males and 14 g in females. At the beginning of the experimental period, body weight averaged 325 g in the males and 195 g in the females. At the beginning of the experimental period, body weight averaged 325 g in the males and 195 g in the females.

The animals were randomly assigned to one of four regimens as follows: Group I, a control group which received the usual ration of Lab-Blox as was given to Group I but it was fed only twice weekly. Group II animals also received 0.4% NaCl in the drinking water when food was withheld. Group III received the same ration of food as Group II but they continued to drink tap water. Group IV received half the normal food ration daily and 0.2% NaCl solution in place of drinking water. The NaCl solutions used in Groups II and IV were more than sufficient to maintain sodium intake at or above control levels.

The reason for adding NaCl to the drinking water was to replace the reduction in sodium intake that resulted from the restricted diets. Animals on unrestricted intake of Lab-Blox have an average sodium intake of 82 mg per day in males and 55 mg in females. The average water intake was about 50 ml per day in males and 40 ml in females. Therefore, the approximate daily sodium intake in Group II animals who were given 0.4% salt solution to drink was 82 mg in males and 66 mg in females. The Group IV animals received approximately half this amount in their drinking water which was calculated to replace the sodium reduction in their diet.

The first three groups each consisted of eight males and five females while Group IV comprised four male rats. Blood pressure was determined by the tail plethysmographic technique; weights were taken when the diet was begun and at 2 and 4 weeks after its initiation. Following the fourth week Groups II and III were re-
turned to normal daily feedings plus tap water. When the rats attained weights similar to those of the control animals their blood pressures were again determined. Group IV was allowed to continue on their diet regimen for a period of 6 weeks in order to observe the effect of a more prolonged but less restrictive diet on blood pressure.

Results. There was a considerable loss of weight in both male and female rats in Groups II and III after 2 weeks of reduced food intake (Table I). The males continued to lose weight throughout the period of food restriction reaching an average level which was 31% below control weight by the fourth week. Female rats on the other hand stabilized their weight after the second week of food reduction.

The blood pressure of the male rats in Groups II and III fell significantly, averaging 16% below that of the control rats after 4 weeks of food restriction (Table I). The range of blood pressure in the male control rats was 166–227 mm Hg prior to the experiment and rose to 178–245 after 4 weeks. The method of statistical analysis used was the unpaired two-tailed t test. The P values given in the table are based on the absolute values. The blood pressure of the female rats in Groups II and III averaged only slightly lower than that of the control rats and the difference was considerably less than in the males and was significant only at 2 weeks after beginning the diet.

The correlation coefficient between change in body weight and change in blood pressure was determined using all of the experimental groups plus the controls. At 2 weeks there was a significant correlation (P < 0.001) between these two variables with r = 0.69. After 4 weeks the correlation was still significant (P < 0.001) and r = 0.62. However, the correlation coefficient was not significant between change in body weight and change in blood pressure when the analysis was done within each experimental group.

The reduced feedings were terminated after 4 weeks at which time Group II and III animals were given food and tap water ad libitum. With refeeding, the body weights and blood pressures increased rapidly and

### Table I: Effect of Weight Reduction on Blood Pressure of Spontaneously Hypertensive Rats

<table>
<thead>
<tr>
<th>Group</th>
<th>2 weeks</th>
<th>4 weeks</th>
<th>Percentage change body weight</th>
<th>Refeeding, 3 weeks</th>
<th>Percentage change blood pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>208 ± 22.9</td>
<td>+5.0</td>
<td>+7.5</td>
<td>108 ± 18.3</td>
<td>+8.5</td>
</tr>
<tr>
<td></td>
<td>118 ± 24.4</td>
<td>-32.0</td>
<td>-20.0**</td>
<td>89 ± 10</td>
<td>+6.6</td>
</tr>
<tr>
<td>Female</td>
<td>204 ± 24.7</td>
<td>-19.9**</td>
<td>-30.9**</td>
<td>157 ± 15.9</td>
<td>+6.2</td>
</tr>
</tbody>
</table>

*Mean grams ± SD.

**P < 0.05

***P < 0.001
WEIGHT LOSS AND BLOOD PRESSURE IN RATS

after 3 weeks reached levels insignificantly
different from those of the control animals
(Table I).

The male rats in Group IV who were
placed on a diet less restricted in calories
than Groups II and III exhibited a more
gradual fall of body weight than the latter.
The reduction averaged 13.2% after 4
weeks. Blood pressure fell 8.5%, which
nearly approached the level of the Group II
and III rats after 4 weeks. A further reduc-
tion in both body weight and blood pressure
was observed after 6 weeks when there was
an average fall of 12.1% in the rats receiving
the diet (Table I). During the same 6-week
period blood pressure in the control animals
rose by an average of 7.8%.

Discussion. The present study indicates
that the elevated blood pressure of the male
SHR is reduced when the animal loses
weight. A relationship between body
weight and blood pressure was further
shown by the prompt return of elevated
blood pressure when the fasted animals
were permitted an unrestricted diet; the rise
in blood pressure paralleled the increase in
body weight. The elevated blood pressure
of the male SHR showed a significant re-
duction during the first 2 weeks after the
animal loses weight. Beyond 2 weeks, how-
ever, and despite further loss of weight
there was no further significant reduction of
blood pressure. The reason for the lack of
continued blood pressure reduction after
the initial 2 weeks was not evident. How-
ever, it was not due to a change in the com-
position or type of food since only the
quantity was altered as compared to the
control. A more likely possibility is that the
relationship between body weight and
blood pressure is not linear over the entire
range of body weight changes but rather
they are related only with regard to moder-
ate reduction. This suggests that there may
be a minimal level of body weight below
which further reductions in weight no
longer are associated with additional falls in
blood pressure.

There have been very few prior studies of
the effects of weight reduction on hyperten-
sion in experimental animals. The only re-
port we found was a study published in 1939
by Wood and Cash (2). These investigators
reported a significant increase in body
weight and blood pressure in both normal
and renal hypertensive dogs fed a high fat
diet.

The relationship between body weight
and blood pressure in man, however, has
been recognized for many years. As early
as 1925, for example, it was found in life
insurance applicants that elevated blood
pressure was five times more frequent in
overweight persons than in the applicants
whose weight was normal (6). Brozek et al.
investigated the effects of a semistarvation
diet in normal volunteers. A 24% reduc-
tion in body weight was associated with a de-
cline of 10.6% in systolic blood pressure
(3). The relative magnitudes of these
changes are similar to those we found in the
SHR. More recently, Reisen et al. (7) found
in overweight patients with mild uncompli-
cated essential hypertension that a diet
which induced an average weight loss of
10.5 kg was associated with a return to
normotension in 75% of the patients.

There was a considerable difference in
this study on the effects of the diet in the
two sexes. Females showed weight loss
comparable to that of the males but much
less reduction of blood pressure. Also, in
contrast with the males the females showed
little or no rise of blood pressure on re-
feeding. The reason for the resistance of the
female rat's blood pressure to change in the
presence of dietary restriction is not appar-
ent. In the human the female seems equally
responsive to weight reduction as the male
(7). In a controlled trial Fletcher found a
highly significant reduction in blood pres-
sure in obese women following weight re-
duction (8). The significance of the differ-
ence remained after correcting for changes
in arm girth.

The mechanism for the fall in blood pres-
sure which accompanies weight reduction
is not clear. On the basis of dietary experi-
ments in a small number of hospitalized
hypertensive patients Dahl concluded that
the antihypertensive effect of food restric-
tion was due to reduced salt intake rather
than to lowered calories (4). Reisen et al.
(7), on the other hand, maintained a high
salt intake with his weight reducing diet and still obtained significant reductions of blood pressure. The present studies in the SHR also indicate that the antihypertensive effect of weight-reducing diets cannot be ascribed to a lowered salt intake since the antihypertensive effect was not prevented by administering excess salt in the drinking water. While it is possible that the lowered salt intake associated with food restriction may have contributed in part to the antihypertensive effect of the diet it did not appear to be the major contributor. Watkin and his associates (9) found in humans that the degree of sodium restriction in the diet must be reduced to 400 mg/day or to one-tenth of the usual daily intake in order to obtain a significant antihypertensive effect. This degree of sodium restriction did not occur in the present study and may explain why the blood pressure falls were similar on the salt-supplemented and non-salt-supplemented rats on caloric-restricted diets.

Other possible mechanisms have been proposed. The release of catecholamines is suppressed during fasting in rats (10) suggesting that the fall in blood pressure may be due to reduced catecholamines. However, no work has been done to determine the importance of this change in catecholamines on the reduction of blood pressure that accompanies reduced food intake. Additional hypotheses that have been advanced to explain the association between obesity and hypertension include increase in blood volume and cardiac output (11) and abnormalities of adrenal steroid secretion (12). The SHR should provide a useful model for studying these and other possible mechanisms that might relate alterations in body weight with changes in blood pressure.
