Hypertension and Exercise

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SUMMARY In such a prevalent disease as hypertension, it is particularly important to examine preventive and therapeutic alternatives as changes in life-style. Repeated physical exercise (physical training) has been shown to cause blood pressure to fall in normotensives and mild hypertensives, whether obese or not. This is followed by other hemodynamic changes characteristic of reduced sympathetic nervous system activity, which can also be found in metabolic and endocrine variables. In addition, there is evidence for an increased adrenergic sensitivity after physical training in circulatory, endocrine, and metabolic variables. In lipolysis regulation, the exact adaptation is located at the GTP-binding protein level between the adrenergic receptor and the cyclase. It is indicative that physical training causes an adaptation in the central sympathetic nervous system and, secondarily, an increased sensitivity of the periphery. This might possibly explain the decreased blood pressure caused by physical training, particularly in mild hypertension where symptoms of increased sympathetic nervous system activity have been observed. (Hypertension 4 (supp III): 111-56—111-59, 1982)

KEY WORDS • hypertension • sympathetic nervous system • peripheral resistance • obesity • insulin • glucose

THE prevalence of hypertension is, of course, dependent on the definition of the condition. It has been reported in 10% of the middle-aged population. In addition, it is not at all certain that the majority of vascular complications of hypertension are derived from this extreme part of the gaussian blood pressure distribution in the population. They may well come from, for example, the next 25% of the distribution curve in susceptible persons. To try to prevent vascular catastrophes by drug treatment, one then would face a situation in which perhaps 25% of the population has to be treated. Obviously, this is not desirable. In this situation, changes in life-style are clearly a better alternative, if feasible.

Prevention and treatment of hypertension by salt restriction have been suggested and debated, and energy intake restriction has recently attracted renewed attention. In this report, some aspects of prevention and treatment of early essential hypertension with regular physical exercise (physical training) are reviewed in both nonobese and obese subjects.

Physical Training and Blood Pressure

Nonobese Subjects

The effects of physical training on blood pressure in normotensive or slightly hypertensive subjects have previously been examined, as a rule, in fairly small samples. It seems reasonable to conclude that a blood-pressure-lowering effect has been obtained in these studies, in normotensive subjects or where an early type of hypertensive disease has been present, without signs of vascular disease. The blood pressure decrease was associated with a decrease in heart rate and cardiac output, while peripheral resistance was found to be unchanged. It is logical that physical training has been found to be effective specifically in hypertensives, where cardiac output and heart rate are elevated, while in hypertensives with increased peripheral resistance, the effect is less clear.

An early phase of essential hypertension, in which increases in blood pressure are associated with elevated heart rate and cardiac output, has been suggested to be due to an increased activity in the sympathetic nervous system (SNS). Consequently, disappearance of these phenomena after physical training might be due to a modification within SNS causing less stimulation at the effector sites of SNS in the periphery.

Obese Subjects

It should be noted that, in the previously reviewed works, the presence of moderate or slight obesity has not always been clearly defined. Information on the effects of clearly obese populations is, however, available, and shows a decrease in blood pressure as well. Hemodynamic variables have not been followed in detail, but heart rate was decreased at rest and during submaximal work, in agreement with previously reviewed work. Instead, body composition and metabolic variables were followed in some detail, and
changes analyzed in relation to changes in blood pressure (table 1). When the patient data were divided along the median of blood pressure decrease after physical training, it was found that these groups did not have different blood pressures from the start. Body fat tended to decrease during training in the group with the least blood pressure decrease, whereas in the half of the data where the blood pressure decrease was substantial, body fat did not change. The lower blood pressure, thus, was not simply due to the fact that obesity was diminished by physical training; instead, blood pressure decreases seemed to follow metabolic variables such as plasma insulin, blood glucose, and plasma triglycerides (table 2). It was not possible to clearly separate out one of these factors as more important than the other in multivariate regression analyses. It might be hypothesized, therefore, that plasma insulin is the primary factor here because plasma insulin, like blood pressure, fell, on the average, which was not the case with blood glucose. In addition, plasma triglyceride concentration is dependent on insulin concentration through known mechanisms, while the reverse is more difficult to understand.

The adaptations in the SNS were not directly followed in this study. This has, however, been performed in several other studies designed in exactly the same manner with the same type of severely obese subjects. Urinary excretion of norepinephrine was elevated in the obese subjects, but did not change with physical training.9

In another study recently completed, an attempt was made to examine the sensitivity of various variables that are regulated by the SNS. This was performed by infusion of a submaximal dose of the β-adrenergic agonist isoproterenol before and after physical training of severely obese subjects (Krotkiewski et al: unpublished data, 1982) (table 3). After physical training, the previously described decreases in blood pressure, heart rate (not shown), and plasma insulin were found, without association to body composition changes. In addition, connecting (C)-peptide, glucagon and gastric inhibitory polypeptide (GIP) decreased. Responses to

### Table 1. Characteristics of Obese Subjects Divided into Two Groups after Median of Blood Pressure Decrease after Physical Training

<table>
<thead>
<tr>
<th></th>
<th>Half of patients with little or no decrease of blood pressure</th>
<th>Half of patients with more decrease in blood pressure</th>
<th>Difference between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure before training (at rest) (mm Hg)</td>
<td>137 ± 23</td>
<td>129 ± 8</td>
<td>ns</td>
</tr>
<tr>
<td>Diastolic blood pressure before training (at rest) (mm Hg)</td>
<td>87 ± 10</td>
<td>87 ± 6</td>
<td>ns</td>
</tr>
<tr>
<td>Decrease of systolic blood pressure with physical training (at rest) (mm Hg)</td>
<td>−1 ± 5</td>
<td>−17 ± 4†</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Decrease of diastolic blood pressure with physical training (at rest) (mm Hg)</td>
<td>−5 ± 5*</td>
<td>−12 ± 2†</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Decrease in body fat with physical training (kg)</td>
<td>−4.4 ± 4.6a</td>
<td>−1.7 ± 2.3</td>
<td>p &lt; 0.10 &gt; 0.05</td>
</tr>
</tbody>
</table>

Significance of decrease: *p < 0.10 > 0.05; †p < 0.05.
ns = not significant.
Values are means ± SD (from Krotkiewski et al., see ref 7).

### Table 2. Stepwise Multiple Regression Analyses of Variables Explaining Blood Pressure Reduction in Obese Subjects after Physical Training (From Krotkiewski et al., 7)

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent variable</th>
<th>Multiple cumulative correlation coefficient</th>
<th>Explained cumulative variance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease in systolic blood pressure during work test (at 100 W)</td>
<td>Plasma triglyceride</td>
<td>0.66</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>+ plasma insulin</td>
<td>0.68</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>+ blood glucose</td>
<td>0.73</td>
<td>54</td>
</tr>
<tr>
<td>Decrease in diastolic blood pressure during work test (at 100 W)</td>
<td>Plasma triglyceride</td>
<td>0.61</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>+ blood glucose</td>
<td>0.69</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>+ plasma insulin</td>
<td>0.72</td>
<td>52</td>
</tr>
</tbody>
</table>

From Krotkiewski et al., see ref 7.
the \(\beta\)-agonist were increased after physical training in a number of variables sensitive to \(\beta\)-adrenergic stimulation. These included blood pressure, heart rate (not shown), as well as insulin, connecting (C-)peptide, and pancreatic polypeptide (PP) concentrations. These results suggested that the \(\beta\)-adrenergic part of the SNS had been sensitized by physical training.

**Adaptations of the Adrenergic Nervous System at the Cellular Level**

Results of other studies have indicated how this might be brought about at the cellular level. Glycerol release from adipocytes was more sensitive to stimulation by catecholamines after physical training,\(^{10, 11}\) and this release can be used as an index of the activity of the catecholamine-sensitive lipase in these cells. Therefore, this was another indication of increased catecholamine sensitivity, which was analyzed in a strict dose-response manner. In addition, it was possible to analyze in more detail what kind of adaptation had taken place in the complex chain of events between the actual hormone stimulus of the receptor and the resulting outflow of the lipolytic product, free glycerol. There was no indication of a change in adrenergic receptor affinity or number; however, the sensitivity of the cyclase was increased. This indicates an action of physical training on the peripheral adrenergic effector cell at the level of the GTP-binding protein level, at least in this system.\(^{12}\)

**Summary of the Adaptation of the Sympathetic Nervous System after Physical Training**

Several of the studies reviewed, in nonobese and obese populations, and in normotensive and slightly hypertensive subjects, indicate that certain SNS-dependent variables are lower at rest after physical training. Furthermore, during identical submaximal workloads, SNS-dependent variables show less response. This is probably due to the fact that, after physical training, a given absolute submaximal workload is performed with less SNS activity, as indicated by measurements of circulating catecholamines.\(^{13}\) Taken together, this may mean that there is now less activity in the SNS both at rest and after certain stimuli to SNS activation, such as exercise. This in turn might be caused by adaptations in the central regulation of SNS activity with less SNS firing. As a consequence, the periphery would become more sensitive to a given amount of adrenergic transmitter after physical training, and this has indeed been observed in several circulatory, endocrine, and metabolic systems that are dependent on SNS stimulation. The nature of such adaptations of the central SNS is at present unknown.

It is of interest, in this connection, to briefly look into a parallel situation with dietary treatment of mild hypertension in obese subjects. Jung et al.\(^{14}\) (as well as Fagerberg et al; submitted for publication, 1982), in a nonrestricted population, have shown that a decreased carbohydrate intake produces a lowering of blood pres-
sure in parallel with a decrease in catecholamine excretion. In this situation, in agreement with the events after physical training, adaptation to a decreased activity in the SNS seems to have occurred.

Role of Insulin

In both the physical training studies and in the dietary treatment studies, plasma insulin concentrations were decreased in parallel with blood pressure. The question arises, however, as to how the insulin might be integrated into the picture. Insulin has been shown to be able to facilitate sodium reabsorption in the distal tubuli of the kidney. It seems possible, therefore, that the effects of physical training on blood pressure might be mediated via a decrease in sodium retention, when insulin concentrations are lowered. This alternative is unlikely in the dietary experiments, however, because here it has been certified that sodium excretion has not been changed. Insulin could, however, also be involved in the adaptations occurring in the SNS, reviewed above. Insulin and carbohydrate metabolism are associated with an increase in catecholamine turnover in SNS synapses. Therefore, a decrease in insulin levels caused by training or diet would consequently decrease SNS activity at this level.

As a final consideration, it is necessary to realize the importance of the association between hypertension and obesity. This has long been known and is stressed by recent epidemiological studies. For example, Berglund et al. (Berglund et al; unpublished data, 1982) examined hypertensive subjects in a free-living, non-selected population. These subjects were frequently obese with enlarged fat cells and had hyperinsulinemia, as well as a decreased glucose tolerance. The type of obesity seems important here. Obese men have more complications from obesity than women, including hypertension. Looking at the sexes separately, one finds that the complications mentioned are associated with abdominal obesity, probably explaining why obese men, typically having more abdominal fat, are sicker than obese women. Circumference measurements in the abdominal region are strongly associated with complications, and, therefore, it is possible that visceral fat is of particular importance for obesity complications, including hypertension (Krotkiewski et al; unpublished data, 1982).

References

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