The aim of our study was to check the responsiveness the chemoreceptor reflex in 28 young mildly hypertensive men (HTS), aged 18-32 years and 25 normotensive male subjects (NTS) aged 19-32 years, before and after 3-months dynamic exercise training. We tested the hypothesis that dynamic training reduces arterial chemoreceptor drive in mild hypertension. Circulatory response to 3-min hyperoxic inactivation of arterial chemoreceptors induced by 70% oxygen breathing was measured before and after training. Arterial blood pressure (BP) was recorded continuously by Finapres method, stroke volume and arm blood flow were registered by impedance reography, heart rate by ECG. Both groups were submitted to moderate 3-months dynamic exercise training. Before training the hyperoxic breathing caused in HTS a significant decrease in systolic BP by 6±1mmHg p<0.01, in diastolic BP by 2±0.6mmHg p<0.01, and in total peripheral vascular resistance (TPR) by 0.24±0.04 TPRU (p<0.01). After training hyperoxia augmented systolic BP by 2.64±1.9mmHg (NS), diastolic BP by 2±1mmHg p<0.05, and TPR by 0.043±0.05 TPRU (ANOVA). In NTS before training brief hyperoxia produced insignificant change in BP and TPR. In NTS after training hyperoxia increased systolic BP by 4.2 mm Hg±1.23 p<0.01 and diastolic BP by 3.1±0.6mmHg p<0.01 respectively and TPR by 0.053±0.02 TPRU. Our results confirm earlier finding on the enhanced arterial chemoreceptor reflex drive in mild human hypertension. We conclude that normalizing arterial blood pressure in subjects with mild hypertension which occurred after 3-months dynamical exercise training is due to attenuation of the sympathoexcitatory chemoreceptor reflex drive by exercise training. The mechanism of this effect requires further study.

Key words: hypertension, chemoreceptor reflex, hyperoxia, hemodynamics, exercise training
INTRODUCTION

Moderate exercise training is a known physiological procedure reducing and preventing arterial hypertension (1 - 4). It seems therefore interesting to observe if moderate prolonged physical exercise training affects sympathoexcitatory arterial chemoreceptor reflex in young mild hypertensive subjects. We have reported augmented drive from arterial chemoreceptors in mild hypertension (5 - 9). In our previous study we observed, that blood pressure is reduced and sympathoexcitatory chemoreceptor reflex attenuated after single physical exercise during long postexercise period (9). We observed also in hypertensive subjects after exercise training a reduction of the power of the low frequency (LF) component of systolic blood pressure oscillation, a marker of sympathetic activation (10). The aim of the present study was to measure the cardiovascular response to brief hyperoxic inactivation of the sympatho-excitatory chemoreceptor reflex in the healthy and in the hypertensive subjects and to check again the reflex responsiveness in both groups after 3-month moderate dynamical exercise training.

SUBJECTS AND METHODS

The study was approved by the Medical University of Warsaw Ethic's Committee on Human Research.

Research material

Each subject gave written consent to participate in the study. 28 young male mildly hypertensive patients (HTS) aged 23±0.9 years, (18-32) and 25 matched normotensive men (NTS) 22.6±0.3 years (19-32) were studied. The systolic blood pressure (SBP) was: 147± 3.5 mmHg and 126 ± 4.5 mmHg; diastolic blood pressure (DBP): 89 ± 2 mmHg and 72 ± 3 mmHg in HTS and NTS, respectively, (p < 0.05). Resting respiratory rate was: 15 ± 0.6 breaths/min and 14 ± 0.7 breaths/min, (p > 0.05) in HTS and NTS respectively. Only male subjects participated in our study to avoid any effects of menstrual cycle on the measurements being studied. All subjects were clinically examinated and found were free of pulmonary, renal, heart diseases and any cause of secondary hypertension excluded. The patients were untreated or pharmacological medication was discontinued for at least two weeks before the start of the study. Experimental procedure was reported in detail before (10).

Training

All subjects undergo 3-month physical training, consisted in dynamic aerobic exercise at a level of 40-50% of VO2max. The VO2max and the value of heart rate calculated for each individual for 40-50% VO2max was determined by submaximal Astrand's test on electrical cycloergometer in Laboratory of Physical Fitness. The subjects exercised 1 hour 3 times per week. The kind of exercise depended on subjects favored dynamic activity: cycling, swimming, running, brisk walking.

Measurements

The chemoreceptor reflex was tested by short lasting breathing a mixture 70% oxygen in air from a 200 liters Douglas bag for a 3-min period with low-resistant, two-way, non-rebreathing and very low dead space valve (Hans Rudolph). Respiratory rate was calculated from chest impedance traces. Heart rate was measured continuously by ECG. Stroke volume and arm blood flow were estimated by tetrapolar impedance reography, and arterial blood pressure recorded by Finapres.
method (Ohmeda model 2300). The all variables were registered on four channels of the multichannel computer data acquisition system and stored on the disc for subsequent analysis. All subjects were tested in the sitting position before and after training.

**Analyses**

The first derivative of the impedance change was used to calculate stroke volume, cardiac output and arm blood flow using Kubicek equation (11). Total peripheral vascular resistance (TPR) was calculated in TPR units (TPRU) from the ratio of mean arterial blood pressure to impedance derived cardiac output. Arm vascular resistance (MVR) was calculated per 100 ml tissue/min in PRU units. The average values of the vascular resistance were calculated over complete respiratory cycles.

**Statistical methods**

Data were assessed for normal distribution by computation of standardized skeweness and standardized kurtosis. Comparisons between the pre-training and post-training effects of hyperoxia in the both groups by two-way, repeated measurements ANOVA and Neuman-Keuls multiple comparison procedure. Comparisons between NTS and HTS were made by one-way analysis of variance. Data are presented as means ± SE.

**RESULTS**

The effect of exercise training on resting SBP, DBP, TPR, respiratory rate and BMI index are presented in Table 1.

<table>
<thead>
<tr>
<th></th>
<th>HTS</th>
<th>NTS</th>
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<tbody>
<tr>
<td><strong>SBP [mmHg]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>before training</td>
<td>147.0 ± 3</td>
<td>126.0 ± 4 *</td>
</tr>
<tr>
<td>after training</td>
<td>128.0 ± 2</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>120.0 ± 3</td>
<td>p &gt; 0.05</td>
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<tr>
<td><strong>DBP [mmHg]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>before training</td>
<td>89.0 ± 2</td>
<td>72.0 ± 3 *</td>
</tr>
<tr>
<td>after training</td>
<td>77.0 ± 1</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>68.0 ± 1</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td><strong>TPR [TPRU]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>before training</td>
<td>1.4 ± 0.11</td>
<td>1.05 ± 0.09 *</td>
</tr>
<tr>
<td>after training</td>
<td>1.0 ± 0.07</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>0.91 ± 0.07</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td><strong>BMI [kg/m^2]</strong></td>
<td></td>
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<tr>
<td>before training</td>
<td>26 ± 0.8</td>
<td>24.6 ± 0.5</td>
</tr>
<tr>
<td>after training</td>
<td>25.7 ± 0.8</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>24.2 ± 0.5</td>
<td>p &lt; 0.05</td>
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<tr>
<td><strong>Res.rate[breath/min]</strong></td>
<td></td>
<td></td>
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<tr>
<td>before training</td>
<td>15.8 ± 0.6</td>
<td>14.7 ± 2.7</td>
</tr>
<tr>
<td>after training</td>
<td>15.2 ± 0.5</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td></td>
<td>14.6 ± 0.7</td>
<td>p &gt; 0.05</td>
</tr>
</tbody>
</table>

* - p < 0.05 in respect to differences between groups, Res.rate - respiratory rate p - significance level in respect to changes within groups
Respiratory rate response to brief hyperoxia in normotensive and hypertensive subjects

In normotensive subjects, the decrease in respiratory rate was 16±2.2% in pre-training and 9.7±1.6% in post-training period (Fig. 1). In the hypertensives - decrease in respiratory rate was 25 ± 1.8% before training, significantly greater than in normotensives (p < 0.01), (Fig. 1). After exercise training no significant difference in the respiratory rate response to hyperoxia was observed between hypertensive and normotensive subjects (p > 0.05), (Fig. 1).

Cardiovascular response to brief hyperoxia in normotensives and hypertensive subjects

In untrained normotensive subjects brief oxygen breathing produced insignificant change in BP (Fig. 2), whereas after exercise training hyperoxia
increased systolic blood pressure by 4.2 ± 1.2 mmHg (p < 0.05), diastolic blood pressure by 3.1 ± 0.6 mmHg, (p < 0.05), (Fig. 2). In untrained hypertensive subjects hyperoxic breathing produced a significant decrease in SBP and DBP,
and after training only slight pressure increase was observed (Fig. 3 - 5). The onset of the hyperoxic blood pressure decrease in hypertensive subjects was observed about 30-40 sec since the beginning of O2 breathing and reached the minimum value after about 60-90 sec.

A significant reduction of TPR during hyperoxia was observed only in untrained hypertensive subjects. The response of TPR is presented in Fig 6.
DISCUSSION

Our results confirm earlier finding suggesting enhanced arterial chemoreceptor drive in mild human hypertension (5 - 9). Inactivation of arterial chemoreceptors by brief hyperoxia resulted in significant decrease in blood pressure and peripheral TPR fall in mildly hypertensive subjects. The observed decrease in respiratory rate in parallel with the decrease in blood pressure during transient hyperoxia is evidently due to inactivation of arterial chemoreceptor activity. It appears as an early disfacilitatory respiratory component (12 -15) related to withdrawal of the peripheral chemoreceptor reflex drive as opposed to later hyperoxic hyperventilation of central origin, due mainly to augmented tidal volume (16). After 3-month moderate exercise training the hypotensive and TPR response to systemic hyperoxia disappeared in mildly hypertensive subjects. Decrease in the respiratory rate induced by brief hyperoxia in trained hypertensive patients was not significantly different from that of healthy subjects suggesting attenuation and normalization of the augmented chemoreceptor reflex activity in hypertensives induced by exercise training. This is the novel finding of our study. It is known that resting ventilatory response to hypoxia is reduced in healthy endurance training subjects (17 - 19). Presumably a decrease in the systolic blood pressure and ventilatory response to isocapnic hypoxia observed in healthy subjects at sea level after endurance training is due to attenuation of the reflex drive the from the carotid body chemoreceptors (17).

To our knowledge, this is the first study in mildly hypertensive patients to evaluate the effects of moderate exercise training on hemodynamic and respiratory response to transient hyperoxic deactivation of the arterial chemoreceptors. The mechanism by which exercise training attenuates the
hemodynamic and respiratory response to brief hyperoxia in hypertensive patients along with the normalization of the blood pressure requires a further study. Possible factors contributing to positive effect of physical exercise normalizing blood pressure in hypertension may include a decrease in the arterial chemoreceptor activity. The effect may be due to increased NO endothelial production reported after physical training (20 - 22). Endogenous nitric oxide inhibits carotid glomus cells and attenuates carotid chemoreceptor activity since inhibition of nitric oxide synthase augments significantly the responsiveness of the arterial chemoreceptors to systemic hypoxia (23, 24). Moderate intensity exercise training due to increased blood stream linear velocity and repeated mechanical shear stress imposed on endothelium improves bioavailability of NO not only in the active muscle group vessels, but also in the systemic circulation (21, 25). Another mechanism of chemoreceptors inhibition may be associated with NO related increase in activity of the efferent inhibitory fibers of the glossopharyngeal nerve supplying carotid bodies, an effect resulting in inhibition of the carotid chemoreceptor discharge (26). Finally, a supposed shift in the interactive functional balance between arterial baro- and chemoreceptor reflexes towards prevalence of the baroreceptor reflex should be also considered (27, 28), since exercise training facilitates cardiac and arterial baroreflex antagonistic to chemoreceptor reflex (29, 30).

In summary our study is in agreement with many findings (e.g. 1 - 4, 9, 20 - 22, 25) on beneficial effect of the moderate exercise training for the blood pressure control in hypertension. We propose that attenuation of the sympathoexcitatory and pressor chemoreceptor reflex contributes to the positive effect of regular exercise in mild human hypertension.

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