Metabolic and body temperature changes during exercise in hyperthyroid patients

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Summary

1. Body temperature, blood glucose, lactate, plasma free fatty acid and noradrenaline responses to exercise were studied in hyperthyroid patients during 30 min exercise on a bicycle ergometer at a work load producing a heart rate of approximately 135–140 beats/min. The results were compared with those obtained in healthy subjects exercising at work loads comparable in terms of oxygen uptake.

2. External auditory canal temperature at rest was 0.5°C higher in hyperthyroid patients than in control subjects but the exercise-induced increases in body temperature were similar in both groups.

3. Pre-exercise blood glucose concentration was higher in the thyrotoxic patients than in normal subjects. During exercise blood glucose decreased markedly in the patients whereas in the control subjects the exercise-induced changes in blood glucose were insignificant.

4. There was no difference between the groups in the pre-exercise blood lactate and plasma free fatty acid concentrations. Significantly greater increases in blood lactate and plasma free fatty acids were found during exercise in hyperthyroid patients than in the control subjects.

5. Resting plasma noradrenaline concentration in the hyperthyroid patients did not differ from that found in normal subjects, but the exercise-induced increases in plasma noradrenaline were greater in the patients than in the control group.

6. On the basis of heart rate, as well as of body temperature and blood lactate differences between the hyperthyroid patients and healthy control subjects, it appears that the patients exercising at similar oxygen uptake as normal subjects were under greater physiological strain.

Key words: body temperature, exercise, hyperthyroidism, noradrenaline.

Introduction

Thyroid hyperfunction is known to impair physical working ability, severe limitation of physical performance being attributable to the thyrotoxic myopathy (Kissel, Hartemann & Duc, 1965). There are relatively few studies of haemodynamic, respiratory and metabolic adaptation to exercise in hyperthyroid patients; Massey, Becklake, McKenzie & Bates (1967) demonstrated that in thyrotoxic patients oxygen consumption at a given work load is greater than in euthyroid subjects, but the increment of oxygen uptake with increasing work load is similar to that found in normal subjects. Respiratory role, pulmonary ventilation, heart rate and cardiac output during exercise were excessive in relation to the oxygen uptake (Bishop, Donald & Wade, 1955; Stein, Kimbel & Johnson, 1961; Massey et al., 1967; Graettinger, Muenster, Silverstone & Campbell, 1959). In normal subjects treated with tri-iodothyronine the pulmonary ventilation and cardiac frequency responses to muscular work were increased but oxygen consumption during exercise did not differ from that before treatment (Massey et al., 1967).
Recent studies in dogs treated with thyroxine or tri-iodothyronine showed that thyroid hormones exerted a marked influence on body temperature and metabolism during prolonged muscular work (Kaciuba-Uścik, Greenleaf, Kozłowski, Brzezińska, Nazar & Ziembas, 1975b), and treatment of dogs with thyroid hormones considerably impairs their capacity for prolonged running (Kaciuba-Uściko & Brzezińska, 1974; Kaciuba-Uścik, Brzezińska & Pohoska, 1976). A significantly greater elevation of body temperature during exercise was found 5 h after an injection of thyroxine (Kaciuba-Uścik et al., 1975b). Both after single administration of thyroid hormones and after chronic treatment of dogs with thyroxine the exercise-induced increase in both plasma free fatty acids and blood lactate concentration was greater than before treatment (Kaciuba-Uścik, Brzezińska & Greenleaf, 1975a; Kaciuba-Uścik et al., 1976). In dogs treated with thyroxine for several days exercise also produced a greater fall in blood glucose concentration and a more rapid depletion of muscle glycogen (Kaciuba-Uścik et al., 1976).

Kaciuba-Uścik et al. (1976) quote studies suggesting that the thyroid hormone-induced hyperthermia and metabolic changes may account for the reduced work performance capacity, and it may be assumed that these factors also contribute to the impairment of exercise tolerance in hyperthyroid patients.

The aim of the present study was to investigate changes in body temperature and blood metabolites during exercise of moderate intensity performed by thyrotoxic patients.

Subjects and methods

We studied 13 patients with thyrotoxicosis of uncomplicated Graves' disease and three patients with a toxic thyroid adenoma, consisting of 12 females and four males. The patients were studied at the time of diagnosis before any treatment. The diagnosis was established by conventional clinical and laboratory methods. Six patients had myasthenic symptoms of varying severity. Patients with congestive heart failure or other diseases were excluded. The physical characteristics and some laboratory data of these patients are shown in Table 1.

The control group consisted of 11 healthy volunteer subjects (eight females and three males). None of the subjects was engaged in any kind of physical activity and their physical working capacity was low. The characteristics of the subjects are presented in Table 1.

Both the patients and control subjects reported to the laboratory after a light uncontrolled meal and rested sitting for about 45 min. They then performed 30 min exercise on a bicycle ergometer (Monark, Sweden). The hyperthyroid patients exercised at a work load giving a heart rate of approximately 135–140 beats/min, loads ranging from 12 to 49 W (75–300 kg/min). The control subjects performed exercise at the work loads of 25–49 W (150–300 kg/min), comparable with those used in the patients in terms of oxygen consumption ($\dot{V}_O_2$). Detailed results are given in Tables deposited as Clinical Science and Molecular Medicine Table 71/17 with the Librarian, the Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE, who will issue copies on request.

ECG was monitored throughout the exercise (chest loads) and arterial blood pressure was measured every 5 min of exercise.

Expired air was collected during 5 min before exercise, between minutes 15 and 17 of exercise and during the last 2 min of exercise, samples being analysed by a Scholander micro-technique. $\dot{V}_O_2$, respiratory quotient (R), oxygen extraction ratio [$EO_2 = 100(\dot{V}_O_2/\dot{V}_E)$%] and mechanical efficiency were calculated. In the patients exercising at a work

<table>
<thead>
<tr>
<th>Table 1. Physical characteristics and laboratory data in the hyperthyroid patients and healthy control subjects</th>
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<tbody>
<tr>
<td>Values are presented as mean ± 1 SD.</td>
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<tr>
<td>Group</td>
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<tr>
<td>Hyperthyroid patients (n = 16)</td>
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<tr>
<td>Control subjects (n = 11)</td>
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</table>
Exercise in hyperthyroid patients

load of 25 W or above mechanical efficiency was calculated according to the following formula:

\[
\text{Mechanical efficiency (\%)} = \frac{\text{Mechanical work performed (W) } \times 60}{\text{total} - \text{resting metabolic rate (J/min)}} \times 100
\]

Body temperature was measured in the external auditory canal (Greenleaf & Castle, 1972), the probe of a thermocouple thermometer (Ellab, Copenhagen) being placed 10–12 mm from the tympanic membrane. Pre-exercise temperature was recorded after 30–45 min rest. Venous blood samples for the plasma free fatty acid, noradrenaline and blood glucose determinations were taken before and immediately after exercise. Lactate concentration was determined in blood taken from a fingertip before exercise and in minute 30 of exercise.

Plasma free fatty acid concentration was determined by modification of the Dole & Meinertz method (Mosinger, 1965), plasma noradrenaline concentration by a spectrofluorimetric method (Anton & Sayre, 1962). Blood glucose was determined by a commercial glucose oxidase method (Fermognost, GDR), and blood lactate by the method of Barker & Summerson, as modified by Ström (1949).

Statistical analysis of the results was performed by t-test for paired data within the groups and for unpaired data between the groups. Unless specifically denoted values are given as mean ± 1 SD.

Results

In the hyperthyroid patients during exercise heart rates attained values of 135–140 beats/min (Table 2). Heart rate stabilized after 5–7 min of exercise and the steady-state value was maintained until the end of exercise; only in two patients was there a rise in heart rate in the last 10 min of exercise. Heart rates of healthy subjects both at rest and during exercise were significantly lower than in the patients (P < 0-01).

Both at rest and during exercise the systolic blood pressure (Table 2) was higher in the thyrotoxic patients than in the healthy control subjects (P < 0-02), whereas the differences in the diastolic blood pressures were insignificant (P > 0-05). The magnitude of blood pressure response to exercise was similar in both groups (P > 0-05).

Despite the significantly greater exercise work load in the control subjects (P < 0-01) than in patients, the differences in oxygen consumption during exercise between these two groups were not significant (P > 0-05). When the oxygen consumption (\(\dot{V}_O_2\)) was compared separately for males and females it appeared that in minute 30 of exercise \(\dot{V}_O_2\) in the hyperthyroid female patients was significantly greater (P < 0-05) than that obtained in the healthy females; the mean values of \(\dot{V}_O_2\) were 806 ± 117 ml/min and 683 ± 62 ml/min respectively. There were no significant differences between the groups in oxygen extraction ratio and respiratory quotient. The average values of estimated mechanical efficiency were lower in the hyperthyroid patients than in the healthy subjects, but the differences were not significant either for the total groups or for males and females calculated separately.

At rest the average temperature in the external auditory canal was higher in the thyrotoxic patients than in the healthy control subjects by 0-5°C (P < 0-01) (Fig. 1). The exercise-induced increases of body temperature in the hyperthyroid patients did not differ from those attained by the control

<table>
<thead>
<tr>
<th>Group</th>
<th>Heart rate (beats/min)</th>
<th>Blood pressure (mmHg)</th>
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<tr>
<td></td>
<td>0</td>
<td>15</td>
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<tr>
<td>Hyperthyroid patients</td>
<td></td>
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<tr>
<td>(n = 16)</td>
<td></td>
<td></td>
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<tr>
<td>0</td>
<td>112 ± 15 (72–132)</td>
<td>138 ± 7 (128–150)</td>
</tr>
<tr>
<td>15</td>
<td>131 ± 18 (105–165)</td>
<td>153 ± 20 (120–180)</td>
</tr>
<tr>
<td>30</td>
<td>65 ± 29 (60–90)</td>
<td>74 ± 25 (55–100)</td>
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<tr>
<td>Control subjects</td>
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<tr>
<td>(n = 11)</td>
<td></td>
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</tr>
<tr>
<td>0</td>
<td>77 ± 15 (64–108)</td>
<td>120 ± 17 (102–148)</td>
</tr>
<tr>
<td>15</td>
<td>115 ± 12 (90–125)</td>
<td>133 ± 10 (120–145)</td>
</tr>
<tr>
<td>30</td>
<td>75 ± 11 (50–95)</td>
<td>72 ± 10 (60–90)</td>
</tr>
</tbody>
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Table 2. Changes in heart rate and blood pressure during exercise in the hyperthyroid patients and control subjects

Results are shown as mean values ± 1 SD with the range in parentheses. Under ‘Blood pressure’ the upper rows of figures are systolic values and the lower rows are diastolic values.
FIG. 1. Exercise-induced changes in body temperature measured in the external auditory canal (mean ± SEM) in hyperthyroid patients (●) and control subjects (○), during 30 min of exercise.

euthyroid subjects (P > 0.05). The mean increases were 0.6 ± 0.07°C and 0.5 ± 0.08°C respectively.

The exercise-induced changes in blood lactate and glucose concentration as well as those in plasma free fatty acids and noradrenaline are presented in the deposited Tables referred to in the Subjects and methods section.

At rest blood glucose concentration was significantly higher in the thyrotoxic patients than in the healthy subjects (P < 0.01). During exercise glucose concentration decreased significantly in the patients (P < 0.01), whereas in the control subjects exercise did not produce any significant change in blood glucose concentration (P > 0.05). There was no difference between the groups in blood lactate concentration (P > 0.05) at rest, whereas during exercise the hyperthyroid patients attained significantly higher values of lactate concentrations than the healthy control subjects (P < 0.01). No statistically significant difference in the resting plasma concentration of free fatty acids was found between the patients and control subjects. In both groups concentration of the free fatty acids increased significantly during exercise (P < 0.01). The magnitude of the response was, however, significantly greater in hyperthyroid patients than in the control subjects (P < 0.01).

The pre-exercise plasma noradrenaline concentration did not differ between the groups (P > 0.05). The exercise-induced increases in the plasma noradrenaline concentration were significantly greater in the patients than in the control group (P < 0.01).

Discussion

The exercise-induced changes in heart rate and blood pressure in the hyperthyroid patients obtained in this study were similar to those previously observed during exercises of shorter (5–7 min) duration (Bishop et al., 1955; Graettinger et al., 1959; Massey et al., 1967). The noteworthy finding is that during 30 min exercise of moderate intensity the steady-state values of both variables were maintained in most patients.

Pulmonary ventilation during exercise in the hyperthyroid patients was within normal limits, when related to the oxygen consumption. Thus we have failed to demonstrate the excessive respiratory response which has been described previously in thyrotoxic patients (Massey et al., 1967; Stein et al., 1961; Bishop et al., 1955). In the present study, however, measurements were not performed before minute 15 of exercise, whereas in these previous studies the duration of the exercise was shorter. According to Massey et al. (1967) the abnormal increase in pulmonary ventilation in the thyrotoxic patients results mainly from the increased breathing frequency. It may, therefore, be that prolonged exercise at light work loads may cause adaptation of the respiratory pattern to oxygen consumption.

In most patients oxygen consumption per unit of work output was higher than in the control subjects. The mean value of the mechanical efficiency was somewhat lower for the hyperthyroid patients than for the control subjects but the difference did not reach statistical significance. It should be noted, however, that these calculations were performed only for the patients who exercised at the work load of 25 W, or above it. Furthermore, the higher lactate concentration in the hyperthyroid patients suggests that the difference in mechanical efficiency may be actually greater than that indicated by calculations because of a possible difference in oxygen debt.

The pre-exercise temperature in the external auditory canal was significantly higher in the thyrotoxic patients than in the healthy subjects, but the increase in body temperature induced by exercise did not differ between these groups. This pattern of the response in the patients may reflect resetting of the body thermoregulatory mechanism (set-point shift) with no change in the sensitivity of the regulatory system.

The exercise-induced increases in plasma free fatty acid and blood lactate concentrations were greater in the hyperthyroid patients than those in the control subjects. Kaciuba-Uscilko et al. (1975a) and Kaciuba-Uścilk & Brzezińska (1976) showed that in dogs treated with thyroid hormones both the excessive plasma free fatty acids and blood lactate responses to exercise could be abolished by the blockade of β-adrenergic receptors. An interplay of thyroid hormones and catecholamines should be therefore considered as a
Elevated lipolytic response and increased lactate production during exercise in hyperthyroidism. The relatively important mechanism responsible for the elevated lipolytic response and increased lactate production during exercise in hyperthyroidism. The augmented lactate production may be a factor contributing to the development of muscle fatigue and thus limiting working ability of hyperthyroid patients.

During exercise the blood glucose fell considerably in most patients, whereas in most control subjects there was a slight rise in glucose concentration. In two patients blood glucose concentration fell below 3 mmol/l during exercise. Hypoglycaemia should be considered as one of the factors limiting exercise performance in these hyperthyroid patients. The fall in blood glucose concentration during exercise in the patients may be in part related to their higher pre-exercise glucose value. However, there was no relationship between the magnitude of response to exercise and the pre-exercise glucose concentration.

Christensen (1973) demonstrated that the basal concentration of plasma noradrenaline is lower in hyperthyroid patients than in healthy humans, whereas hypothyroid patients show an increased noradrenaline concentration in blood. He suggested an inverse relationship between thyroid status and catecholamine release, which reflects a compensatory adjustment of the sympathetic nervous system to the effect of thyroid hormones on the cardiovascular system. This conclusion was further supported by the study of Ghione, Pelligrini, Buzzogioli, Carpi, Valori & Donato (1974). We found no difference between the plasma noradrenaline concentration in the hyperthyroid patients and control subjects at rest when sitting. After exercise, however, the patients had higher noradrenaline concentrations than the control subjects.

It has previously been shown that in healthy humans an increase in sympathetic activity during dynamic exercise is related to the relative work load, e.g. the proportion of exercise $\dot{V}O_2$ to the subjects’ aerobic capacity ($\dot{V}O_2$ max.) (Kozłowski, Brzezińska, Nazar & Kowalski, 1972). Differences in the relative work loads between hyperthyroid patients and the healthy control subjects might thus explain the difference in the plasma noradrenaline response. However, this is not consistent with the above suggestion of a feed-back inhibition of the adrenergic activity in hyperthyroidism. Another possibility is that the higher concentration of noradrenaline in hyperthyroid patients results from delayed inactivation of circulating noradrenaline (Harrison, 1964). Whatever the mechanism might be, higher concentration of circulating noradrenaline in the hyperthyroid patients during exercise seems to be an important factor which may contribute to the excessive haemodynamic and metabolic response to exercise.

References


Christensen, N.J. (1973) Plasma noradrenaline and adrenaline in patients with thyrotoxicosis and myxoedema. Clinical Science and Molecular Medicine, 45, 163–171.


