A STUDY OF PITUITARY-THYROID FUNCTION DURING EXERCISE IN MAN

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Summary : Exercise induced modulations in circulatory T_4, T_3 and TSH were monitored in 14 healthy euthyroid male volunteers undergoing exercise on a bicycle ergometer at 750 KPM for 20 minutes. TSH response to 100 μg TRH was also studied in 4 exercising and 4 resting subjects. Serial blood samples were obtained before, during and after the exercise. Serum T_4 exhibited a significant decrease ($P<0.05$) from 9.6 ± 0.49 $\mu g/dl$ (mean$\pm$SE) to 8.3 ± 0.47 $\mu g/dl$ at 20 min after the termination of the exercise, whereas a significant decrease ($P<0.01$) in T_3 levels from 158 ± 9 *ng/dl* to 144 ± 8.2 *ng/dl* was recorded at 40 min after the termination of the exercise. The basal TSH levels as well as the sensitivity of the pituitary thyroid axis, monitored as overall TSH response, reflected by the sum of TSH values at different time intervals and the maximum rise over the basal levels (ΔTSH) remained unaltered after exercise.

These observations suggest that hormone secretion by the thyroid and its responsiveness to endogenous TSH are maintained after exercise. The decrease in circulatory T_4 and T_3 could be due to an increase in degradation of the hormones or may reflect a generalized adaptation phenomenon. The exact mechanism and significance of these alterations remains to be elucidated.

Key words : thyroid function Exercise TSH response to TRH

INTRODUCTION

The exercise stress is associated with signs and symptoms of early thyrotoxicosis like hypermetabolism, excessive perspiration, fatigability, tachycardia, increased oxygen consumption and heat production in the body. It is possible that hypermetabolism associated with physical activity could be due to increased activity of the thyroid gland. However, studies on thyroid function during exercise have revealed discordant observations. Increased (9, 15) decreased (1, 5) as well as unaltered (2, 3, 8) thyroid gland function has been reported during exercise in man. Irvine (7) observed an increased absolute turnover of thyroxine (T_4) in nonathletic individuals after 6 days of daily bouts of muscular exercise by track running. De Nayar *et al.* (5) recorded a decrease in serum free T_3 after a brief bout of strenuous exercise, whereas Terjung and Tipton (15) reported an increase in serum T_4 after submaximal exercise in man. Balsam and Leppo (1) observed a decrease in plasma T_4 levels and no change in plasma triiodothyronine (T_3) in men undergoing physical training for six weeks.

Similarly, though pituitary secretion of thyrotropin (TSH) is well accepted as the main regulator of thyroid activity and the "set point" of pituitary-thyroid axis is modulated by hypothalamic secretion of thyrotropin releasing hormone (TRH), its role during exercise remains unknown. Terjung and Tipton (15) observed an increase in plasma T_4 and unaltered TSH levels following exercise in man. The question as to where and how exercise acts to influence TSH secretion remains unresolved. It is possible that exercise stress might be altering the sensitivity of the pituitary thyroid axis. The present study details exercise induced alterations in circulatory levels of T_4, T_3, TSH and TRH induced TSH secretion in healthy euthyroid male volunteers undergoing controlled exercise on a bicycle ergometer.

MATERIAL AND METHOD

The study was performed in 14 healthy euthyroid male volunteers. Their mean $\pm$SE, height, weight and age were 169$\pm$1.42 cm, 52.5$\pm$0.49 *kg* and 19.46$\pm$0.22 yr respectively. It was ensured that subjects selected had neither proteinuria nor any other evidence of impaired renal, hepatic or endocrine function. None of the subjects studied received medications viz. salicylates, penicillin or dilantin which are known to displace thyroid hormones from binding proteins. The subjects presented in the laboratory between 8 and 9 a.m. An intravenous polythene catheter was inserted into the antecubetal vein and kept patent by a slow infusion of normal saline. The subjects rested in seated position 20–30 min before the first (zero time) blood sample was withdrawn. Each subject exercised for 20 min on a bicycle ergometer at 750 kilopond meters per min. Serial blood samples were obtained at 0, 10, and 20 min of exercise as well as 20, 40 and 60 min during the recovery period. To evaluate the effects of exercise on hypothalamo-pituitary-thyroid axis, TRH stimulation test was performed in 4 subjects 20 min after the exercise and in 4 control subjects. Each subject received 100 μg of synthetic TRH (Hoechst) iv as a bolus and blood samples were collected at 0, 20, 40, 60 and 90 min interval. Sera were separated and stored at –20°C. T_4 and T_3 levels were measured in the serum using radioimmunoassay technique (14, 11). 8-anilino-1-naphathalene sulfonic acid (ANS) was used to dissociate the thyronines from binding proteins (60 μg/tube in T_4 RIA and 150 μg/tube in T_3 RIA). Upto 100 *ng*/tube of 3, 5–diiodo-L-thyronine (T_2) and 3, 3' 5' triiodothyronine (reverse T_3, rT_3) showed no significant displacement of ^{125}I-T_4 or ^{125}I-T_3 in their respective RIAs. Lack of significant cross reaction by other thyroid hormone analogues and metabolites has been reported previously (12). The sensitivity of T_3 RIA was 25 pg and that of T_4 250 *pg*/tube. When known quantities of T_4 and T_3 were added to hormone free plasma, 96–102% could be recovered at three different concentrations. The inter and intra-assay variabilities were less than 12%. Serum TSH was measured by a double antibody RIA (10, 13). The sensitivity of the assay was 0.5 $\mu u/ml$. Human TSH and its specific anti-serum were generouly

supplied by the National Pituitary Agency NIAMDD, Bethesda, Md., and human TSH standard 68/38 was kindly provided by the Division of Biological Standards NIMR, London, England. All samples of the study for different estimations were processed in one assay to avoid larger intra-assay variations.

Statistical analyses were done by analysis of variance (treatment by subject design) and student's 't' test.

RESULTS

The heart rate (mean±SE) of these subjects at 0, 10 and 20 min of exercise and 20, 40 and 60 min in the recovery period were 82.8±2.84, 172.4±4.01, 178±4.2, 106.4±3.6, 94±3.16 and 86.7±3.54 beats/min respectively. Fig. 1 shows serum TSH, T_3 and T_4 before during and after the exercise. Serum T_3 levels before exercise varied between 100 to 200 *ng/dl* with a mean of 168±9 *ng/dl*. The mean values of 155±8 *ng/dl* and 156±8 *rg/dl* at 10 and 20 min of exercise were not significantly ($P>0.05$) different from the mean of pre-exercise values. A significant decrease ($P<0.01$) in T_3 levels to 144±8.2 *ng/dl* and 130±6.9 *ng/dl* was recorded at 40 and 60 min during the recovery period.

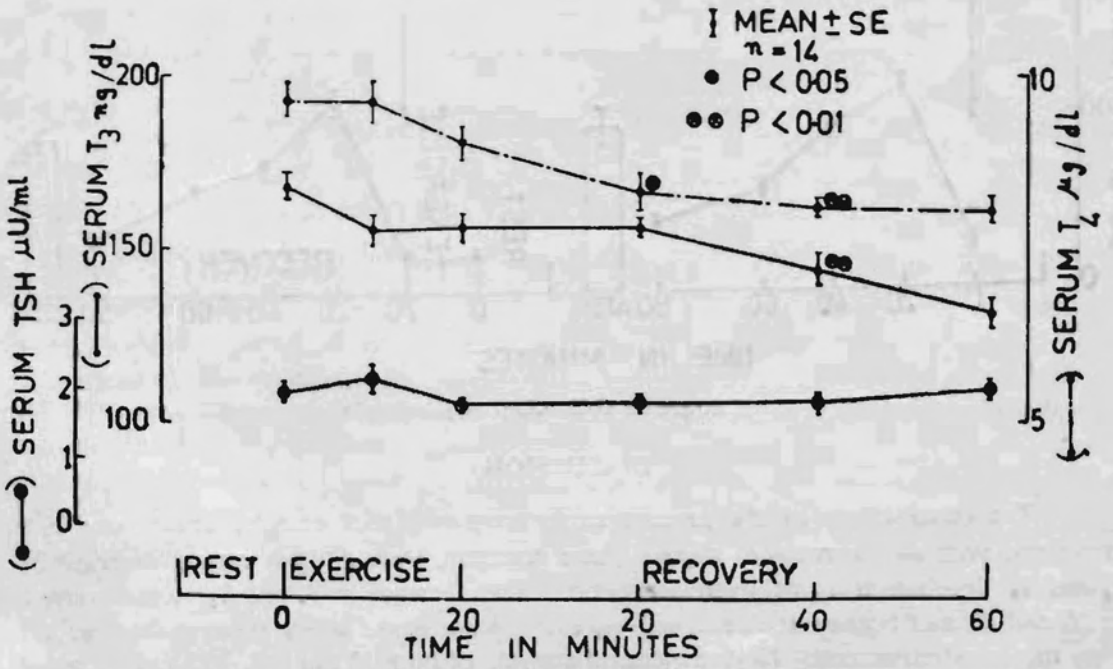

Fig. 1 : Alterations in circulatory levels of T_4, T_3 and TSH before, during and after the exercise.

The mean serum T_4 before exercise was 9.6±0.49 *μg/dl* (range 6 to 13.4. *μg/dl*). Like T_3, serum T_4 also did not exhibit any significant ($P>0.05$) alterations at 10 (9.6 ±0.57 *μg/dl*) and 20 (9.0±0.5 *μg/dl*) min during the exercise period. Serum T_4 levels 20 min after the termination of exercise showed a significant decrease ($P<0.05$) to a mean value of 8.3±0.47 *μg/dl*. The mean T_4 values of 8.1±0.35 and 8.0±0.43 *μg/dl* 40 and 60 min after the termination of the exercise respectively were significantly lower ($P<0.01$) than the mean of preexercise values. Serum TSH, from an initial preexercise value of 2.0±0.33 *μU/ml* showed a slight but non significant fall ($P>0.05$) to 1.82±0.26 *μU/ml* at 20 min of exercise. The mean TSH levels at 20, 40 and 60 min of recovery were 1.86±0.25, 1.35±0.21 and 2.04±0.36 *μU/ml* respectively. These values were not significantly different ($P>0.05$) from the mean of preexercise values.

Fig. 2 shows TSH response to TRH in 4 healthy euthyroid subjects after the exercise and in 4 control subjects. TRH administration consistently increased TSH levels in all the subjects. The peak rise in TSH levels was recorded at 20 min. The basal, peak as well as increments over the basal levels (ΔTSH) were not significantly altered ($P<0.05$) by the exercise stress.

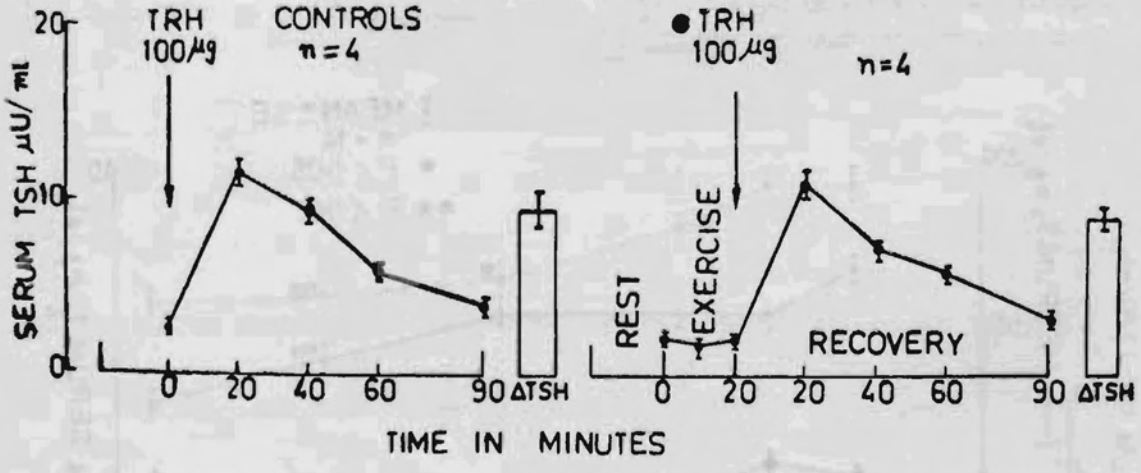

Fig. 2 : TSH response to TRH (100 *μg*, iv) in non-exercising (controls) and exercising subjects.

DISCUSSION

The observations of the present study suggested that exercise stress was not associated with an increase in thyroid gland function, instead there was a decrease in T_4 and T_3 levels in the post exercise period. The decrease in T_4 and T_3 was observed at 20 and 40 min post exercise respectively and the decreased levels were maintained till sixty min of observations. Nevertheless, the levels of both T_4 and T_3 did not decrease to the hypothyroid range and remained within the euthyroid limits. Circulatory levels

of TSH, both basal and after TRH administration, which reflected sensitivity of the pituitary thyroid axis, remained unaltered by the exercise stress.

There is a considerable amount of discrepancy in literature on the effects of exercise on circulating levels of T_4. Irvine (7) studied T_4 degradation in athletes after training. Throughout the training period, T_4 degradation rate exceeded thyroidal secretion rate resulting in decreased plasma protein bound iodine (PBI) levels. Balsam and Leppo (1) studied T_4 and T_3 metabolism in men after a six week programme of physical training. The training resulted in an increase in metabolic clearance rate of T_4 but did not change plasma T_3 levels. In contrast, though metabolic clearance rate of T_4 was not altered, plasma T_3 was decreased in these subjects. In addition, they also observed a slight but significant increase in urinary clearance of T_4 and T_3 but no change in faecal hormonal clearance. As in the present study monitoring of T_4 and T_3 was limited to exercise period and 60 min of post-exercise, the results of earlier studies cannot be compared in toto. The exact factors responsible for decreased levels of T_4 and T_3 during post exercise period remain speculative. These changes could be secondary to fluid volume shifts, blood flow or plasma binding of the hormones (7). However, the T_4 binding capacity of TBG has been reported as increased whereas that of TBPA as decreased after exercise (15).

A decreased conversion of T_4 to T_3 may also contribute towards lowered T_3 levels after exercise. Normally, a major portion of T_3 originates from peripheral conversion of T_4 to T_3. During stressful conditions like nonthyroidal systemic diseases (4), starvation (16) and exercise (9) most of T_4 is converted to hormonally inactive 3, 3' 5' – T_3 (reverse T_3) instead of the hormone 3, 5, 3' – T_3. This would lead to lowering of both T_4 as well as T_3 in the plasma. Another possible cause of decreased T_4 and T_3 levels could be enhanced degradation rates of the hormones after exercise. Irvine (7) recorded a 75% higher T_4 degradation rate in exercising athletes as compared to resting subjects. Similarly, an enhanced degradation rate for T_3 and increased urinary excretion of T_4 and T_3 has been reported after physical training (1).

The exact impact of decrease in T_4 and T_3 levels during the post-exercise period on pituitary secretion of TSH remains speculative. An increase in TSH secretion was expected following lowering of T_4 and T_3 in the plasma. However, we could not record any change in basal TSH or TRH induced rise in TSH in our study. Our observations on unaltered TSH levels following exercise are in agreement with that of Terjung and Tipton (15). The lack of significant alterations in TSH levels indicate that either alterations in T_4 and T_3 in the circulation are independent of pituitary secretion of TSH or secretion and clearance of TSH are enhanced after exercise, leaving the circulatory levels unaltered. In fact, the feedback regulation of TSH is more closely related to free T_4 and T_3, than the concentration of their bound counterparts. The free T_4 levels have been reported as unaltered during exercise (1).

The physiological significance of decrease in T_4 and T_3 levels following exercise remains to be elucidated. With the increased expenditure of energy and associated increased respiration there may be an increase in utilization of thyroid hormones resulting in lowering of hormone levels in the plasma. In addition, a decreased availability of thyronines at tissue levels might be an adaptive mechanism to protect the exercising tissues from high exposure to thyroid hormones during the hypermetabolic state. Thus, decreased serum T_4 and T_3 in the presence of unaltered sensitivity of the pituitary gland and no clinical manifestations of hypothyroidism is an intriguing thyroid relationship which requires further investigations.

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