

Effect of Thyroxine on the Rate of Collagen Breakdown in Young Thyroidectomized Male Rats

Collagen constitutes about 30 % of the total protein content in the mammalian organism, being a major component of the connective tissue of these animals (7). Its rate of synthesis and degradation is affected by genetic, nutritional, hormonal and nervous factors. Thyroxine is one of the hormones which has been observed to influence the rate of collagen turnover. Patients suffering from hyperthyroidism have been reported to show high values of hydroxyproline in urine (10), whereas thyroxine (T₄) replacement of patients suffering hypothyroidism partly restored the output of hydroxyproline and consequently, the rate of collagen metabolism (1). The purpose of this short communication is to report the effect of thyroidectomy and T₄ replacement on the rate of growth and collagen breakdown in young rats. It has been long known that the urinary output of hydroxyproline may be used as an *in vivo* index of the rate of collagen catabolism (5, 6).

Intact and thyroidectomized (T_x) Wistar male young rats (about 120 g) were housed in individual non-metabolic cages. Thyroidectomy was performed four days before the beginning of the experiment. For three days, rats were allowed to eat *ad libitum* a purified diet containing 18 % lactalbumin (3). Then, animals were divided into three hormone-treated groups and transferred to individual metabolic cages for daily collection of urine. Groups were arranged as follows: intact, receiving vehicle (0.9 % NaCl); T_x, receiving the same vehicle; and T_x, receiving 2 µg of T₄ (Sigma) per 100 g b. w. per day. Injections

were given i. p. during a 21-day experimental period. Rats were fed *ad libitum* the same diet mentioned above. Body weight changes and food intake were daily recorded. Complete 24-h urine excretion was collected from individual rats, and then pooled every three days within each experimental group. Urinary hydroxyproline was assayed as described by WOESSNER (11) and IBBOT (4).

At the end of the experiment, all rats were semianaesthetized with ether and decapitated. Immediately, liver and several hind limb muscles (gastrocnemius, tibialis anterior, soleus and extensor digitorum longus) were carefully excised and wet weighed. Serum triiodothyronine was determined by radioimmunoassay (Corning Medical Diagnostic, Medfield, Mass., USA). The data were statistically evaluated by conventional one-way analysis of the variance.

Results of the experiment are summarized in table I. As compared to the intact control rats, a significant reduction ($p < 0.05$) in the rate of growth, food intake, liver weight and hydroxyproline output was observed in the T_x rats receiving vehicle injection. Administration of 2 µg of T₄ to T_x rats restored the rate of growth, food intake and liver weight; however, it failed to increase hydroxyproline output. No significant differences were observed in the weight of the dissected hind limb muscles.

These results suggest that thyroidectomy of young rats brought about a marked reduction in the rates of both growth and collagen breakdown, as well as in the

Table 1. Body weight (b. w.) changes, food intake, liver and muscle weights and urinary output of hydroxyproline (OHproline) of intact and thyroidectomized (T_x) young male rats receiving intraperitoneal injection of either vehicle (0.9 % NaCl) or 2 μ g of thyroxine (T_4) per 100 g b. w. daily during 21 days.

Animals were killed by decapitation at the end of the 21-day experimental period. Immediately, livers and hind limb muscles (gastrocnemius, tibialis anterior, soleus and extensor digitorum longus) were excised and wet weighed. Entries are mean values ($\pm$ SEM) from ten rats in each group unless otherwise indicated. For the muscle weight the sum of the four excised muscles in each animal was computed.

Group	B. w. gain (g/day)	Food intake (g/100 g b.w.)	Liver weight (g/100 g b.w.)	Muscles weight (mg/100 g b.w.)	OHproline ^a output (μ g/100 g b.w.)	Serum T_3 (ng/ml)
Intact + vehicle	7.6 $\pm$ 1.4	15.2 $\pm$ 1.5	5.0 $\pm$ 0.8	1634 $\pm$ 23	131 $\pm$ 36	1.5 $\pm$ 0.2
T_x + vehicle	1.9 $\pm$ 0.8*	10.4 $\pm$ 1.9*	2.7 $\pm$ 0.7*	1654 $\pm$ 34	79 $\pm$ 37*	N. D.
T_x + T_4	7.1 $\pm$ 2.0	14.8 $\pm$ 2.0	4.0 $\pm$ 0.7	1649 $\pm$ 37	84 $\pm$ 20*	1.45 $\pm$ 0.1

* $p < 0.05$, as compared to the intact rats receiving vehicle injection (one-way ANOVA).

^a Entries are mean values ($\pm$ SEM) of the seven determinations carried out each three days during the 21-day experimental period. N.D. = Not detectable.

weight of liver (an organ which together with skeletal muscle, contains a substantial amount of connective tissue in the whole organism). The reduction of collagen breakdown observed in T_x rats was similar to that seen in the rate of myofibrillar protein breakdown in similar animals (2). Although T_4 replacement fully restored growth and liver mass, it was not able to increase the rate of collagen breakdown showed by T_x rats. This observation contrasts with our own findings (2, 9) and those of others (8) in which a similar T_4 replacement given to T_x rats completely restored both growth and muscle protein turnover. In conclusion, the response of collagen turnover to T_4 treatment seems to be much slower than that of the whole body or skeletal muscle.

Key words: Hydroxyproline, Collagen metabolism, Thyroxine, Liver, Muscle.

Palabras clave: Hidroxiprolina, Metabolismo del colágeno, Tiroxina, Hígado, Músculo.

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