

29.

REVUE ROUMAINE DE BIOLOGIE

SÉRIE DE ZOOLOGIE

TOME 14

1969

N° 3

TIRAGE À PART

SEX-DEPENDING EFFECT OF 17α -METHYL-ANDROST-5-ENE- 3β , 17β -DIOL ON THE THYROID FUNCTION OF WHITE RATS

BY

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The action of madiol on the thyroid function was studied by ^{32}P and ^{131}I uptake and by the determination of the conversion index (I_c).

^{32}P and ^{131}I uptake and I_c were not modified in the male rats, but their values significantly decreased in the case of female rats, pointing to functional disturbances of the female thyroid gland.

In the present work radioisotopes were used for estimating thyroid function after administration of 17α -methyl-androst-5-ene- 3β , 17β -diol (madiol). In previous works we showed different responses of the adrenals, endocrine pancreas and lymphatic system in male and female rats [2], [5], [6].

The action of anabolic steroids on the endocrine system is little known. However, its physiological state can modify essentially the metabolic pathways of proteins, carbohydrates and lipids [3], [7].

MATERIAL AND METHODS

Adult male and female white rats weighing 130–148 g. b. w. were used. The animals were kept under normal conditions and they were given daily 0.5 mg madiol (Biofarm) per 100 g b. w. for 30 days. After madiol administration an isotonic solution of $3\mu\text{Ci N}_2\text{H}^{32}\text{PO}_4$ was injected to one group of animals 4 h before sacrificing them. Another group was injected with $2\mu\text{Ci Na}^{131}\text{I}$ and after 24 h the rats were killed by decapitation.

The thyroid gland was measured on a torsion balance, dissolved in 1 N KOH and kept for 24 h at 39°C . Fresh blood was collected in oxalate-containing tubes and centrifuged at 2000 R. P.M. 0.5 ml of plasma were passed through a MERCK-3 (Cl^-) exchange resin column to sepa-

rate protein-bound and inorganic ^{131}I [8]. The radioactivity of samples was determined by a B_2 type apparatus for β -rays and by a gamma-scintillation counter with NaI (T_1) crystal (KFKJ, Nc-104) for γ -rays.

RESULTS

Radioiodine assay of the thyroid capacity to elaborate hormones is the most widely used method. This test is based upon the well-established relation between the avidity of this gland for iodine and its functional state. Iodine is used in the synthesis of thyroxine and triiodothyronine, which are secreted into blood stream for distribution to the tissues where they serve as key metabolic regulators. The rate at which the thyroid accumulates radio iodine from an administered dose is a useful index of its function.

In our experiments, chronic treatment of male and female white rats with madiol did not change significantly ^{131}I uptake by the thyroid in the case of males. At the same time, madiol had an evident action upon the thyroid of females. A reduced capacity of this gland to accumulate ^{131}I was observed, as can be seen in table 1.

Table 1

Effect of madiol treatment upon different indices of thyroid gland function and ^{131}I conversion, depending on sex

| | | Male | | Female | |
|--|-----------------|---------|---------|---------|---------|
| | | Control | Treated | Control | Treated |
| Thyroid weight (mg) | \bar{X} | 23 | 29 | 30 | 39 |
| | $\pm \text{ES}$ | 2.1 | 2.2 | 2.2 | 1.0 |
| | n | (12) | (12) | (12) | (12) |
| | p | — | <0.1 | — | <0.01 |
| ^{32}P incorporation (c/m/mg) | \bar{X} | 2.59 | 2.84 | 1.83 | 0.46 |
| | $\pm \text{ES}$ | 0.10 | 0.19 | 0.13 | 0.04 |
| | n | (12) | (12) | (12) | (10) |
| | p | — | >0.05 | — | <0.01 |
| ^{131}I incorporation (c/m/mg) | \bar{X} | 17801 | 18698 | 14056 | 9244 |
| | $\pm \text{ES}$ | 734 | 1414 | 1440 | 1341 |
| | n | (10) | (10) | (12) | (12) |
| | p | — | >0.05 | — | <0.02 |
| Per cent accumulation of ^{131}I in the thyroid* | \bar{X} | 36.5 | 42.5 | 48.5 | 30.5 |
| | $\pm \text{ES}$ | 5.3 | 4.2 | 4.1 | 6.4 |
| | n | (10) | (10) | (12) | (12) |
| | p | — | >0.05 | — | <0.02 |
| $I_c = 100 \frac{\text{PB}^{131}\text{I}}{\text{T}^{131}\text{I}}$ | \bar{X} | 78.1 | 79.4 | 63.0 | 53.2 |
| | $\pm \text{ES}$ | 3.6 | 2.9 | 2.1 | 1.7 |
| | n | (12) | (12) | (12) | (12) |
| | p | — | >0.05 | — | <0.01 |

c/m/mg = count per minute and mg fresh tissue

* It was calculated by the formula $I\% = 100 \frac{\Lambda_\theta}{\Lambda_\varepsilon}$, where Λ_θ is the total radioactivity of thyroid gland and Λ_ε is the total number of administered impulses.

Thyroid weight and ^{32}P uptake by the thyroids of females changed significantly too. These data showed a dysfunction of the thyroids treated with madiol *in vivo*.

In order to estimate the amount of labelled hormones in the plasma in the presence of inorganic radioiodine, advantage is taken of the strong binding of thyroxine to the plasma proteins [8]. The ratio between plasma-labelled protein-bound iodine level (PB ^{131}I) and total radioiodine level (T ^{131}I) represents the conversion index (I_c) for a given quantity of plasma. I_c -value was determined in male and female white rats after madiol administration. A decrease from 63 to 53.2 per cent was observed in females.

DISCUSSIONS

The action of androgens and anabolic steroids on the thyroid function is not yet clear [1], [5], [7]. Feldman and Carte [5] showed that some synthetic anabolic steroids (e. g. 17α -methyl- 17β -hydroxy-androst-1,4-diene-3-one, 17α -ethyl- 17β -hydroxy-19-norandrost-4-ene-3-one) had no effect upon ^{131}I uptake by the human thyroid gland. The same authors showed that testosterone- 17β -propionate and 17α -ethyl- 17β -hydroxy-19-norandrost-4-ene-3-one decreased the amount of protein-bound ^{131}I in the plasma.

Our results showed that madiol caused a dysfunction of the thyroid gland and of the iodine-utilisation by the thyroids of females. In males we did not find any changes. These data can explain the reduced effect of madiol in the case of females, where the well-known anabolic action of madiol was significantly diminished [3], [6].

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Received December 2, 1968

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