EFFECT OF AN ANTITHYROID AGENT (AMMONIUM PERCHLORATE) ON ADRENAL CORTICAL FUNCTION

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After administration of ammonium perchlorate no clear connection was found between the plasma concentration of 11-hydroxycorticosteroids and the binding of iodine by the blood proteins.

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A link between the blood level of the thyroid hormones and adrenal cortical function has frequently been demonstrated experimentally [3-5, 8].

It appeared interesting to study these relationships during prolonged administration of antithyroid substances.

EXPERIMENTAL METHOD

Experiments were carried out on 320 male albino rats receiving ammonium perchlorate (APC) either as a single intravenous injection in a dose of 50 mg/kg or by prolonged administration (in a dose of 1 μg/kg daily for 6 months by mouth). The concentration of the 11-hydroxycorticosteroids (11 HCS) in the blood plasma and adrenal tissues [7] and the level of protein-bound iodine (PBI) in the plasma [2] were determined 7.5 min, 6 and 16 h, and 1, 3, 5, 7, and 10 days, in the case of a single injection of APC, and also 1 and 2 weeks, and 1, 2, 3, and 6 months after the experiment began (in the case of prolonged administration of APC).

EXPERIMENTAL RESULTS

The plasma 11 HCS concentration 7.5 min after injection of APC was increased to 41.5 ± 5.6 μg%, and in the adrenals to 50 ± 0.61 μg/g (control 19.7 ± 0.23 μg/g). After 6 h the concentration of hormones in the plasma had risen sharply—to 7.3±0.34 μg%, and in the adrenal tissues to 3.78±0.41 μg/g, with a further increase after 16 h to 25.9±3.7 μg% in the plasma and to 84.1±9.3 μg/g in the adrenals. The 11HCS level returned to its initial value by the 3rd day of the experiment. Intravenous injection of APC caused a rapid fall in the PBI level. For instance, after 7.5 min its plasma concentration was 2.4±0.3 μg% (control 4.7 ± 0.61 μ%). The PBI level reached a minimum after 24 h (1.2 ± 0.14 μg%), and it did not reach its initial level again until the 10th day. In the case of prolonged administration of APC the 11 HCS concentration was increased during the first 2 weeks of the experiment; in the plasma to 20.3±3.5 μg% (control 13.4±1.94 μg%), and in the adrenal tissues to 60.1±7.2 μg/g (control 21.4±2.7 μg/g). At later times the 11HCS concentration in the plasma and adrenal tissue was lowered; one month after the beginning of the experiment the 11HCS concentrations were 4.68 ± 0.53 μg% and 8.2 ± 0.94 μg% respectively, after 3 months 3.6 ± 0.41 μg% and 6.7 ± 0.74 μg%, and after 6 months 2.4±0.36 μg% respectively. Throughout the experiment the blood PBI level was lowered, its values 2 weeks and 1, 3, and 6 months after the beginning of the experiment being 2.2 ± 0.32, 1.8 ± 0.28, and 2.7±0.4 μg% respectively (controls 3.1 ± 0.35 μg%).

The results obtained do not indicate that adrenal cortical function bears a direct relationship to the serum PBI level after administration of APC. The increase in 11HCS level in the first minutes of the experiment can perhaps be attributed to the effect of an excess of active thyroid hormones formed because of rupture of their bond with the blood protein (as shown by a decrease in the PBI concentration in the early stages of poisoning); it is difficult to rule out under these circumstances the possibility of a direct effect

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of APC on 11HCS production. Subsequently the increase in 11 HCS concentration inhibited ACTH production, leading to depression of the hormonal function of the adrenal cortex, which we observed 6 h after administration of APC. The increase in 11HCS concentration after 16 and 24 h was probably due to the direct action of APC on hormone formation processes because it was in this period that accumulation of Cl^{35}-labeled APC in the adrenal cortex reached a maximum. During prolonged administration of APC we found an increase in the plasma 11 HCS concentration in the first two weeks of the experiment, followed by a sharp decrease in their level below the control value, in association with a low plasma PBI level throughout the experiment. The increase in 11HCS concentration in the first two weeks of the experiment cannot therefore be attributed to the direct effect of thyroid hormones [1, 6]. It is possibly the result of direct stimulation of hormone formation in the adrenal cortex by APC. The decrease in 11HCS production in later stages of the experiment was due to their functional exhaustion and not to inhibition of ACTH production. Absence of a direct connection between adrenal cortical function and the PBI level is also demonstrated by the fact than an increase in the PBI concentration to the control level (6 months of the experiment) did not produce the anticipated increase in 11HCS concentration.

LITERATURE CITED

1. S. G. Genes, Uspekhi Sovr. Biol., 60, No. 3, 411 (1965).
2. S. B. Barker, M. Humphrey, and M. H. Soley, J. Clin. Invest., 25, 55 (1951).
3. E. J. Baumann and D. Marine, Endocrinology, 36, 400 (1945).
4. K. Eik-Ness and K. R. Brizzel, Am. J. Physiol., 184, 371 (1956).
5. C. P. Leblond and H. E. Hoff, Endocrinology., 35, 229 (1944).
6. J. Roche, R. Michel, and P. Johan, C.r. Soc. Biol., 153, 255 (1959).
7. R. H. Silber, R. D. Busch, and R. Oslapas, Clin. Chem., 4, 278 (1958).
8. M. Kh. Zarrow and J. C. Zarrow, Proc. Soc. Exp. Biol. (N. Y.), 76, 620 (1951).