SENSITIVITY OF HYPERTHYROID RABBITS TO PRESSOR EFFECT OF ADRENALIN

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Findings are described which oppose the view that sensitivity of adrenergic receptors is increased in thyrotoxicosis.

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Investigations of the sensitivity of hyperthyroid animals to catecholamines revealed by the severity of changes in the arterial pressure have not yielded consistent results [2-10].

In the present investigation this problem was examined by measuring responses to adrenalin in rabbits in various stages of experimental thyrotoxicosis.

EXPERIMENTAL METHOD

Experiments were conducted on male rabbits weighing 2.5-3.5 kg. Some of the animals (18) acted as controls, while the others were fed thyroid extract in doses of from 0.4-2.2 g daily for 28 days. Some (20) animals were investigated on the 14th day of experimental thyrotoxicosis, others (22) on the 28th day. Adrenalin was injected quickly in a dose of 2.5 μg/kg into the exposed jugular vein of the animals anesthetized with urethane (1 g/kg intravenously). The time of injection and the pressure in the carotid artery were recorded on a photorecording oscillograph. The pressure was measured by an electromanometer.

EXPERIMENTAL RESULTS

The mean arterial pressure in the animals of the control group was 95 ± 1.38 mm.* After injection of adrenalin it rose to 136.2 ± 44.3 mm, an increase of 41.2 ± 4 mm, or 43.3% of the initial value.

The original mean pressure in animals receiving thyroid extract for 2 weeks was 118.5 ± 4.15 mm. After injection of adrenalin it rose to 157 ± 5.7 mm, i.e., by 38.5 mm or by 32.4% of the initial value. Although the difference between the absolute increases of arterial pressure in the control and experimental animals was not significant, the increase expressed as a percentage of the initial value was significantly ($P < 0.05$) lower than in the controls.

In the rabbits receiving thyroid extract for 4 weeks the initial pressure was 124.6 ± 2 mm. After injection of adrenalin it rose to 157 ± 3 mm, i.e., by 32.4 mm or by 26.6% of the initial value. The increase in the mean arterial pressure in this group of animals was smaller than that in the controls by a statistically even more significant margin ($P < 0.001$).

The results demonstrate that with progressive development of experimental thyrotoxicosis in rabbits, adrenalin causes a progressively smaller increase in the mean arterial pressure.

Analysis of the times of onset and development of the pressor response to adrenalin revealed the following pattern. An increase in arterial pressure of the control rabbits appeared on the average after 3.6 ± 0.13 sec. In rabbits receiving thyroid for 14 days this time was increased to 4.13 ± 0.2 sec, and in the animals receiving thyroid for 28 days, to 4.3 ± 0.19 sec. The values obtained in both experimental groups differed significantly from the controls ($P = 0.03$ and $P < 0.001$, respectively). The delay in the onset of the response to adrenalin in the hyperthyroid animals became particularly obvious, bearing in mind that the

*Here and subsequently, $M \pm m$.

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velocity of the blood flow is greater in such animals [1]. This means that the adrenalin must have reached the specific adrenergic receptors of the arterial system sooner.

The time taken for the pressor response to adrenalin to develop, i.e., the time between the onset and the maximum of the response, was also increased in the experimental animals. In the controls its mean value was 3.14 ± 0.15 sec, in the animals receiving thyroid extract for 14 days it was increased to 3.46 ± 0.36 sec, and in the animals of the third group to 4 ± 0.33 sec. The difference between the times of development of the pressor response to adrenalin in the animals of the control and the last experimental group was statistically significant ($P = 0.002$).

The rate of return to a normal mean pressure was estimated from its height 10 sec after the maximal increase. During this period the arterial pressure in the control rabbits fell on the average by 32 mm, or by 78%, compared with by 18.6 mm or 47% in the animals receiving thyroid for 14 days and with 14 mm or 43% in animals receiving thyroid for 28 days. The difference between the results in both experimental groups and in the control group was statistically significant, and as the thyrotoxicosis increased progressively in severity, the significance of the difference increased ($P < 0.02$ and $P < 0.001$, respectively).

Injection of adrenalin into the control animals led to an increase not only in the mean, but also in the pulse pressure, from 26 ± 0.8 initially to 40 ± 1.46 mm at the moment of maximal increase of the mean pressure. No significant increase in the pulse pressure could be detected in the animals of either experimental group under the influence of adrenalin.

In the dose used, adrenalin caused moderate slowing of the heart rate in the animals of all groups. Neither in the severity of the bradycardia nor in the changes in heart rate after injection of adrenalin could any difference be discovered between the control and experimental animals.

The results demonstrate that experimental thyrotoxicosis in rabbits is accompanied by a progressive delay in the onset and development of the pressor response to adrenalin. The magnitude of the response also was smaller in hyperthyroid animals. The arterial pressure, when raised by the action of adrenalin, also took longer to return to normal. This last finding could be attributed to lowering of monoamine oxidase activity in the vessel walls [11] and to inhibition of breakdown of injected adrenalin. However, this explanation is not in accord with data indicating that monoamine oxidase inhibitors do not potentiate effects of catecholamines.

On the whole, the results described above do not support the view that the sensitivity of adrenergic receptors is increased in thyrotoxicosis.

LITERATURE CITED

1. L. M. Gol'ber, V. I. Kandror, and K. M. Ester, Abstracts of Proceedings of the 10th Congress of the I. P. Pavlov All-Union Physiological Society [in Russian], Vol. 2, No. 1, 216, Moscow-Leningrad (1964).
2. E. B. Gorbovitskii, Vascular Reactions in Experimental Renal Hypertension and Experimental Hyperthyroidism [in Russian], Candidate Dissertation, Moscow (1951).
3. P. P. Gusach, In the book: Proceedings of the 2nd Conference of the Ukrainian Society of Pathophysiologists [in Russian], Uzhgorod (1962), p. 135.
4. V. S. Sumbaev, Pat. Fiziol., No. 5, 57 (1961).
5. L. Ya. Fishchenko, In the book: Goiter [in Russian], Kiev (1956), p. 68.
6. O. E. Hepler and J. P. Simonds, Proc. Soc. Exp. Biol., New York, 34, 534 (1936).
7. F. G Miculicich, Arch. Exp. Path. Pharmak., Bd.162, S.484 (1931).
8. J. E. Murray and J. J. Kelly, Am. Intern. Med., 51, 309 (1959).
9. J. Page and J. M. McCubbin, Circulation, 5, 390 (1952).
10. D. S. Riggs et al., J. Pharmacol. Exp. Ther., 101, 31 (1951).
11. A. Spinks and J. H. Burn, Brit. J. Pharmacol., 7, 93 (1952).