BIPHASIC CHARACTER OF THE HYPOCALCEMIC ACTION OF THYROCALCITONIN

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Experiments on rabbits showed that intravenous injection of the thyrohormone thyrocalcitonin sharply reduces the blood calcium level in two phases. The first phase occurs sooner after injection of the hormone, while the second reaches its maximum after 12 h.

A study of the dynamics of thyrocalcitonin (TCT) action in experiments on animals, together with the results of clinical observations [4-6], indicates that this hormone has the property of producing a marked decrease in the blood calcium concentration. As most investigators point out, the hypocalcemic effect observed is transient in character, and the action of TCT ends 3-4 h after its administration.

The authors have shown [2] in experiments in vitro that TCT forms complexes by interaction with the protein components of the blood serum or homogenates of some tissues. Injection of such mixtures into rabbits led to a decrease in their blood calcium concentration, but in these cases the action of the hormone reached its maximum after a considerable time interval [2].

Analysis of these results suggested that the action of TCT might be biphasic in character. The present investigation was undertaken to test this hypothesis experimentally.

EXPERIMENTAL METHOD

A Soviet preparation of TCT obtained from bovine thyroid glands by a modified method of Gudmundsson et al. [3], was used in the investigation. Its activity was 300 units/mg. Experiments were carried out on rabbits of both sexes weighing 2-3.5 kg. The animals were transferred to a minimal diet for 16-18 h before the experiments began. TCT was injected intravenously into the animals of each group (not less than 10 rabbits per group) in doses of 1, 10, or 17 μg/kg made up in 0.5-1 ml physiological saline. Blood for testing was taken from the marginal vein of the ear before injection of TCT and 2, 4, 8, 12, 14, 16, 18, 20, and 24 h thereafter. The serum calcium concentration was determined by complexiметric titration with 0.001 N EDTA solution in the presence of murexide as indicator.

EXPERIMENTAL RESULTS AND DISCUSSION

It will be clear from Fig. 1 that the blood calcium concentration of the control rabbits (animals receiving physiological saline) remained virtually unchanged during the 24 h. Meanwhile, 2 h after injection of 10 μg/kg TCT, the blood calcium level fell by 2.06±0.139 mg%; 4 h after injection the calcium concentration was almost back to its original level (differing from it by only 0.39±0.031 mg%). In the next 4 h the calcium concentration was essentially unchanged, but later it fell again, to reach its lowest level (a decrease of 2.41±0.072 mg%). In the next 4 h the calcium concentration was essentially unchanged, but later it fell again, to reach its lowest level (a decrease of 2.41±0.072 mg%) 12 h after injection, when it

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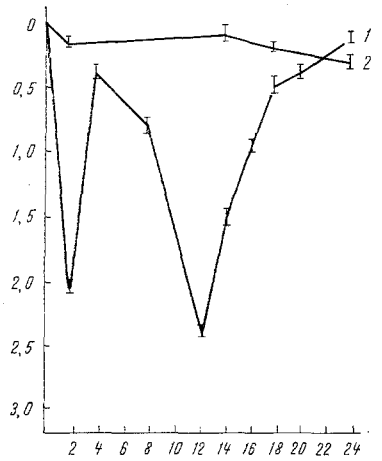

Fig. 1. Change in blood calcium concentration of rabbits after intravenous injection of TCT in dose of 10 μg/kg (1) and of 1 ml physiological saline (2). Abscissa, time (in h); ordinate, change in blood calcium concentration (Δ_{Ca}; in mg%).

gradually began to rise again so that after 24 h the hypocalcemic response in the animals was finally ended (deviation from the initial level only 0.11±0.026 mg%).

The absence of any regular relationship between the degree of the manifested hypocalcemic effect of TCT and the dose of the preparation is interesting: injection of a larger dose of the hormone (17 μg/kg) into the rabbits caused a smaller decrease in the blood calcium level at the maximum of the second phase (12 h) than injection of a much smaller dose (10 μg/kg) of TCT.

An earlier investigation [2] revealed the ability of certain organs, notably the myocardium, to bind thyrocalcitonin. This suggests that TCT, like most other hormones, exists in the body either in a free or in a bound state. It can accordingly be supposed that the first phase of the hypocalcemic action of TCT is due to the direct effect of free TCT, while the second phase is due to gradual liberation of TCT from the complexes formed by interaction between this hormone and the chemical components of the tissues. At the same time, the unlimited capacity of the myocardium to bind TCT, established in experiments in vitro, as well as the fact that the biphasic hypocalcemic reaction in animals develops in response to injection of very small doses of TCT, contradict this hypothesis to some extent.

After peripheral administration of TCT to rabbits, the authors have shown that the calcium concentration in the cerebrospinal fluid of the animals rises sharply, while its blood level simultaneously falls [1]. This suggests that the first phase of the hypocalcemic effect of TCT is associated with its influence on the central mechanisms regulating the calcium level in the body.

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