Effect of histamine on adrenal 17-hydroxycorticoid secretion in unanesthetized dogs

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SUZUKI, TATUZI, KENJI HIRAI, HARUHIKO YOSHIO, KEN-ICHI KUROJII, AND KAZUKUNI YAMASHITA. Effect of histamine on adrenal 17-hydroxycorticoid secretion in unanesthetized dogs. Am. J. Physiol. 205(5): 847-848. 1963. — Dogs with previously sectioned dorsal spinal roots (T11-L4) were used in experiments for collecting the adrenal venous blood without anesthetizing or evoking any pain. Intravenous injection of histamine in doses of 0.05-1.0 mg/kg body wt. was demonstrated to produce a marked acceleration of 17-hydroxycorticoid secretion. The time courses of changes in the secretion rate after injection of varying doses of histamine are compared.

THE EFFECT OF HISTAMINE on the pituitary-adrenocortical system has been evaluated by indirect indices. It was reported that an injection of histamine caused a significant lymphopenic (1, 2) or eosinopenic response (3-6). Injection of histamine was also proved to produce a marked fall in adrenal ascorbic acid concentration (3, 7-11). A direct evaluation was performed by Endroczl et al. (2). They estimated the corticoid content of the adrenal venous blood collected from anesthetized cats and demonstrated a definite increase in corticoid secretion produced by subcutaneous injection of histamine. However, no description of the time course of the accelerated corticoid secretion was made in their paper.

In the present study we have attempted to evaluate directly the effect of histamine on the adrenal 17-hydroxycorticoid (17-OHCS) secretion rate in unanesthetized dogs and to determine the exact time courses of the 17-OHCS secretion in response to varying doses of histamine.

METHODS

The experiments were carried out on mongrel dogs weighing 11-19 kg. The adrenal venous blood for estimation of the secretion rate of 17-OHCS was sampled from unanesthetized dogs, as was done in our previous studies (12-15), by a modification of the method of Satake, Sugawara, and Watanabe (16). In order not to evoke any pain at the period of adrenal venous blood collection, dorsal spinal roots (T11-L4) were cut under sodium pentobarbital anesthesia 3 weeks or more prior to the experiments.

On the day before experiments the lumboadrenal vein was exposed through the lumbar route and a small glass cannula connected with a short rubber tube was inserted into the vein lateral to the adrenal gland. A silk thread was passed loosely around the adrenal vein between the vena cava and the adrenal gland. This thread was pulled gently at the period of blood collection in order to direct the blood flow to the exterior through the cannula and the rubber tube. Heparin sodium was used to prevent blood clotting.

Experiments were started as a rule about 18 hr after the adrenal vein cannulation. After two adrenal venous blood samples were collected, histamine hydrochloride dissolved in saline solution was injected intravenously in 60 sec in doses of 0.05-1.0 mg/kg body wt. At 5, 20, 40, 60, 90, and 120 min after histamine injection, the adrenal venous blood was collected during a period of 20-120 sec. The adrenal venous blood samples were iced immediately after collection and centrifuged. The adrenal venous plasma was analyzed for 17-OHCS by the method of Nelson and Samuels (17).

RESULTS

Dogs 1 and 2, injected with 1.0 mg/kg of histamine, began to struggle within 20 sec after the start of histamine injection. In five others, injected with 0.05-0.5 mg/kg histamine, deep and rough respiration without struggle was observed. The frequency of respiration increased in all cases. The rate of heartbeat increased in dogs 1-5, while it remained unaltered in dogs 6 and 7. No definite changes in body temperature were found after histamine injection.

The data concerning the adrenal 17-OHCS secretion rate are shown in Table 1. The 17-OHCS secretion rate before histamine injection was 0.05-0.29 µg/min per
The effect of histamine on the corticoid secretion was evaluated quantitatively by the direct determination. That a small amount of histamine, such as 50 μg/kg, acts on the pituitary-adrenocortical system to induce an increase in corticoid secretion, as observed by Fuche and Kahlson (1) with an indirect method, was confirmed in the present study by the direct evaluation of adrenal 17-OHCS secretion rate.

Since histamine produces a marked effect on blood pressure and other physiological functions, the effect of histamine on the adrenocorticotrophic hormone (ACTH) secretion of the adrenohypophysis could be secondary to these changes. That psychic stimulation caused by histamine poisoning increases ACTH secretion is not very convincing, since the depletion of adrenal ascorbic acid has been found to be induced by histamine in anesthetized animals (11).

It has been well established that histamine accelerates the adrenal medullary secretion (18-20). Thus there is a possibility that histaminic action on the pituitary-adrenocortical system may be mediated by the adrenal medullary hormone. However, Fuche and Kahlson (1) and Gordon (3) inferred that the adrenal medullary secretion was not essential in the histamine effect on the pituitary-adrenocortical system. On the other hand, Semonsen and Sawyer (5) concluded that the effect of subcutaneous histamine on the adrenohypophysis was mediated at least in part via the adrenal medulla. The direct action of histamine on the adrenohypophysis, which was observed by Fortier (4), was denied by Schally and Safran (91).

The data of the present study do not allow a decision among several possible mechanisms. Elucidation of the exact mechanism for the histaminic action on the adrenocortical secretion awaits further investigation.

## DISCUSSION

The effect of histamine on adrenocortical activity has been studied by a number of investigators. Most of them, however, evaluated the adrenocortical activity with indirect indices such as lymphopenic response (1, 2), eosinopenic response (3-5) and a depletion of adrenal ascorbic acid (3, 7-10). In the present study the excitatory effect of histamine on the corticoid secretion was evaluated quantitatively by the direct determination. That a small amount of histamine, such as 50 μg/kg, acts on the pituitary-adrenocortical system to induce an increase in corticoid secretion, as observed by Fuche and Kahlson (1) with an indirect method, was confirmed in the present study by the direct evaluation of adrenal 17-OHCS secretion rate.

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## REFERENCES