

AGE DIFFERENCES IN THE EFFECT OF ACTH ON ALDOSTERONE SECRETION IN RATS

L. V. Magdich

UDC 612.453.018:612.66]-06:612.433.451.018

KEY WORDS: age; aldosterone; ACTH.

Age changes in the mineralocorticoid function of the adrenal cortex have not yet received due attention from research workers. There is no general agreement regarding changes in the aldosterone concentration in the peripheral blood during aging. According to some workers [5], for instance, the aldosterone concentration in the peripheral blood of rats does not change with age, whereas according to other workers, it falls significantly [9]. Age changes in aldosterone secretion and in its regulation during aging have not been studied. The role of ACTH in the regulation of the mineralocorticoid function of the adrenal cortex has recently been discussed in detail. There is a report in the literature that ACTH has no significant effect on the zona glomerulosa of the adrenal cortex [11]. However, the regulatory effect of ACTH on aldosterone secretion is at present accepted by most investigators [2, 8, 10].

The possible change in the mineralocorticoid function of the adrenal cortex during aging is indirectly supported by much evidence of changes taking place in the concentrations of potassium and sodium ions in different organs in old age [3, 4].

The aim of this investigation was to study age differences in aldosterone secretion and its regulation by ACTH.

TABLE 1. Effect of ACTH on Rate of Aldosterone Secretion in Adult and Old Rats

Dose of ACTH, units/100 g	Rate of aldosterone secretion, ng/h	
	adult animals	old animals
0,05	$4,25 \pm 0,51$	$2,58 \pm 0,43$
	$3,73 \pm 0,73$	$2,94 \pm 0,29$
	$n=8; P<0,3$	$n=8; P<0,1$
0,5	$4,22 \pm 0,64$	$2,08 \pm 0,58$
	$4,44 \pm 0,71$	$3,57 \pm 0,49$
	$n=8; P<0,5$	$n=8; P<0,01$
1	$5,04 \pm 0,79$	$2,57 \pm 0,43$
	$9,28 \pm 1,38$	$4,84 \pm 1,06$
	$n=10; P<0,01$	$n=10; P<0,01$
5	$4,34 \pm 0,65$	$2,23 \pm 0,37$
	$10,37 \pm 2,54$	$2,06 \pm 0,83$
	$n=8; P<0,01$	$n=8; P>0,5$

Legend: 1) Control data in numerator, experimental data in denominator. 2) n - Number of investigations; P - probability of significance of differences between control and experiment.

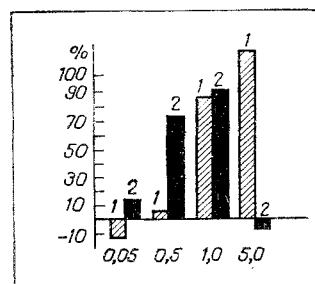


Fig. 1. Change in rate of aldosterone secretion under the influence of ACTH in adults (1) and old (2) rats (in % of initial level). Abscissa, dose of ACTH (in units/100 g body weight); ordinate, rate of aldosterone secretion (in % of initial level).

Laboratory of Endocrinology and Laboratory of Physiology, Institute of Gerontology, Academy of Medical Sciences of the USSR, Kiev. (Presented by Academician of the Academy of Medical Sciences of the USSR D. F. Chebotarev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 89, No. 7, pp. 19-20, July, 1980. Original article submitted June 6, 1979.

EXPERIMENTAL METHOD

Male Wistar laboratory rats of two age groups were used: adult (6-8 months) and old (28-30 months). To study the rate of aldosterone secretion the left adrenal vein was cannulated, and blood flowing from the adrenal was collected for 30 min. The hormone concentration in adrenal venous blood was determined by a radioimmuno-logic method using the special kits from Cea-Ire-Sorin (France). Aldosterone secretion was investigated before and 30 min after injection of ACTH. To determine age changes in the regulation of aldosterone secretion, ACTH was used in the experiments over a wide range of doses: from 0.05 to 5 units/100 g body weight. The ACTH was injected into the femoral vein.

EXPERIMENTAL RESULTS

During aging the aldosterone concentration in the peripheral blood of the Wistar rats was found to diminish. In adult male rats, for instance, the aldosterone concentration in the peripheral blood was 23.89 ± 1.98 ng%, falling in the old rats to 18.23 ± 0.96 ng%. A significant decrease was observed in the rate of aldosterone secretion in the old animals (Table 1). As Table 1 shows, the rate of secretion of aldosterone was 41.2% lower in the old animals than in the adult rats.

In the next series of experiments the effect of different doses of ACTH on aldosterone secretion was studied in adults and old male rats. The threshold dose of ACTH enabling the sensitivity of the zona glomerulosa of the adrenal cortex to be judged, and a large dose, enabling the so-called reactivity to be judged, were determined as the first step in the experiments. These results are shown in Table 1 and Fig. 1. The absolute values of the change in the rate of aldosterone secretion under the influence of ACTH are given in Table 1, whereas changes in the rate of secretion of the hormone, as a percentage of the initial level, are shown in Fig. 1.

In old animals the sensitivity of the zona glomerulosa to ACTH is increased. As Table 1 and Fig. 1 show, for old animals the threshold dose was 0.50 unit/100 g body weight, whereas in adult animals it was 1 unit/100 g. Injection of ACTH in a dose of 0.5 unit/100 g did not change the rate of aldosterone secretion in the adult animals and led to an increase in its secretion in old animals by 71.6%.

After injection of ACTH in a dose of 1 unit/100 g the increase in secretion was approximately the same in the adult and old animals: 84.1% in the adults and 88.3% in the old rats. However, as Table 1 shows, in absolute values the increase in the rate of aldosterone secretion after injection of ACTH in a dose of 1 unit/100 g body weight was significantly greater in the adults than in the old animals.

Particularly significant age differences were found after injection of ACTH in a dose of 5 units/100 g. In that case the intensity of aldosterone secretion in the adult animals rose by 116.0%, whereas in the old animals it was virtually unchanged.

In the old animals the functional activity of the zona glomerulosa of the adrenal cortex was thus reduced, as also was the intensity of secretion of the principal mineralocorticoid, aldosterone. It is interesting to note that the rate of aldosterone secretion in old age falls more than its concentration in the peripheral blood. This fact requires special analysis. However, it can be tentatively suggested that it is linked with age differences in aldosterone metabolism, its binding with proteins, and its distribution in the tissues.

The level of hormonal regulation depends not only on the hormone concentration, but also on the characteristics of responses of the tissues to its action. It has been shown [6,7] that sensitivity of certain tissues to the action of hormones increases during aging whereas their reactivity decreases. We know that in old animals smaller doses of ACTH cause changes in the glucocorticoid and androgenic function of the adrenal cortex [1]. The results now obtained show some measure of agreement with all these facts. In old animals the threshold doses of ACTH stimulating aldosterone secretion are reduced, i.e., the sensitivity of the zona glomerulosa of the adrenal cortex to ACTH increases. Meanwhile, the reactivity and amplitude of the changes with an increase in dose of ACTH are reduced with age.

The results of this investigation of the mineralocorticoid function of the adrenal cortex lead to the conclusion that aldosterone secretion and its regulation by ACTH change during aging.

LITERATURE CITED

1. V. I. Bekker, "Functional state of the adrenal cortex during aging," Author's Abstract of Candidate's Dissertation, Kiev (1967).
2. K. V. Druzhinina, in: *Hormone Biochemistry and Hormonal Regulation* [in Russian], Moscow (1976), p. 228.

3. L. P. Kuprash, "Age changes in water and electrolyte metabolism (clinical and experimental investigation)," Author's Abstract of Doctoral Dissertation, Kiev (1974).
4. O. A. Martynenko, in: Mechanisms of Aging [in Russian], Kiev (1963), p. 290.
5. V. N. Slavnov and G. V. Valueva, in: Endocrinology. Republican Inter-Institute Collection [in Russian], No. 6, Kiev (1976), p. 87.
6. V. V. Frol'kis, Fiziol. Zh. SSSR, No. 7, 857 (1965).
7. V. V. Frol'kis, N. V. Svechnikova, et al., Fiziol. Zh. (Ukr.), No. 3, 330 (1963).
8. N. A. Yudaev and K. V. Druzhinina, Probl. Endokrinol., No. 4, 59 (1967).
9. C. Flood, C. Gherondache, G. Pincus, et al., J. Clin. Invest., 46, 960 (1967).
10. R. Horton, J. Clin. Invest., 48, 1230 (1969).
11. R. E. McCaa, C. S. McCaa, et al., Circulat. Res., 32, 356 (1973).

EFFECT OF COLCHICINE ON SECRETION OF ALVEOLAR SURFACTANT IN THE INTACT AND REGENERATING RAT LUNG

L. K. Romanova

UDC 612.212.014.1.014.462.8:612.6.03]-014.46:615.277.3:547.944.6

KEY WORDS: surfactant; secretion; colchicine; regeneration of the lung.

Synthesis of the combination of surface-active substances constituting the surfactant, located on the cellular lining of the alveoli of the lung and responsible for their stability, takes place in type II alveolocytes [6, 7]. It has been shown by electron microscopy that surface-active substances of phospholipid nature are present in the cell as osmiophilic lamellar bodies known as intracellular surfactant [3]. Under ordinary physiological conditions the surfactant is secreted from type II alveolocytes by a merocrine type of mechanism through exocytosis from the apical surface of the cells facing the alveolar lumen [4].

As recent investigations have shown, the level of secretion of surfactant can be modified by the action of various factors. Hyperventilation and other factors stimulate surfactant secretion [6, 8, 9]. Colchicine and vinblastine as a rule depress it [5, 6]. The intracellular mechanisms of regulation of surfactant secretion have not yet been adequately studied. It might be supposed that the restriction or stimulation of surfactant secretion are linked either with changes in the level of metabolism in the type II alveolocytes and the intensity of synthesis of phospholipids or with delay or acceleration of the release of surfactant from these cells into the alveolar lumen.

It was accordingly decided to study changes in the character and level of surfactant secretion under the influence of colchicine, which selectively inactivates the cytoplasmic microtubules that play an important role in the secretory process [10].

EXPERIMENTAL METHOD

Noninbred male rats weighing 220-250 g were used. The animals were divided into four groups. From the rats of group 1 63% of the weight of the lungs (the whole left lung and the diaphragmatic lobe of the right lung) was removed and at 1 p.m. on the 4th-5th day after the operation intramuscular injections of colchicine (from "Merck") began in a dose of 0.1 mg/100 g body weight per injection.

In the course of the 24 h before sacrifice each animal received six injections of colchicine at intervals of 4 h. The total dose of colchicine was 0.6 mg/100 g body weight. From the rats of group 2 63% of the weight of the lung tissue was removed, and physiological saline was injected intramuscularly (0.3 ml per injection). On the rats of group 3 a mock operation was performed and colchicine was injected in the same dose as that given to the rats of group 1. Animals of group 4 underwent the mock operation only. The rats of all groups were

Laboratory of Pulmonology, Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 89, No. 7, pp. 21-25, July, 1980. Original article submitted June 6, 1979.