Some Mechanisms of Kidney Aldosterone Reception and Its Regulation for Damage of the Sciatic Nerve in Rats

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UDC 616.61−007:616.8−02:577.175.532

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol.115, No. 4, pp.352−354, April, 1993
Original article submitted November 23, 1992

Key Words: *aldosterone; mineralocorticoid receptors; nerve damage; adrenoblockers*

The hormone of the adrenal cortex, aldosterone, is the most important animal and human mineralocorticoid regulating active sodium transport across the mucous epithelial membranes of various organs, and, primarily, through the kidney tubule epithelium [7,9, 11]. Aldosterone accomplishes its effects via a complicated system of mineralocorticoid receptors [8,10]. However, a disturbance of kidney sensitivity to aldosterone has been revealed in animals with certain alterations of the nervous system. It has been established that aldosterone injections have practically no effect on sodium resorption in the kidneys of rats with a damaged sciatic nerve [1]. The flow of pathological nerve impulses elicited by the nerve damage causes disruptions in the mineralocorticoid receptor apparatus, including the hormone-receptor complex [3].

The aim of the present investigation was to study the effects of sympathetic nervous system stimulators and blockers on kidney aldosterone reception in animals with a damaged sciatic nerve.

MATERIALS AND METHODS

Experiments were carried out on male Wistar rats weighing 200 g. The sciatic nerve was cut in the upper third of the femur, and 0.2 ml of a 2 % formalin solution was injected into its central portion. The animals were administered propranolol i.p. in a dose of 0.2 mg per 100 g weight twice a day. L-DOPA was injected i.p. 1 mg per 100 g once a day, which reportedly [5] results in a stable increase of the norepinephrine concentration in the urine. 6-Hydroxydopamine (6-OHDA) i.p injections (10 mg per 100 g weight) were performed twice: on the day of sciatic nerve damage and 7 days later. The animals underwent bilateral adrenalectomy 3 days before the experiment to prevent all aldosterone receptors from binding with the endogenous hormone. Aldosterone was injected i.p. in a dose of 36 ng (1×10^{-10} mol) per 100 g weight 14 days after the nerve damage. To distinguish the specific from the nonspecific binding some animals were injected both with ^{3}H-aldosterone and its unlabeled analog in a dose which produced a 500-fold and 200-fold increase of the cytoplasmic and nuclear hormone levels, respectively. The rats were decapitated 10 min (cytoplasm) or 20 min (nuclei) after the aldosterone injection. All operations with the biological material were performed in the cold (0-4°C). The nuclei were isolated according to the method in [6]. The purity of the nuclear fraction and the number of nuclei in a unit of suspension volume were determined using a light microscope; the nuclei were stained with Azure II. The cytoplasm was obtained by 90-min centrifugation of the homogenate at 105,000 g, followed by treatment with dextrane-coal mixture in order to remove unbound ^{3}H-aldosterone. The samples of cytoplasm and nuclei were transferred to 10 ml of ZhS-8

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(Presented by P.V.Simonov, Member of the Russian Academy of Medical Sciences)

0007-4888/93/0004-0367$12.50

TABLE 1. Specific ^{3}H−Aldosterone Accretion by the Rat Kidney

Experimental conditions	Cytoplasm ^{3}H-aldosterone, pg per mg cytoplasmic protein		Nuclear ^{3}H-aldosterone, pg per 1×10^8 nuclei	
Control	1.1±0.13		16.2±0.87	
Nerve section	0.7±0.08.	$p=0.032$	8.0±0.33.	$p<0.001$
Control	2.2±0.23	12.0±0.71		
Nerve section + propranolol	2.2±0.14.	$p=1$	11.5±0.79	$p=0.772$
Control	2.3±0.11		13.8±1.31	
Nerve section + L−DOPA	1.3±0.10.	$p<0.001$	6.7±0.36.	$p=0.001$
Control	1.8±0.11			
Nerve section + 6−OHDA	1.6±0.18.	$p=0.341$		

scincillator, and their radioactivity was determined with a scintillation counter. The results were processed statistically.

RESULTS

It was established that treatment with propranolol, a blocker of both the central and peripheral β-adrenergic structures, prevented a decrease of ^{3}H-aldosterone binding with the mineralocorticoid receptors of the tubule cells in rats with a cut sciatic nerve (Table 1). Propranolol produced the same effect even when injected only on the 8th day after damage of the nerve [3]. 6-OHDA produced a selective degeneration of the catecholamine structures and, accordingly, a decrease of the norepinephrine content in the peripheral organs and tissues; it also quite effectively prevented an alteration of ^{3}H-aldosterone receptor binding in the kidneys of rats with a cut sciatic nerve (Table 1).

However, denervation of the kidney performed on the 7th day of nerve injury [3] in animals with a cut sciatic nerve does not cut off the "humoral" pathway of damage to the kidney mineralocorticoid receptors [7]. When performed on the day of nerve section, it presents the same effect as propranolol [2].

At the same time, administration of the sympathetic activator L-DOPA induced a still more pronounced decrease of ^{3}H-aldosterone accumulation in the animals with a damaged sciatic nerve (Table 1).

Thus, the pathological nerve impulses coming from the proximal end of the injured nerve result in alterations of the kidney tubule cells, including changes of the state of the mineralocorticoid receptors. As a consequence, the sensitivity to aldosterone is lowered, resulting in disturbances in the water-salt metabolism and ionic homeostasis. This is also confirmed by the results obtained in experiments with L-DOPA injections which demonstrated that the pharmacological stimulation of the organism's adrenergic activity and sympathetic tonicity causes further alterations of aldosterone reception in the kidneys of rats with a cut sciatic nerve.

On the other hand, experiments with an interruption of the reflex arc by either neurotropic drugs or kidney denervation demonstrated a normalization of mineralocorticoid receptor function in animals with a damaged nerve. Treatment of such animals with the β-adrenergic blocker propranolol demonstrated that the simultaneous interruption of the pathological impulses, reaching the kidney from the focus of nervous system damage both via the sympathetic nerves and via the adrenergic system of the brain and the hypothalamic-pituitary-peripheral endocrine glands system provides better protection of the mineralocorticoid kidney receptors from the alterative processes induced by the nerve injury than interruption of the nerve pathway alone either by kidney denervation or by distruction of the adrenergic nerve endings with 6-hydroxydopamine. It can be concluded that both central nervous and humoral mechanisms determine the function of the cellular and molecular structures which regulate kidney reception of aldosterone in animals.

The results obtained suggest that adrenoreceptor blockers may be used to attenuate the effect of factors altering the molecular mechanisms of cellular sensitivity to hormones for local damage of the nervous system.

REFERENCES

1. Ya. I. Azhipa and G. A. Filyashina, *Izv. Akad. Nauk. SSSR, Ser. Biol.*, No. 1, 19-25 (1989).
2. Yu. A. Akimov, Ya. I. Azhipa, A. A. Rodionov, *et al., Ibid.*, No. 1, 106-113 (1991).
3. Yu. A. Akimov, A. A. Rodionov, A. I. Grishchenko, *et al., Ibid.*, No. 6, 897-905 (1991).
4. Yu. A. Akimov, A. I. Grishchenko, and Ya. I. Azhipa, *Biol. Membrany*, 9, No. 10-11, 1143-1144 (1992).
5. F. I. Komarov, I. S. Zavodskaya, E. V. Moreva *et al.*, in: *Some Mechanisms of Gastroduodenal Pathology: Experimental and Clinical Evidence* [in Russian], Moscow (1984), p. 182.
6. J. Chauveau, G. Moulle, and C. Rouiller, *Exp. Cell Res.*, 11, No. 2, 317-321 (1956).
7. J. Crabbe, *J. Clin, Invest.*, 40, No. 11, 2103-2105 (1961).
8. I. S. Edelman, *Adv. Biosci.*, 7, 267-275 (1971).
9. R. S. Levin, *J. Endocr.*, 45, No. 2, 315-348 (1969).
10. D. Marver, in: *Biochemical Action of Hormones*, Vol. 12, New York-London (1985), pp. 385-431.
11. E. J. Poss, W. J. Ready, and A. Rivera, *J. Clin. Endocr. Metab.*, 19, 289-294 (1959).