MECHANISM OF ACTION OF NEUROHYPOPHYSEAL HORMONES ON SODIUM EXCRETION AND DIURESIS

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Administration of pituitrin, vasopressin, and oxytocin to rats during spontaneous micturition increases diuresis and sodium excretion by reducing tubular reabsorption. In adrenalectomized rats these preparations have no diuretic effect and increased sodium excretion is observed only after administration of vasopressin. After hypophysectomy the diuretic effect of the preparations disappears but they still increase sodium excretion. It is postulated that the diuretic effect of the neurohypophyseal hormones is connected with activation of the pituitary–adrenal system, whereas some additional mechanism is involved in their effect on sodium excretion.

KEY WORDS: *diuresis; sodium excretion; posterior pituitary lobe hormones; pituitary–adrenal cortex system.*

Pituitrin and vasopressin reduce water diuresis and often increase sodium excretion [4, 9]. This effect of antidiuretic hormone (ADH) on mammalian kidney function is associated with increased synthesis of cyclic AMP [10, 11, 18]. Meanwhile, during spontaneous micturition in rats and dogs, a diuretic effect of neurohypophyseal hormones with a subsequent parallel increase in salt excretion has been found [2, 5, 12, 13]. This action of these hormones is unconnected with any direct effect on the kidney [3].

EXPERIMENTAL METHOD

Experiments were carried out on 210 albino rats weighing 160-200 g kept in metabolic cages on a constant food and water intake. The effect of pituitrin (20 milliunits/100 g), vasopressin (20 milliunits/100 g), and oxytocin (100 milliunits/100 g, intraperitoneally) on the 24-h water intake, diuresis, and excretion of sodium, potassium (flame photometry), and creatinine (Folin's method) was studied in intact, adrenalectomized, and hypophysectomized [1] animals. Completeness of removal of the pituitary was verified by examination of the region of the sella turcica after death of the animals. The rats were used in the experiments 5 days after the operation. Adrenalectomized animals received DOCA (0.5 mg/100 g daily) by way of replacement therapy. The experiments were carried out 3 days after the operation. The effect of neurohypophyseal hormones on the ascorbic acid concentration in the adrenals also was studied [14].

EXPERIMENTAL RESULTS

After administration of the neurohypophyseal hormones to the rats with normal micturition a diuretic effect accompanied by increased sodium excretion was observed

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TABLE 1. Effect of Neurohypophyseal Hormones on 24-h Diuresis in Intact and Adrenalectomized Rats (M ± m)

Type of experiment	Number of experiment	Water intake	Diuresis	Sodium	Potasiium	Creatinine (in mg)
		ml		meq		
Effect of pituitrin						
Control	16	18,0±1,41	5,6±0,89	8,2±1,25	568±77	2,3±0,26
Experiment	16	17,9±1,13	10,0±1,44	38,2±9,25	651±63	2,0±0,12
P			<0,01	<0,01		
The same after adrenalectomy						
Control	19	20,5±1,37	9,7±0,96	21,5±3,34	562±45	1,3±0,25
Experiment	19	19,5±1,49	9,6±0,96	25,9±3,6	546±48	1,2±0,15
Effect of vasopressin						
Control	16	17,0±0,92	5,7±0,78	9,4±1,52	658±67	2,2±0,22
Experiment	16	16,8±1,55	9,6±1,35	31,4±3,22	769±105	2,2±0,28
P			<0,02	<0,02		
The same after adrenalectomy						
Control	24	18,0±0,84	8,9±0,71	15,5±3,07	797±60	1,6±0,16
Experiment	24	17,9±0,79	9,0±0,68	36,8±6,35	580±87	1,7±0,15
P				<0,001		
Effect of oxytocin						
Control	17	20,8±1,22	7,0±0,72	11,7±1,34	498±45	2,5±0,24
Experiment	17	21,0±1,56	10,8±0,87	62,1±15,45	734±37	2,7±0,32
P			<0,01	<0,001		
The same after adrenalectomy						
Control	21	18,6±1,10	8,7±0,89	23,0±5,80	580±62	1,7±0,16
Experiment	21	16,6±1,27	8,0±0,75	24,6±6,80	435±68	1,4±0,14

Note. Here and in Table 2, level of significance (P) is shown only where difference is significant ($P < 0.05$).

TABLE 2. Effect of Neurohypophyseal Hormones on 24-h Diuresis in Intact and Hypophysectomized Rats (M ± m)

Type of experiment	Number of experiment	Water intake	Diuresis	Sodium	Potassium	Creatinine (in mg)
		ml		meq		
Effect of pituitrin						
Control	19	18,8±1,65	6,3±0,58	9,7±1,27	858±65	2,1±0,17
Experiment	19	17,9±1,05	9,7±1,14	42,5±6,78	863±48	1,9±0,14
P			<0,01	<0,001		
The same after hypophysectomy						
Control	30	21,7±0,94	12,4±1,0	14,5±1,48	830±76	1,6±0,12
Experiment	29	22,5±1,09	13,3±1,0	61,0±8,0	793±71	1,6±0,13
P				<0,001		
Effect of vasopressin						
Control	16	17,9±0,78	4,4±0,41	12,0±1,18	654±96	3,4±0,26
Experiment	16	18,3±0,99	9,7±1,27	37,8±4,47	680±55	3,3±0,25
P			<0,001	<0,001		
The same after hypophysectomy						
Control	19	20,0±1,06	10,0±0,75	12,7±2,64	923±100	2,6±0,24
Experiment	19	22,0±1,36	10,9±0,90	37,1±6,4	982±104	2,4±0,29
P				<0,001		
Effect of oxytocin						
Control	20	21,6±0,78	8,0±0,54	13,5±1,29	619±51	3,1±0,18
Experiment	20	22,0±0,78	13,8±0,72	48,2±3,48	622±51	3,3±,017
P			<0,001	<0,001		
The same after hypophysectomy						
Control	20	24,5±1,80	15,8±1,32	17,5±1,92	696±70	2,2±0,24
Experiment	20	23,0±1,85	14,7±1,35	37,2±5,55	664±71	2,2±0,25
				<0,001		

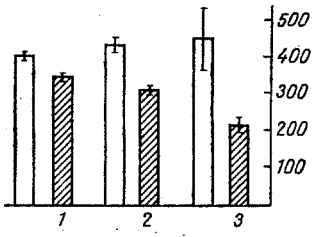

Fig. 1. Effect of neurohypophyseal hormones on ascorbic acid concentration in adrenals of rats 6 h after a single injection. Unshaded columns — control; shaded columns — after administration of: 1) pituitrin, 2) vasopressin, 3) oxytocin. Ordinate, ascorbic acid concentration (in mg%).

(Table 1). This effect depended on a decrease in tubular reabsorption, for the 24-h excretion of creatinine, a measure of filtration, was unchanged. This agreed with previous observations in the writer's laboratory [2, 12].

Considering that the direct effect of ADH on the kidney is expressed as increased reabsorption of water in the distal tubules, the diuretic action of neurohypophyseal hormones must be assumed to be due to extrarenal factors. Since adrenocortical hormones (glucocorticoids) increase the excretion of water and salt [7, 8, 15], the action of neurohypophyseal hormones was investigated after adrenalectomy. Experiments to study the effect of pituitrin, vasopressin, and oxytocin on spontaneous diuresis in adrenalectomized rats showed no diuretic effect of the hormones in this case, and sodium excretion continued only after the administration of vasopressin (Table 1). These results agreed with those of corresponding experiments on dogs [3]. The fact was noted that after adrenalectomy, despite replacement therapy, much more sodium was excreted in 24 h than in the same experiments before the operation. The increased sodium loss possibly created an unfavorable background for the action of pituitrin and oxytocin in increasing sodium excretion.

The hormones given caused a marked decrease in the ascorbic acid concentration in the adrenals (Fig. 1), in agreement with observations by other workers [19].

The decrease in the ascorbic acid concentration in the adrenals confirmed that the diuretic action of the neurohypophyseal hormones could be linked with increased glucocorticoid production.

Since neurohypophyseal hormones can stimulate ACTH secretion [6, 16, 17], it was suggested that the cause of the phenomena studied could be the effect of octapeptides on the adenohypophysis. Experiments on hypophysectomized animals receiving pituitrin, vasopressin, and oxytocin showed that no diuretic effect developed under these conditions but the effect on sodium excretion continued (Table 2).

It can accordingly be concluded that the diuretic action of the neurohypophyseal hormones takes place with the participation of the pituitary—adrenal cortex system, whereas the effect on sodium excretion, although to some extent linked with the adrenals, also requires the participation of some additional mechanism that requires further study.

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