ROLE OF ALDOSTERONE IN THE INITIAL STAGE OF TWO FORMS OF EXPERIMENTAL VASORENAL HYPERTENSION

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The role of the mineralocorticoid function of the adrenals in rats was studied during the development of two forms of experimental vasorenal hypertension (stenosis of one renal artery while the opposite kidney remains intact, and ischemia of the solitary kidney). The sodium-retaining action of aldosterone was blocked immediately after the operation by Verospiron. In rats with unilateral stenosis of the renal artery and the opposite kidney intact, a marked increase in the daily urinary aldosterone excretion was observed; in animals with ischemia of the solitary kidney no activation of adrenal mineralocorticoid function was observed. Verospiron sharply inhibited the development of the first form of renal hypertension but did not affect the blood pressure in rats with stenosis of the artery of the solitary kidney.

KEY WORDS: vasorenal hypertension; aldosterone; Verospiron.

An increase in aldosterone output is observed in experimental renal hypertension mainly in the early stages of the disease [4] whereas in the chronic phase the aldosterone level is usually within normal limits. However, the mineralocorticoid function of the adrenals is not always activated in the acute stage of renal hypertension. The response of the adrenal cortex has been shown to depend on the form of vasorenal hypertension [8, 9, 13, 14]: In the case of stenosis of one renal artery while the second kidney is intact, the adrenal mineralocorticoid function is increased, whereas in ischemia of the solitary kidney aldosterone production is unchanged. Admittedly, this view is not universally accepted [6]. On the other hand, marked hyperaldosteronism does not always lead to elevation of the arterial blood pressure (BP), for example, in edema, heart failure, and so on. Even when hypertension and hyperaldosteronism are combined it is difficult to be certain whether the latter is the cause of the raised BP.

In an attempt to shed light on this problem the effect of blocking the sodium-retaining effect of aldosterone on the development of two forms of vasorenal hypertension was studied in rats.

EXPERIMENTAL METHOD

Experiments were carried out on 102 male rats weighing 180-250 g. The right renal artery was constricted in 54 of these animals [3]. In the rest one kidney was removed 1 week before the production of ischemia in the second kidney. Immediately after stenosis of the artery, administration of 12.5 mg Verospiron (an analog of aldactone, which blocks the sodium-retaining effects of aldosterone in the distal renal tubules; a product of Gedeon Richter, Hungary) in 1 ml aqueous solution into the esophagus was commenced on half of the animals of each group. The remaining animals received tap water. Every week in all the animals the systolic pressure was measured in the caudal artery by a photoplethysmographic method and the 24-hourly urinary aldosterone excretion was determined by thin-layer chromatography [12]. The animals were killed 4 weeks after the operation.

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TABLE 1. Dynamics of BP (in mm Hg) in Rats with Two Forms of Vasorenal Hypertension (M±m)

Form of hypertension	Group	Before operation	Weeks after production of renal ischemia			
			1	2	3	4
Unilateral stenosis of renal artery	Control	107,8±3,7	135,0±5,5	146,4±6,5	155,7±6,5	153,1±9,8
	P		<0,001	<0,001	<0,004	<0,001
	Experim. (Verospiron)	110,9±2,6	102,5±6,4	121,4±5,3	124,5±3,1	127,5±4,2
	P				<0,001	<0,001
Ischemia of solitary kidney	Control	115,8±4,2	110,0±3,3	115,8±10,5	137,0±4,3	138,6±5,5
	P				<0,002	<0,007
	Experim. (Verospiron)	118,6±2,6	118,0±5,5	120,1±4,0	135,8±6,1	134,0±5,4
	P				<0,001	<0,05

TABLE 2. Urinary Aldosterone Excretion (in μg/day) in Rats with Two Forms of Vasorenal Hypertension (M±m)

Form of hypertension	Group	Before operation	Weeks after production of renal ischemia			
			1	2	3	4
Unilateral stenosis of renal artery	Control	1,03±0,21	1,83±0,21	1,23±0,11	1,24±0,11	1,68±0,04
	P		<0,01			<0,001
	Experim. (Verospiron)	0,90±0,15	1,13±0,02	1,52±0,14	1,26±0,08	2,38±0,31
	P		<0,005	<0,005	<0,005	<0,003
Ischemia of solitary kidney	Control	1,11±0,08	1,38±0,19	1,11±0,18	1,23±0,15	1,22±0,04
	Experim. (Verospiron)	1,03±0,03	0,75±0,14	1,83±0,29	1,27±0,04	1,69±0,08
	P			<0,05		<0,02

EXPERIMENTAL RESULTS AND DISCUSSION

In rats with unilateral stenosis of the renal artery and the opposite kidney intact, and not receiving Verospiron, the BP reached a maximum 3 weeks after the operation. Ischemia of the solitary kidney also led to the development of persistent hypertension (Table 1).

In rats with the first form of hypertension the urinary aldosterone excretion was greatly increased 1 week after the operation. After 2 and 3 weeks the 24-hourly urinary aldosterone excretion fell to normal, and toward the end of the experiment (4 weeks) it again rose a little. In rats with ischemia of the solitary kidney the aldosterone excretion remained substantially unchanged throughout the experiment (Table 2).

In rats with unilateral renal ischemia (the opposite kidney intact) Verospiron completely inhibited the development of hypertension for 2 weeks. The BP of these animals started to rise only after the third week of the experiment. This increase could be due to tachyphylaxis of the animal to Verospiron during its prolonged administration [2]. However, the rise of BP was still much less than in control rats with the same form of hypertension. In animals with ischemia of the solitary kidney Verospiron had no effect on the development of hypertension.

The results of these experiments point clearly to the pathogenetic difference between the two forms of vasorenal hypertension in rats. In the animals with unilateral renal ischemia and the opposite kidney intact, the early increase in aldosterone production and sodium retention in the body was evidently one of the basic conditions for the development of hypertension, for removal of this condition prevented the BP from rising. The important role of adrenal mineralocorticoid function in this form of vasorenal hypertension is confirmed by other evidence of activation of the adrenal cortex [1, 4, 7, 10, 11].

Meanwhile, in the animals with stenosis of the artery of the solitary kidney hyperaldosteronism was frequently absent [9, 13, 14] and, as these experiments showed, blocking the sodium-retaining effect of aldosterone did not prevent hypertension from developing. The role of aldosterone in this form of hypertension and, in particular, in the phase of its development was not therefore significant. The increase in its production sometimes observed in this type of hypertension can be regarded as nothing more than a factor aggravating the disease.

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