THE RENIN CONTENT IN THE KIDNEYS OF PERSONS HAVING DIED OF HYPERTONIC DISEASE AND IN RABBITS WITH EXPERIMENTAL COARCTATION HYPERTONIA AND CHOLESTEROL ATHEROSCLEROSIS

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The role of the kidney factor in hypertonic disease has not been definitively cleared up. In the working out of this problem, naturally, interest attaches to the investigation of the renin content in the kidneys in hypertonic disease.

In the literature there are only a small number of articles on this question, and the work described in them dates from before the discovery of the enzymatic process between renin and hypertensinogen.

Our object was to determine the renin content in the kidneys of persons who had died of hypertonic diesease (in the various forms of this disease) and also in the kidneys of rabbits eith experimental coarctation hypertonia and cholest erolatherosclerosis.

METHODS

In order to obtain extracts of renin from the kidneys of patients who had died of hypertonic disease we worked immediately after autopsy. For comparison we also determined the renin in the kidneys of patients who had died from various traumas.

The kidneys of rabbits with experimental coarctation of the aorta and cholesterol atherosclerosis were taken soon after the animal was killed. The kidneys of healthy rabbits were used as a control.

To obtain preparations of renin the cortex of the kidneys, dried with alcohol and ether, was extracted with a 2% solution of sodium chloride.

We judged the amount of renin in the extracts obtained, and thus in the kidneys, from the blood-pressure reaction in dogs in an acute experiment in which we injected the renin preparations and injected hypertensin obtained after the incubation of renin with hypertensinogen at a temperature of 37° for 15 minutes, followed by precipitation of the proteins with a volume of alcohol four times as large. The hypertensinogen was prepared from normal horse serum by fractional precipitation of the globulins with ammonium sulfate. Hypertensin has a certain advantage over renin: the presence of a smaller amount of renin can be detected by using it than by the direct injection of the same enzyme into the animal.

The acute experiment was performed on dogs weighing 5 to 15 kg under morphine-barbamil* narcosis.

*Barbamil = amytal – translator.

The extracts were injected into the jugular or femoral vein. The pressure in the artery was recorded on a kymograph.

In the first part of the work of determining the renin in the kidneys of persons who had died from hypertonic disease, we always injected into a dog an amount of renin preparation corresponding to 2 g of kidney tissue.

In the work with the rabbits we were able to judge the amount of renin by the reaction of the blood pressure after injection of the dog with hypertensin.

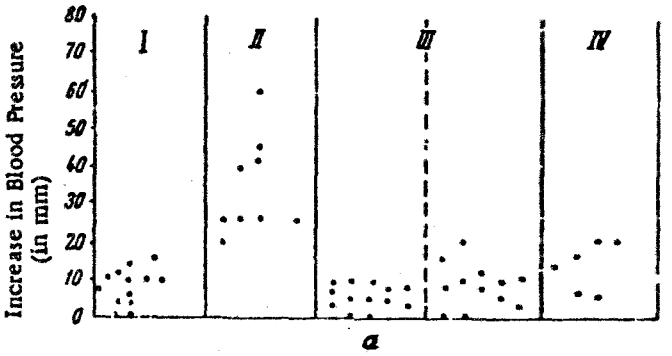
The experiments were arranged as follows. On the same day extract of renin was prepared from the kidneys of a healthy and an experimental rabbit. The content of renin in the preparations was determined from their ability to form hypertensin on incubation with hypertensinogen. In order to obtain the most exact results we looked for the optimum ratios of concentration of the enzyme and of the substrate obtained from each pair of kidneys examined, and this permitted us to judge the amount of renin in the kidneys of the healthy and the sick rabbit. The hypertensin obtained in the incubation of renin from the kidneys of the healthy and the sick rabbit was tested on the same dog.

RESULTS

We investigated the renin content in the kidneys of 4 groups of persons who had died. The first group consisted of 14 persons ranging in age from 18 to 57 who had died of various injuries. A period of 12 to 25 hours elapsed between death and autopsy. The rise of blood pressure in dogs on injection of the extract from the kidneys of these patients in an acute experiment did not exceed 15 mm.

The second group consisted of 7 patients with hypertonic disease with a malignant course and of 4 with symptomatic malignant hypertonia, a total of 11 persons, ranging in age from 29 to 51. All these patients died with symptoms of kidney insufficiency (uremia). A period of 5 to 30 hours elapsed from death to autopsy. When the extracts from kidneys of these patients were injected into dogs the rise in blood pressure varied from 20 to 80 mm. The renin content in the blood of 7 persons was investigated while they were alive, but it was detected in only four [1].

In the third group were 25 patients with hypertonic disease with a usual course, ranging in age from 22 to 69, including 13 with a predominant heart affection. The time elapsing from death to autopsy was 3 to 30 hours. The rise in blood pressure in dogs on injection of the extracts from the kidneys of patients with a predominant heart infection did not exceed 10 mm. When dogs were injected with extract from the kidneys from the remaining patients of this group the maximum rise in their blood pressure was 20 mm. Pronounced sclerosis of the kidneys was detected on autopsy in 11 patients of this group.



Rise in blood pressure in dogs on injection of extract from kidneys of persons who had died from hypertonic disease. I) Patients who died of various injuries; II) Persons who died from malignant hypertonia; III) Patients with hypertonic disease with usual course (a – with predominant heart affection); IV) Patients with chronic nephritis.

The fourth group consisted of 6 patients with chronic nephritis, aged 25 to 52; a period of 3 to 30 hours elapsed from death to autopsy. On the injection of extract from the kidneys of these patients the blood pressure rose 5-20 mm.

From the data adduced (see figure) it follows that the greatest rise in blood pressure in the dogs was observed with the injection of preparations of renin isolated from the kidneys of the patients with hypertonic disease taking a malignant course. Extracts from the kidneys of persons who had died of injuries evoked a slight rise in the blood pressure, a fact that indicated that the renin content in the kidneys of these individuals was not high. An even smaller rise in the blood pressure was observed in the case of hypertonic disease with predominant heart affection.

Since the time elapsing from death to autopsy varied with different individuals in our investigations, we conducted experiments to determine the influence of postmortem autolysis on the renin content.

In the experiments of the first series a preparation of renin was obtained from part of a kidney of a freshly killed dog and the amount of amino groups in this tissue was determined. The remaining part of the kidney was kept at a temperature of 10 to 18° for 2-48 hours. At fixed time intervals the amount of renin and of amino groups was determined in this tissue (the former biologically and the latter by Pope and Stevens' method). The amount of amino groups in the kidney increased with the passage of time, indicating autolysis of the kidney tissue under the indicated conditions. The amount of renin, however, either decreased slightly or remained constant (Table 1).

In the experiments of the second series one kidney was taken from a freshly killed dog and a preparation of renin was made from it. The dog's body was kept at a temperature of 8-10°. After 12 or 18 hours the second kidney was removed, and a preparation of renin was made from it also. No differences were noted in the amount of pressor substance in the two kidneys.

TABLE 1

Influence of Autolysis of Kidney Tissue on Its Content of Renin and Amino Groups

Time of examination of kidney tissue (after death of animal)	Temperature	Amount of amino groups (in mg per 1 g of renal cortex	Rise in blood pressure under influence of hypertensin (in mm mercury)	
Immediately		0.76	20	
17 hours later	18°	2.54	22	—
Immediately		1.36	10	
48 hours later	19°	3.07	10	—
Immediately		0.8	—	30
22 hours later	19°	4.37	—	30
Immediately		1.45	15	—
10 hours later		2.35	16	—
Immediately		0.98	6	12
18 hours later	18°	2.50	4	10
Immediately		0.64	30	30
24 hours later	18°	0.93	30	32
Immediately		1.40	22	26
22 hours later	19°	2.07	—	8
Immediately		0.69	—	15
4 hours later	19°	0.94	—	17
7 hours later	19°	0.05	—	17
Immediately		0.57	—	15
2 hours later	19°	0.76	—	17
4 hours later	19°	0.95	—	16
6 hours later	19°	1.23	—	16
Immediately		1.44	—	14
22 hours later	20°	2.01	—	20
48 hours later	20°	2.62	—	20
Immediately		0.80	—	2
24 hours later	18°	0.92	—	2
48 hours later	18°	2.48	—	2
Immediately		0.28	—	22
20 hours later	20°	0.75	—	16

TABLE 2

Content of Renin in Kidneys of Rabbits with Experimental Ischemia of the Kidneys

Date	No. of rabbit	Duration of Hypertonia	Blood pressure (in mm)	Rabbit	Rise in blood pressure (in mm mercury)	
					on injection of hypertensin	on injection of renin
Oct. 14				Healthy	28	32
				with hypertonia	34	36
Nov. 22	4	2 months	180	Healthy	38	—
	4	2 "		with hypertonia	42	—
Dec. 19	29	1 month 4 days	180	Healthy	18	10
				with hypertonia	28	28
Jan. 15	33	2 "	160	Healthy	22	—
				with hypertonia	22	—
Feb. 4	21	3,5 "	250	Healthy	16	
				with hypertonia	28	
Mar. 19	9	5 "	190	Healthy	34	13
				with hypertonia	34	12
Feb. 25	7	4 "	180	Healthy	20	—
				with hypertonia	30	—
May 29	45	1 "	190	Healthy	14	—
				with hypertonia	20	—
June 25	44	1 month 16 days	190	Healthy	28	—
				with hypertonia	38	—
May 25	40	3 " 15 "	180	Healthy	28	—
				with hypertonia	68	—

Note: The amount of preparation of renin and of hypertensin injected in the rabbits was the same in all the experiments – 2 ml.

The results of the experiments show that postmortem autolysis does not affect the quantity of renin in the kidneys, and therefore, the data obtained on the varying content of renin in the kidneys of persons who had died from various forms of hypertonia, and also of patients who had died of injuries, are fully comparable among themselves, and they indicate the presence of pressor substance in the kidneys while the patients were alive, and not its postmortem formation.

The second part of the work was performed on rabbits. Ten rabbits with experimental coarctation of the aorta, and 10 healthy rabbits, were examined for renin content in the kidneys. The duration of the hypertonia was from 1 month 4 days to 5 months.

As the experiments showed, in 2 cases out of 10 the blood pressure was the same on injection of extracts from the kidneys of healthy rabbits and extracts from the kidneys of rabbits with experimental coarctation hypertonia; in the other 8 cases it was higher when extracts from the kidneys of the sick animals were injected (Table 2)

In order to determine to what extent the change which we observed in the renin content in the kidneys was specific, we investigated the change in the renin content in the kidneys of 17 rabbits with experimental cholesterol atherosclerosis (16 healthy rabbits were also examined as a control). In this series of experiments a highly contrasting picture was observed. In 10 of the 17 animals with experimental cholesterol atherosclerosis the amount of renin in the kidneys was less than in the healthy rabbits. In 3 cases the renin content in the kidneys of both experimental and healthy rabbits was the same; in only 4 cases was there more renin in the kidneys of experimental rabbits than in the normal rabbits. We found no evidence that the renin content depended on how pronounced the atherosclerosis of the aorta was.

Thus; while the renin content in the kidneys of rabbits with coarctation of the aorta was higher than the normal amount, in the kidneys of rabbits with experimental cholesterol atherosclerosis it was in most cases less than in healthy animals.

LITERATURE CITED

[1] Yu. A. Serebrovskaya, Yu. D. Vadkovskaya and L. E. Petrova, Ter. Arkh. Vol. 25, No. 1, pp. 56-62 (1953)