FILTRATION AND REABSORPTION OF THE DENERVATED KIDNEY UNDER NORMAL CONDITIONS AND UNDER THE INFLUENCE OF VARIOUS NEUROTROPIC SUBSTANCES

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Many authors have reported [5, 7, 16, 20] that there is no functional difference between an intact and a denervated kidney, either under normal conditions, or when there is an increased load (water, salt, dehydration etc). On the other hand, many other investigators have found that the denervated organ is not functionally equivalent to the intact kidney: there is a lag of water diuresis [9, 10, 11, 17], and in response to salt loads there is an increased excretion of chlorides [6, 11], and water and sodium [18, 19].

Widely divergent results have been obtained on studies of filtration and reabsorption: some authors [5, 6, 7, 15] found no difference between the intact and denervated organs, while others [18] found an increased reabsorption without any appreciable alteration of filtration in the denervated kidney. Some investigators [8] found that filtration and reabsorption in the denervated kidney fluctuated.

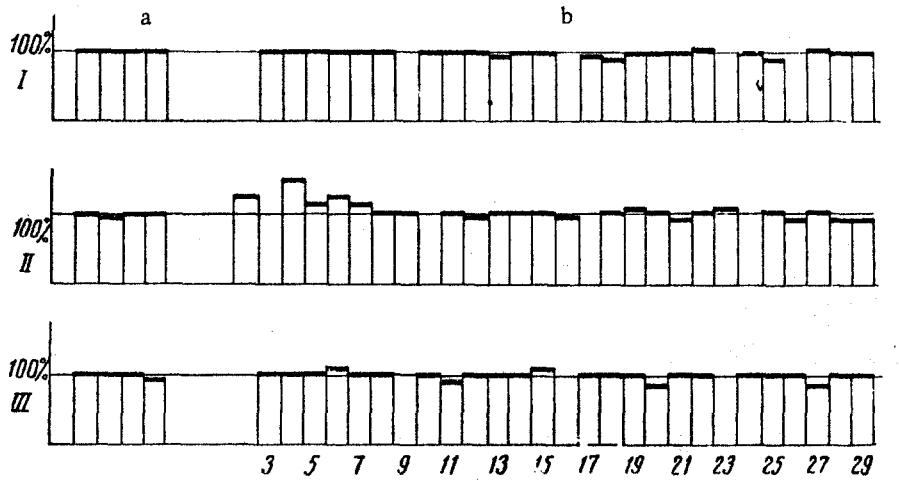

Fig. 1. Ratio of the diureses of the left (denervated) and right (unoperated) kidney, expressed as a percentage. a) Experiments before denervation; b) experiments after denervation; I) dog Dinka; II) dog Naida; III) dog Chernushka. The figures on the horizontal axis indicate the days after the operation.

The object of the present investigation has been to make a comparative study of filtration and reabsorption in the intact and denervated kidney, under normal conditions, and under the influence of various neurotropic substances which alter diuresis.

METHOD

The method of Pavlov-Orbeli was used in 309 experiments on 12 dogs. In eight, one kidney was denervated by the usual method (division of the visible nerve branches, removal of the adventitia with the vessels and the ureter, and subsequent treatment with phenol solution).

The effect of denervation was investigated for a month after the operation, because it has been reported, and confirmed recently [8], that nerve endings are to be found in the kidney $1\frac{1}{2}$ months after denervation. The experiments were carried out in the morning 14-16 hours after the animals had fed; they lasted 5-6 hours, during which time every 20 minutes recordings were made of spontaneous diuresis, and of diuresis after a water load (30-40 ml of a 10% water-milk mixture per kg weight). During the experiment we repeatedly determined filtration and reabsorption in terms of endogenous creatinin, which was measured in the urine by Folin's method, and in the body by Folin's method as modified by E. B. Berkhin [1]. In two dogs, in addition, a study was made by Fol'gard's method of the excretion of chlorides. In some experiments blood flow (plasma flow) was measured by the use of cardiotrast. In some of the experiments we also investigated the influence of novocain (10-15 mg/kg intravenously) and of aminasine (0.5-1 mg/kg intravenously) during spontaneous and water diuresis.

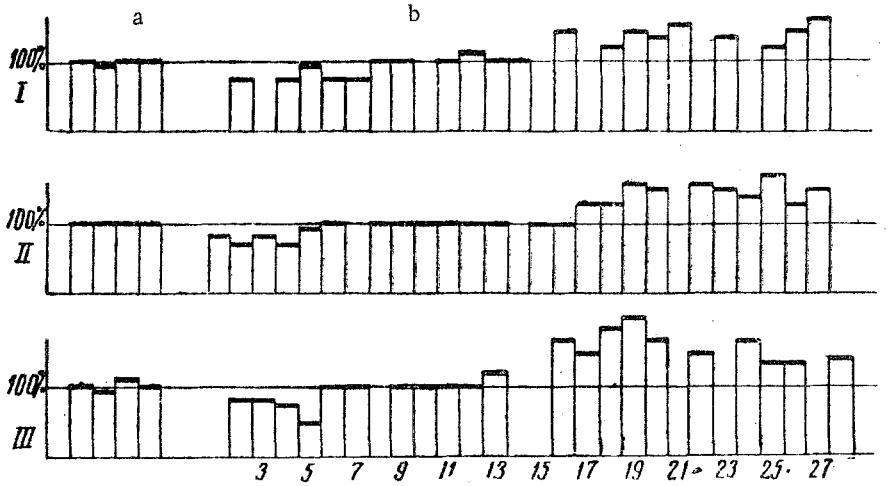

Fig. 2. Ratio of tubular reabsorption of the left (denervated) kidney and reabsorption (taken as 100%) of the right (intact) kidney. a) Experiments after denervation; I) dog Katun'; II) dog Chernushka; III) dog Naida. The figures on the horizontal axis indicate days after the operation.

TABLE 1. Diuresis and Excretion of Chlorides Before and After Denervation of the Left Kidney

Time	dog Dinka				dog Chernushka			
	Diuresis (in ml per min)		Amount of Chlorides (in mg)		Diuresis (in ml per min)		Chlorides (in mg)	
	Right kidney	Left kidney	Right kidney	Left kidney	Right kidney	Left kidney	Right kidney	Left kidney
Experiments of 12/II/1959 (before denervation)								
10 hours 20 minutes	2.8	3.0	27.1	27.3	3.4	3.4	36.4	35.0
10 " 40 "	3.0	3.0	27.0	27.6	3.2	3.2	32.0	32.0
11 " 00 "	3.4	3.4	31.3	30.6	3.2	3.2	32.0	31.3
11 " 20 "	2.8	2.8	26.6	27.4	3.0	3.0	28.8	29.4
11 " 40 "	3.0	3.0	27.9	27.9	2.8	2.8	28.0	28.2
Experiments of 17/III/1959 (after denervation)								
10 hours 20 minutes	2.0	2.0	34.0	32.4	1.2	1.2	12.0	12.2
10 " 40 "	1.0	1.0	10.4	11.0	1.4	1.4	14.0	13.8
11 " 00 "	1.2	1.2	13.2	13.8	1.2	1.2	13.6	12.4
11 " 20 "	1.2	1.4	13.2	15.4	1.0	1.0	9.6	9.5
11 " 40 "	1.2	1.2	11.7	12.6	1.0	1.0	9.0	9.5

RESULTS

In control experiments carried out before denervation it was shown that the extent of the diuresis, filtration, and reabsorption of each kidney, and the rate of excretion of chlorides varied during the different days of the experiment. We were most interested in the ratio of the corresponding quantities for the two kidneys. It was fairly constant: in most of the animals the left and right kidneys functioned synchronously, liberating the same amount of

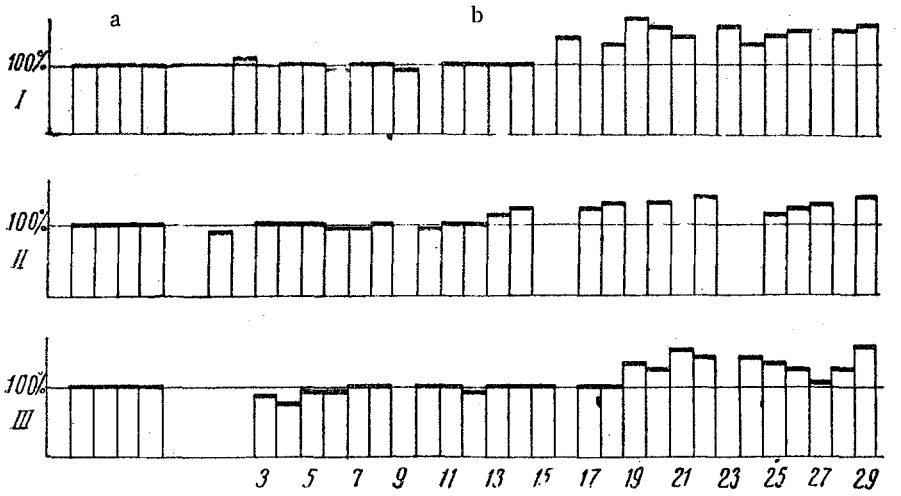

Fig. 3. Ratio of the glomerular filtration of the left (denervated) kidney and filtration (taken as 100%) of the right (intact) kidney. a) Experiments before denervation; b) experiments after denervation; I) dog Katun'; II) dog Naida; III) dog Chernushka. The figures on the horizontal axis indicate days after the operation.

urine and chloride. The amounts of glomerular filtration, renal plasma flow, and tubular reabsorption were approximately the same in both kidneys. The ratio of the amounts of urine excreted by the two kidneys after denervation showed no change in 4 dogs, and in 3 it was disturbed only for the first 5-7 days, and then recovered (Fig. 1). In one dog only did the denervated kidney excrete less urine than the other during the whole period of observation.

TABLE 2. Influence of Novocain on Diuresis, Filtration, and Reabsorption of the Intact (Right) and Denervated (Left) Kidney (dog Sil'va, weight 23 g. Experiment of 9/XII/1958)

Time	Diuresis (in ml per min)		Concentration index for creatinine		Filtration (in ml/min)		Percent reabsorption	
	Right kidney	Left kidney	Right kidney	Left kidney	Right kidney	Left kidney	Right kidney	Left kidney
Before the injection of novocain								
10 hours 40 minutes	0.41	0.22	58.0	94.8	23.8	20.8	98.28	98.94
11 " 00 "	0.40	0.21	61.0	101.2	24.4	21.2	98.34	99.01
After the injection of 0.01 g/kg novocain intravenously								
11 hours 20 minutes	0.32	0.17	76.0	124.6	24.3	21.2	98.68	99.20
11 " 40 "	0.65	0.30	48.0	89.7	31.2	26.9	97.91	98.88
12 " 00 "	0.75	0.40	42.0	65.0	31.5	26.0	97.62	98.46
12 " 20 "	0.75	0.40	34.0	57.2	25.5	22.9	97.06	98.25

From an analysis of more than 1000 clearance periods, the phasic nature of the changes of reabsorption and filtration in the denervated kidney were clearly established. In the first 5 days after denervation, in most of the dogs reabsorption was reduced in the denervated kidney below its value in the other; it then increased, and from the 12-18th day until the end of the observation period, reabsorption in the denervated kidney was greater than in the other (Fig. 2).

During the first days after denervation, glomerular filtration did not undergo any marked change, and from about the 10-12th day onwards it was greater than in the unoperated kidney (Fig. 3). An exception was the dog Sil'va, in whom the filtration rate on the denervated side was far below that on the other. As a result of denervation, the renal plasma flow was increased, and the filtration fraction thereby reduced, which indicated a reduction in tone chiefly of the efferent vessels of the glomeruli. Consequently, the period of enhanced glomerular filtration on the denervated side corresponded approximately with the period of increased reabsorption; as we pointed out above, diuresis did not undergo any great change. The denervation did not alter the excretion of chlorides with the urine (Table 1).

TABLE 3. Influence of Aminasine on the Water Diuresis, Filtration, and Reabsorption of the Intact (Right) and Denervated (Left) Kidney (dog Dinka, weight 12 kg. Experiment of 24/III/1959)

Time	Diuresis (in ml per min)		Concentration index for creatinine		Filtration (in ml/min)		Percentage reabsorption	
	Right kidney	Left kidney	Right kidney	Left kidney	Right kidney	Left kidney	Right kidney	Left kidney
At 11.00 hours a water load of 500 ml was given								
11 hours 00 minutes	0.06	0.06	302.0	426.5	18.1	25.5	99.66	99.76
11 " 20 "	0.13	0.13	152.9	212.0	19.8	27.5	99.34	99.52
11 " 40 "	1.30	1.35	16.7	21.1	21.7	28.4	94.04	95.24
At 11.40 hours 0.5 mg/kg aminasine were injected intravenously								
12 hours 00 minutes	1.00	1.00	17.5	21.6	17.5	21.6	94.28	95.32
12 " 20 "	0.90	0.85	18.0	23.5	16.2	1.9	94.44	95.74
12 " 40 "	0.85	0.85	17.7	23.5	15.0	1.9	94.35	95.74
13 " 00 "	0.70	0.68	21.4	29.4	15.0	2.0	95.32	96.60

To determine the effect of innervation on the increased diuresis induced by a water load, in 72 experiments we compared the water diureses of the intact and denervated kidneys. According to published reports [3, 14], the first phase of water diuresis is associated chiefly with nervous influences from the digestive tract. We therefore paid attention principally to the urinary excretion during the first 40-80 minutes after drinking. In 67 out of 72 experiments it was found that the change of water diuresis was the same in both kidneys; the change of diuresis, filtration, and reabsorption was expressed as a percentage of the original values.

It was interesting to compare the response of the intact and denervated kidneys to the injection of drugs influencing urinary excretion. Under these conditions the effect of the innervation might show up more strongly. We therefore studied the influence of novocain and aminasine on the function of the intact and of the denervated kidney. In our experiments novocain strongly inhibited diuresis through an increased reabsorption, a result in line with published reports [2, 18]. Diuresis did not change spontaneously, but in many experiments it was actually increased 20-60 minutes after the injection of novocain, chiefly on account of a reduced reabsorption. In 14 experiments on dogs in which one kidney had been denervated, we measured diuresis and filtration and reabsorption before and after the injection. In all the experiments, whether the novocain was given during a period of spontaneous or of water diuresis, the denervated and intact kidneys responded in the same way (Table 2).

It has been reported [13] and our previous observations have shown [4, 12] that aminasine has an antidiuretic influence which is increased during a water diuresis, and that the effect is brought about by an increased reabsorption and a short-lasting reduction of filtration. In 18 experiments we studied the influence of aminasine on urinary secretion in animals in which one kidney had been denervated. In 14 experiments the responses of both kidneys to the aminasine injection were the same (Table 3), and in 4 the reduction of the diuresis was more marked on the denervated side. This latter effect was due chiefly to a marked increase of reabsorption on the denervated side.

From our experiments we may draw the following conclusions: 1) renal denervation causes no fundamental changes of spontaneous or water diuresis; 2) after 1-2 weeks, there occurs a period when filtration and reabsorption is increased on the denervated side; 3) alterations of function induced by the injection of novocain or aminasine are the same in the intact and in the denervated kidney.

SUMMARY

Chronic experiments on 8 dogs were made to study the effect of renal denervation on spontaneous and water diuresis, filtration and reabsorption, chloride excretion and renal blood flow; the observations were made during the first month after the operation. From the 10-12th day after denervation onwards, filtration and reabsorption in the denervated kidney were greater than in the intact one; there were no material changes of diuresis or chloride excretion. The intact and denervated kidneys reacted in the same way to novocain and aminasine (chlorpromasine) administration.

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