CHANGES IN FILTRATION, REABSORPTION, AND RENAL OUTFLOW IN DOGS GIVEN WATER BY VARIOUS ROUTES

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(Received January 15, 1957. Presented by Active Member of the AMN SSSR V. N. Chernigovskii)

In studying water diuresis, we have become interested in changes occurring in the kidneys in response to giving large amounts of fluid. Determination of glomerular filtration and reabsorption in the tubules has shown which process accounts for the increased diuresis occurring after normal drinking, or after parenteral injection of fluid. Also, because urinary excretion is closely associated with renal blood supply, we have studied the effect of a water load on the renal circulation.

Most authors hold that in water diuresis there is a reduced reabsorption, while filtration does not increase, and may even be reduced [5, 6, 11]. Other workers have observed both a reduced reabsorption and an increased filtration [7, 8]. H. Ludemann and his co-workers [9], who worked with large water loads, ascribed the increased diuresis chiefly to an increase in the filtration rate.

The few published reports on alterations to the renal circulation resulting from water diuresis are based mainly on acute experiments. A.Walker and his co-workers [12] measured the blood flow through the kidney with a Rein stromuhr, and collected the urine by a catheter; they found that renal flow plays no part in the increased diuresis resulting from a water load or from mercury diuretics, and is only slightly increased after the injection of purines. V. V. Zakusov [4] who used the same method, found there was an increased renal blood flow and diuresis in response to diuretics, but discovered no definite relationship between them. We have read no published accounts of results obtained in chronic experiments. Very little work has been done on changes in the filtration rate, tubular reabsorption, and renal circulation induced by a parenteral injection of fluid.

METHOD

The investigations were carried out on dogs with ureteric fistulas. The urine was collected, as a rule, at 15 minute intervals, ans it was therefore possible to observe changes in the reabsorption and renal circulation. In most of the experiments, the water load consisted of 30 ml per kg body weight of water mixed with 10 % milk; intraveous injections of isotonic sodium chloride solutions were given, and in other experiments glucose solutions were used; the volume of fluid injected was 20-25 ml per kg body weight, and it was given at a rate of 20 ml per minute.

The filtration and reabsorption were measured by the creatinin method. The urine creatinin was determined by the well-known Folin method, while for the blood creatinin (endogenous creatinin) we used our own modification of the method [1]. The renal blood flow, or more accurately the "plasma flow" was measured by the use of phenol red. We found no published method of measuring renal blood flow in animals using phenol red, and therefore in collaboration with E. V. Chaikovskaya [2] we first worked out an appropriate method using a

TABLE 1

Effect of a Water Load on Filtration and Reabsorption (dog Damka, experiment No. 2, April 12, 1952)

Time (hours min.)	Amount of urine (in ml)		Concentration of creatinin (in mg %)		Concentration index	Filtration (in ml/min)	Reabsorption	Filtrate, excreted č urine
	total	per min.	in urine	in blood			in percentage	
10.00—11.00	12	0,20	168,1	1,02	164,70	32,94	99,39	0,61
(Water load of 500 ml given at 11 a.m.)								
11.30—	57	1,90	37,0	—	36,27	68,91	97,24	2,76
12.00	122	4,07	13,5	--	13,92	56,65	92,82	7,18
12.30	91	3,03	13,9	0,97	14,33	43,42	93,02	6,98
13.00	62	2,07	31,2	—	32,15	66,65	96,89	3,11
13.30	40	1,33	18,9	—	19,49	25,93	94,87	5,13
14.00	14	0,47	34,2	—	34,20	16,07	97,08	2,92
14.30	31	1,03	38,8	1,00	38,80	39,96	97,42	2,58
15.00	13	0,43	51,8	—	51,80	22,27	98,07	1,93
15.30	6	0,20	102,0	—	102,00	20,40	99,02	0,98

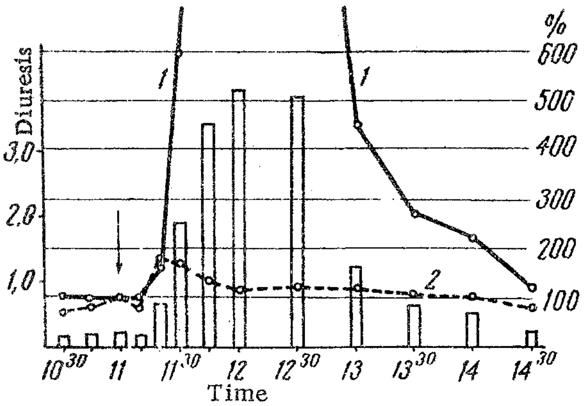

Fig. 1. Effect of a water load on filtration, reabsorption, and diuresis (dog Astra, weight 17 kg). 1) Portion of filtrate not reabsorbed, expressed as percentage of original value; 2) filtration (in ml per minute) as a percentage of initial value; arrow – dog drinks 500 ml of water; columns – diuresis in ml/minute.

single injection of a suspension of the dye in oil. Altogether, 52 experiments were carried out on 14 dogs; 227 measurements of filtration and reabsorption and 185 determinations of renal blood flow were made.

RESULTS

Experiments with a water load showed that diuresis occurred together with a marked reduction in reabsorption; in some cases the reduction was from 99–98 to 93–89%, and accompanied a 7–to 10–fold increase in diuresis. In most instances the filtration varied over the normal limits, or else increased, but this had a very much smaller influence on the diuresis. No reduction in filtration after a water load was observed.

Table 1 shows the results of one of the experiments. During the period of maximum diuresis, at 12 o'clock, the filtration had increased 1.7 times, but the reabsorption had fallen from 99.4 to 92.8% (the fluid which had been filtered and not absorbed increased from 0.6 to 7.2%, i.e., by 12 times). Thus, the increased filtration would correspond to an increase in diuresis of 1.7 times, while the reduced reabsorption would lead to a rise of 12 times, making 20 times in all; these figures agreed with the amount of urine collected.

Fig. 1 shows graphically the results of one of these experiments, in which the urine was collected at 10-minute intervals during the first half hour after giving the water. For the sake of clearness, instead of showing the amount of reabsorption as a percentage, the percentage of the unabsorbed filtrate is plotted, i.e., the amount excreted with the urine. It can be seen that the increased diuresis results chiefly from the marked reduction in reabsorption, although in the first 30–45 minutes, there is also an increased filtration.

In the first 15–30 minutes, in most experiments, renal blood flow increased considerably. Subsequently, it was was maintained at a fairly constant rate, or, more frequently, it fell in spite of the maintained high rate of diuresis which reached its maximum level at the end of the first hour (Fig. 2).

TABLE 2

Effect on Filtration and Reabsorption of Injected Physiological Saline (dog Krasotka, experiment , January 12, 1954)

Time (hours min)	Amount of urine (in ml)		Concentration of creatinin (in mg%)		Concentration index	Filtration (in ml per min)	Reabsorption	Filtrate excreted c̄ urine
	total	per min	in urine	in blood			Percentage	
11.00 —								
11.15	8	0,53	57,14	—	55,47	29,40	98,20	1,80
11 30	9	0,60	59,26	—	57,53	34,52	98,26	1,74
11.45	7	0,47	60,61	1,03	58,84	27,65	98,30	1,70
Between 11: 35 and 11: 50 a.m.,300 ml of 0.85% NaCl solution was given intravenously								
12.00	31	2,07	37,50	—	36,41	75,37	97,25	2,75
12.15	34	2,27	25,00	—	24,27	55,09	95,88	4,12
12.30	26	1,73	20,70	—	21,12	36,54	95,26	4,74
12.45	19	1,27	22,22	—	22,67	28,79	95,59	4,41
13.00	16	1,07	26,32	0,98	26,85	28,73	96,27	3,73
13.30	27	0,90	28,17	—	28,74	25,87	96,52	3,48
14.00	22	0,73	37.50	—	38,26	27,93	97.39	2,61

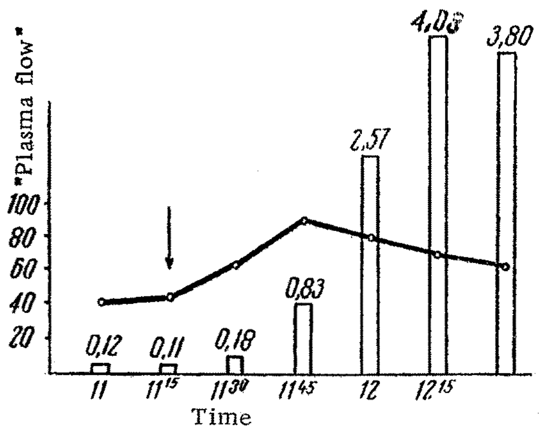

Fig. 2. Effect of a water load on renal circulation and diuresis (dog Rozka, weight 15 kg). Curves – renal "plasma flow" as determined by phenol red, in ml/ minute; columns – diuresis in ml/ minute; arrow – dog drinks 500 ml of water.

In approximately one third of the experiments, after the water load there was either no change or else an insignificant increase in renal circulation. Thus, there was no direct correspondence between diuresis and renal blood flow.

Consequently, water diuresis after drinking occurs chiefly through reduced reabsorption. It remains to be seen whether the increased diuresis following parenteral injection of fluid is caused by the same mechanism. We have found only one published report [10] dealing with differences in renal function after intravenous injection of isotonic solutions of sodium chloride and glucose: in the first case it appeared that filtration increased while reabsorption remained unchanged, while in the second, on the contrary, the diuresis was caused by a lowered absorption.

The experiments we performed all gave the same results, which are shown in Table 2 and Fig. 3. It can be seen from Table 2 that the increased diuresis in the first 15 minutes after giving fluid intravenously is chiefly due to a greatly increased filtration rate; no great reduction in reabsorption occurred. However, even by the second 15 minute period, the increased diuresis was contributed equally by changes in filtration and in reabsorption. In the third 15 minute period, filtration had returned to its normal value, while reabsorption continued to fall. Subsequently, the high level of diuresis was maintained through reduced reabsorption, while filtration remained within normal limits.

Fig. 3 shows the same result. The initial increase in diuresis depends mostly on filtration, and subsequently it is maintained by reduced absorption. In this experiment, the filtration rate remained raised for a longer period than in the previous one.

Determination of filtration and reabsorption by intravenous injection of a 4.9% glucose solution, showed that the relationship described above is maintained: the initial increase in diuresis is associated chiefly with an increased filtration, while subsequently it is maintained by reduced reabsorption. In this way, we can

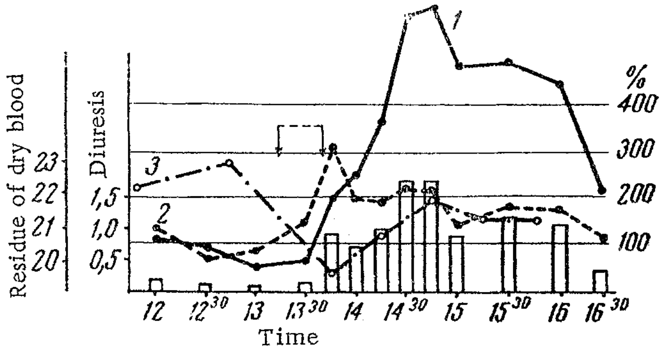

Fig. 3. Effect of an intravenous injection of 400 ml of physiological saline (shown by arrow) on filtration, reabsorption, diuresis, and dry blood residue (dog Kusachka, weight 11 kg). 1) Unabsorbed portion of filtrate, as percentage of original value; 2) filtration (in ml per minute) as a percentage of the original value; 3) dry blood residue as percentage; arrows — dog given 400 ml water; columns — diuresis in ml per minute.

TABLE 3

Effect of Injecting Physiological Saline on Renal Blood Flow (dog Rozka, experiment March 15, 1955)

Time	Volume of urine		Concentration of phenol red (in mg%)		Concentration index	Blood flow (in ml per min)
	total	per minute	in urine	in blood		
12.15—12.30	2,5	0,17	404,0	0,94	429,8	73,07
12.30—12.45	3,2	0,21	481,9	0,97	496,8	104,33
Between 12:43 and 12:57 a.m., 300 ml of 0.85% NaCl solution was given intravenously						
12.45—13.00	29,0	1,93	84,7	0,96	88,2	170,22
13.00—13.15	17,0	1,13	59.5	0,92	64,7	73,11
13.15—13.30	8,0	0,53	133,3	0,88	151,5	80,30

definitely refute the claim referred to above [10] that extra saline is excreted by increased filtration, and glucose by reduced reabsorption.

We have shown that when fluid is injected, filtration plays a more important part in causing the increased diuresis, than when the water is given by mouth. We have yet to explain what causes the increased filtration at the end of the injection. It would seem reasonable to suppose that it is the result of hydremia, which produces an increased filtration pressure. Having observed the hydremic reaction to parenteral fluid injections, we showed that it is more constant than the same reaction in response to food which we demonstrated previously [3]. Immediately after the injection of the fluid, in most experiments a dilution of the blood was observed. However, just as in the experiments in which the water was given by mouth, the degree of hydremia did not correspond to the subsequent course of the diuresis.

If a comparison is made of the change in filtration and reabsorption with change in the dry blood residue (see Fig. 3), then it is easily seen that the time of greatest filtration increase coincides with the maximal dilution of the blood. In cases where no definite hydremia was observed from the very beginning, the increased diuresis was brought about by reduced reabsorption and not by increased filtration.

Thus, there is good reason to suppose that the increased diuresis following intravenous injection of fluid is at first due to an increased filtration, which is brought about by the increased dilution of the blood. Subsequently, the increase is maintained chiefly by reduced reabsorption, while changes in filtration contribute comparatively little, i.e., the condition at this stage is similar to that obtaining when fluid is given by mouth.

Just as when fluid was given by mouth, results of renal blood flow measurements as affected by parenteral injection of fluid were varied. In some, there was no blood flow change, while in most experiments there was an increase. One clear difference was that when giving water by mouth, the maximum increase in blood flow usually occurred 30 minutes after drinking, while when the fluid was injected, the maximum flow always occurred directly at the end of the injection. In most cases the increased blood flow was confined to this period (Table 3); only in one experiment of the twelve was the maximum increase in blood observed after an interval of 30 minutes.

Whether the water was given orally or parenterally, there was no correlation between the changes in blood flow and diuresis.

The work we have done has refined our knowledge of changes in renal filtration and reabsorption when water is introduced by different routes, and has shown that increased blood flow is not an important factor in water diuresis. The reasons for the observed increase in renal circulation during water diuresis and its relationship to filtration rate require further investigation.

SUMMARY

The work was carried out on dogs with ureteric fistulas. They were given 30 mg/kg of water plus 10% milk to drink; 20-25 ml per kg body weight of isotonic solutions of sodium chloride and glucose were injected intravenously at a rate of 20 ml per minute. Filtration and reabsorption were measured in terms of creatinin clearance, while renal blood flow was determined by injecting an oily suspension of the dye phenol red. Water diuresis occurs after drinking by virtue of a greatly reduced reabsorption. In some cases the diuresis was caused by an increased filtration. Diuresis increased rapidly after intravenous injection of fluid, and this was mainly due at first to increased filtration, but later to diminished reabsorption. The initial increased filtration is accompanied by a pronounced hydremia following the intravenous injection. In the majority of experiments, the renal blood flow was increased during the first 15-30 minutes after drinking, as well as after the intravenous injection.

Later, however, no relation was found between the rates of renal blood flow and diuresis.

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