CHANGES IN URINE EXCRETION AFTER INJECTION OF EPINEPHRINE IN THE RENAL ARTERY

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Some researchers have noted a decrease in diuresis under the effect of epinephrine [1, 2, 5, 6, 7, 9-12] and others have indicated a marked polyuria [4, 8]. According to the data of B. A. Pakhmurnyi [3], two phases can be distinguished in the effect of epinephrine: an initial inhibition of diuresis with its subsequent appreciable increase. Most authors consider that the leading mechanism in the changes of diuresis under the effect of epinephrine is its effect on the vascular apparatus of the kidneys resulting in a change of glomerular filtration [9, 10, 12]; a number of investigators arrived at the conclusion that resorption of water is enhanced by epinephrine [1, 2, 3].

However, in most experiments epinephrine was injected into the general blood stream. Under such conditions it is difficult to differentiate the immediate effect of epinephrine on renal tissue and its effect caused by shifts in the work of the cardiovascular system, endocrine glands, etc., which affect the process of urine excretion. A study of the action of epinephrine on isolated kidneys [13] or on a heart lung-kidney preparation [14] also does not solve the problem conclusively, since the character of the effect can be inadequate for this preparation to affect intact animal kidneys.

We studied the character and mechanism of the effect of epinephrine on diuresis when injected directly into the renal atery, having thus excluded the side effects of epinephrine.

EXPERIMENTAL METHOD

The experiments were set up on random-bred dogs. Under morphine-hexenal anesthesia we made a median incision, the intestine was moved aside, and a fine hypodermic needle, which was connected by a rubber tube to reservoirs containing solutions of the investigated substances, was inserted into the left renal artery. Under constant pressure a normal saline solution was infused into the renal artery at a rate of 0.5-1.5 ml/min. After a control background of diuresis was established, a solution of one of the investigated preparations was injected into the artery for 5-15 min in place of the physiological salt solution.

The urine was collected at 5 min intervals from each ureter separately by means of vinyl chloride catheters, which were inserted up to the renal pelves through an incision in the ureter. The character of the changes in the processes of glomerular filtration and the resorption of water in the renal canals was judged by the purification from endogenous creatine or inulin. The content of creatine or inulin in the blood and urine was determined by the usual methods. To maintain a high background of diuresis, an isotopic sodium chloride solution was infused at a rate of 1-4 ml/min into the shin vein of the dogs during the entire experiment.

Our task was to study the immediate effect of the investigated preparations on the kidney tissue, therefore we selected doses which, on passing through the kidney and entering the general blood circulation, did not cause noticeable changes in the activity of the other kidney.

In all we made 82 injections of epinephrine and other preparations in 20 animals.

EXPERIMENTAL RESULTS

The injection into the renal artery of epinephrine in a concentration of 1:100,000-1:200,000 at a rate of 1-1.5 ml/min (0.3-1 μg/kg/min) caused inhibition of diuresis in most experiments. Oliguria was accompanied both by a decrease in filtration and by an increase of resorption of water in the renal tubules (Fig. 1A). However, in certain experiments a decrease in urination occurred only by an enhancement of the resorption processes (Fig. 1B). Moreover, sometimes the decrease of diuresis was observed with an increase of glomerular filtration ; the creatine coefficient in these cases was appreciably increased (Fig. 1C). These experiments indicate that epinephrine can directly affect not only the vascular apparatus of the kidney, but also the epithelia of the tubules and processes of water resorption.

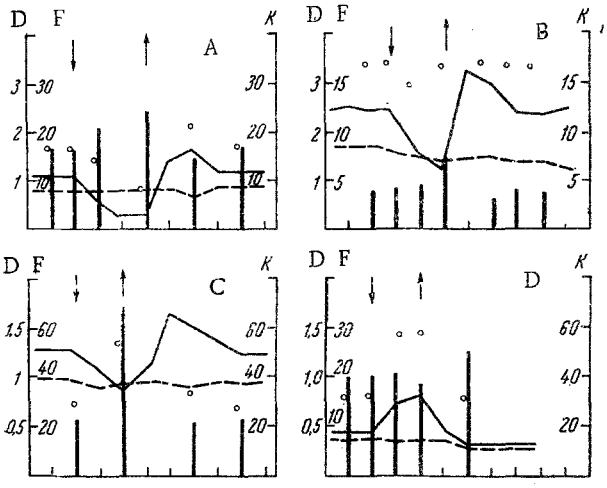

Fig. 1. Effect of epinephrine injection into renal artery on diuresis. In each graph the time (every 5 min) is plotted on the abscissa and diuresis (D) and filtration (F) (in ml/min) on the ordinate on the left, and on the right is the creatine or inulin coefficient (K). The solid line is diuresis from the stimulated kidney; the dashed line is diuresis from the contralateral kidney; the circles denote filtration; the columns, the coefficient; the arrows, the start and end of epinephrine injection.

A change in diuresis under the effect of epinephrine in our experiments occurred immediately after the start of injecting the preparation and lasted during the entire infusion period, and often for 5-20 min after it stopped. Diuresis later returned to the normal level or more frequently exceeded it, whereas diuresis from the contralateral kidney remained unchanged (see Fig. 1A, B, C). Evidently such polyuria depends on local changes in the kidney caused by the preceding action of epinephrine.

When the dose of epinephrine was reduced to 0.02-0.04 mg/kg/min, its injection into the renal artery evoked a slight increase of diuresis with an increase of filtration (Fig. 1D), and sometimes with a certain decrease of tubular resorption of water. The polyuric effect of epinephrine was less persistant than its oliguric effect.

It was of interest to compare the effect of epinephrine on the urinary function of the kidney with the effect of ephedrine, which blocks amino acid oxidases, thus enhancing the effect of endogenous sympathomimetic amines. We set up a series of experiments with the injection of ephedrine sulfate into the renal artery. The preparation was injected as a 0.01-0.05% solution at a rate of 1.-1.5 ml/min, i.e., in a dose of 3-13 μg/kg/min.

Small doses of ephedrine increased urination from the corresponding kidney up to 163-284% in comparison with the initial level (Fig. 2A). Here we observed a decrease in water resorption in the renal tubules, whereas filtration remained unchanged. Diuresis of the contralateral kidney did not vary.

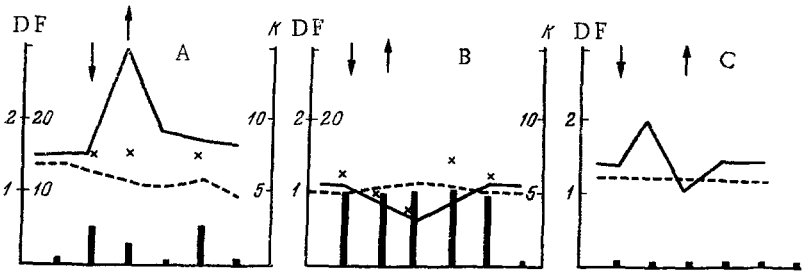

Fig. 2. Effect of ephedrine injection in renal artery on diuresis. Arrows indicate start and end of ephedrine injection. Other designations are the same as in Fig. 1.

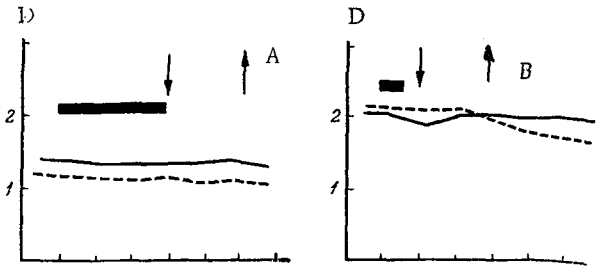

Fig. 3. Effect of epinephrine injection renal artery on diuresis with concomitant action of chlorpromazine (A) and dihydroergotamine (B). The black rectangle denotes injection into renal artery of chlorpromazine (A) or dihydroergotamine (B). The other designations are the same as in Fig. 1.

When the ephedrine dose was increased to 10-13 μg/kg/min, we noted the opposite effect: diuresis declined. A major role in this was played by a drop in glomerular filtration, whereas water resorption increased slightly (Fig. 2B). In a number of experiments we observed a mixed picture: excretion of urine increased at the start of ephedrine injection, and then dropped (Fig. 2C).

We can conclude on the basis of these experiments that the immediate effect of ephedrine on kidney tissue differs somewhat from that of epinephrine. This is noticeable at small doses which, while not changing filtration, does markedly suppress water resorption in the tubules. The effect of large doses of ephedrine, just as of large doses of epinephrine, is attended by a change in the functions of the vascular and tubular apparatus of the kidney.

In the next series of experiments we studied the effect of epinephrine on diuresis after a preliminary injection of adrenolytic preparations into the renal artery. A 10-15 min infusion of a chlorpromazine solution in a 1:650 concentration sometimes reduced the oliguric action of epinephrine, and in some experiments completely eliminated it (Fig. 3A). Smaller doses of this preparation did not change the action of epinephrine on diuresis. The stronger adrenolytic dihydroergotamine in a dose of 0.5-1 mg completely eliminated epinephrine inhibition of urine excretion (Fig. 3B).

Therefore, when epinephrine was injected into the renal artery, the changes in diuresis of the dogs were in many respects similar to those observed upon injection of this preparation into the general blood stream. Our experiments confirmed the possibility of different changes in diuresis under the effect of epinephrine depending on its dose [6, 10]. With small doses (0.02-0.04 μg/kg/min) we observed an increase in urine excretion, and with large doses, its inhibition. The effect of small doses of epinephrine is first of all felt on the vascular apparatus of the kidney, which is indicated by the change in the filtration capacity of the kidneys. Evidently, a spasm of the abducting arterioles occurs and the filtration pressure increases.

With large doses of epinephrine, the enhancement of water resorption in the renal tubules is of prime importance since this causes an inhibition of diuresis. In most cases filtration in the glomeruli is reduced. However, inhibition of urine excretion can occur without a decrease in filtration, and sometimes even with its appreciable enhancement. A further increase in the dose of epinephrine led to a marked drop in filtration and decrease in diuresis even to anuria.

In our experiments we did not observe a polyuric phase of action of epinephrine in a form such as was described in the work of other authors. Evidently, the occurrence of this phase depends on the extrarenal factors [3]. However, the initial increase of diuresis following epinephrine-induced oliguria is related to the direct effect of epinephrine on the renal tissues.

The effect of epinephrine on urogenous processes is accomplished through the adrenergic systems which are blocked by adrenolytic substances – dihydroergotamine and large doses of chlorpromazine, since after a preliminary injection of these preparations into the renal artery epinephrine no longer had an oliguric effect.

This method of injecting the studied substances in one of the renal arteries permits us to say with confidence that the observed effects of these preparations depended on their immediate influence on the cell elements of the kidney. Secondary effects of these preparations from their entering the general circulation were precluded, since if this had been so,changes would have occurred in the function of the contralateral intact kidney.

SUMMARY

In acute experiments on dogs a study was made of the effect produced by adrenalin on the urine secretion following administration of the preparation into one of the renal arteries; the second kidney served as control. As established, low adrenalin doses (0.02-0.05 μg/kg/min) stimulated urine secretion mainly at the expense of increased filtration; a dose of 0.3-1 μg/kg/min adrenalin inhibited the diuresis, decreasing filtration and intensifying water reabsorption in the tubules. The action of adrenalin on the kidney was eliminated by dihydroergotamine and large aminazine doses. Low doses of ephedrine increased diuresis at the expense of depressed water reabsorption in the tubules; similarly to adrenalin high doses of the preparation inhibited the diuresis.

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