EFFECT OF NARCOTICS ON RENAL CIRCULATION OF HEALTHY DOGS AND OF DOGS WITH EXPERIMENTAL HYPERTENSION

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The experimental work of Warthin, Caroline and Thomas [7] and of E. B. Berkhin [1, 4] is devoted to the effect of narcotic substances on the renal circulation. The first authors observed a decrease in the renal blood flow of dogs under the influence of pentobarbital (by the phenolsulfonphthalein clearance-coefficient). E. B. Berkhin observed a decrease in the renal filtration of dogs under the influence of narcotics. In two clinical works devoted to this problem, there is a difference of opinions: M. Ya. Ratner [4] reported that renal blood flow decreases during barbamil* sleep (by the phenolsulfonphthalein clearance coefficient), while N. A. Ratner [5] using the same method, observed an increase in the "effective renal blood flow" during the action of chloral hydrate and barbamil. Both investigations were carried out on patients with hypertension.

Since the data regarding the effect of narcotic substances on the renal circulation are insufficient and vary, further investigation of this problem is essential. Such investigations have a practical aspect as well, since narcotics are widely and successfully used in the treatment of hypertension. These circumstances induced us to carry out the present work. Taking into account the early inclusion of renal ischemia in the general pathogenetic chain of hypertension, we considered it essential to set up experiments on animals with experimental renal hypertension as well as on healthy dogs.

EXPERIMENTAL METHOD

The work was carried out on female dogs (2 healthy ones and 3 with experimental renal hypertension), whose perineum had been pierced previously by a catheter in order to facilitate the collection of urine. Renal hypertension was produced by constricting both renal arteries for two seconds. When the experiments began, the hypertension had lasted from 1 to 3 years.

The blood pressure was determined by Korotkov's auscultatory system on the common carotid artery which was brought out into a cuff of skin. The renal circulation (peritubular and corpuscular) was investigated by means of parallel determinations of the diodrast and endogenous creatinine clearance coefficients. The diodrast concentration in the blood did not exceed 5 mg% in all the experiments, diuresis was not less than 1 ml per minute. Urine was collected and blood samples taken at 15 minute intervals.

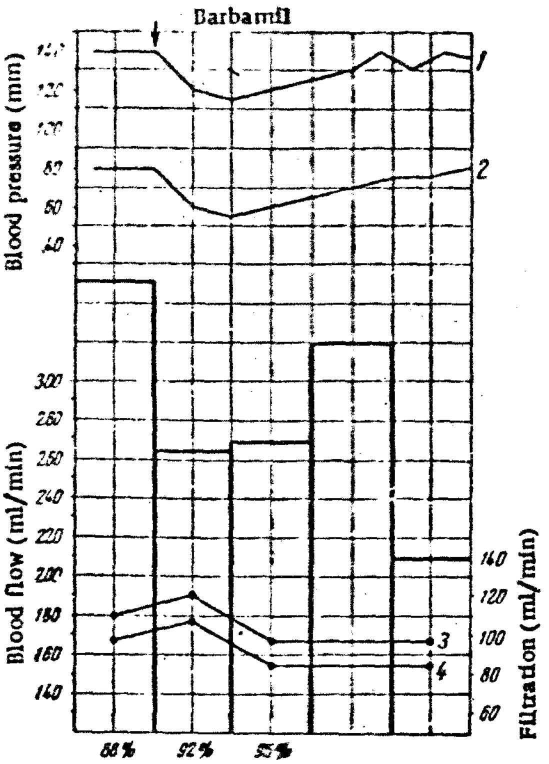
The amount of reabsorption and the filtration fraction were calculated from the data of the experiment.

Chloral hydrate was administered as a 3 g dose in starch solution in an enema; medinal as 0.015-0.02 mg/kg and barbamil as 0.01 mg/kg in salt solution intravenously; luminal as 0.01-0.015-0.02 mg/kg internally. The indicated doses had a slightly soporific effect. In all, 14 experiments were carried out.

* Amytal.

EXPERIMENTAL RESULTS

The soporific effect developed faster during parenteral and slower during enteral administration of the substances under investigation. As the soporific effect developed, the arterial pressure decreased. This decrease was less obvious in healthy dogs (10/7 to 17/20 mm) than in dogs with hypertension (30/35 mm). Similarly, the blood flow in the kidneys decreased, more in the peritubular vessels than in the glomeruli.



Lowered blood pressure (1 – systolic, 2 – diastolic), decreased renal blood flow (by the diodrast clearance coefficient; columns) and filtration (3 – by the creatinine clearance coefficient, 4 – amount of diuresis per minute) of the dog Vesta under the influence of barbamil. The figures below indicate the extent of reabsorption. Each column corresponds to a 15-minute period of observation.

The kidneys of healthy dogs and of dogs with hypertension reacted to approximately the same extent. The diodrast clearance coefficient decreased 50-63% under the influence of chloral hydrate, 30-43% under that of medinal and barbamil, 30-53% of luminal. The creatinine clearance coefficient fell 28-46% during administration of chloral hydrate, 8-30% under the influence of medinal and barbamil and 11-29% of luminal. The maximums of the two coefficients did not always coincide in time. The filtration fraction always increased; the reabsorption rose; diuresis decreased from 3.4-8.5 (before the experiment) to 1.4-5.8 ml per minute. The onset time of the maximum change, as well as the extent of the changes in renal circulation did not coincide with the initiation and extent of changes in the blood pressure in the majority of cases (see illustration). The blood pressure always changed relatively less than the renal blood flow. This is especially evident when narcotics were administered internally, when a small decrease in the blood pressure was accompanied by a marked decrease in renal circulation.

DISCUSSION OF RESULTS

It is impossible to establish a direct connection between the changes in renal circulation under the influence of narcotics and their depressand effect on the central nervous system or their moderate effect on the contractile elements of the kidney vessels. With these two assumptions, an increase in kidney circulation could be expected, since N. G. Gavrilov's work [3] has shown that when chloral hydrate solution is passed through an isolated kidney, its vessels expand. The depression of the central nervous system and of its vasculomotor center by narcotics leads to a lowering of the blood pressure. The observed decrease in renal circulation cannot, however, be regarded as a direct consequence of this decrease in blood pressure as a passive reaction. The changes in the renal circulation in our experiments, as indicated above, were always much more pronounced than the changes in the blood pressure; the duration of these changes also varied. The time and maximum of the changes in the peritubular and glomerular blood vessels did not coincide; the lowering of the blood pressure was more evident in the former than in the latter, supplying a basis for the supposition that there is a spasm of the efferent glomerular vessels.

It is known that one of the basic factors which determine kidney filtration is height of the blood pressure. Therefore the supposition can be made that the drop in blood pressure is the reason for the development of an active compensatory reaction by the kidneys, which is evidenced by the exclusion of part of the renal nephrons and by spasm of the efferent vessels of the glomerulus. The presence of such a reaction explains the relatively greater decrease in renal circulation in comparison with the decrease in the systemic blood pressure. A considerable number of nephrons is excluded from the circulation during the normal work of the kidneys. Thus, in Cannon's opinion [6], exclusion of up to 2/3 of all the nephrons is possible without substantial changes in the urine secretion of the kidneys. The significance of the compensatory reaction of the renal vessels to lowered blood pressure, as we suppose, is that, during lessened blood inflow, the metabolic processes remain at a sufficiently high level in the nephrons open for blood circulation that hypoxia of the kidneys does not develop, in connection with which, apparently, renin is not formed.

Reflexes from the renal interoceptors, as well as reflexes from the pressoreceptors of the sinocardial and aortic zones, may be significant in the formation of this compensatory reaction.

When the kidneys of dogs with experimental renal hypertension are ischemic, the reaction of the renal circulation to lowering the blood pressure developed with the same regularity as in healthy dogs. Its relative extent is close to the extent of the reaction of the healthy kidney vessels, although the hypotensive effect is more pronounced.

This can be connected with the complication of the reaction of the cardiovascular system in this case by the "removal" of some of the spasm of the systemic vessels.

The methods we used permitted the determination of the force of the blood circulation of the nephron – the working part of the kidney – but did not make it possible to judge the force of the interstitial circulation which is responsible for the efficiency of the nephrons. The problem of the interstitial blood circulation and its adequacy for the work of the nephrons has not been worked out at all. Maybe, the explanation of many unclear aspects of the work of the kidneys is there.

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* Published in Russian.