OSMOREGULATORY FUNCTION OF THE LIVER IN EXPERIMENTAL ASCITES

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Experimental ascites in dogs does not abolish the antidiuretic effect of 3% sodium chloride injected into the portal circulation but it does block the sodium-excretory components of the reaction.

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The osmoreceptors of the liver are of considerable importance [1, 2] as the initial elements of complex osmoregulatory reflexes. Injection of hypertonic sodium chloride solution into the portal circulation inhibits diuresis and increases sodium excretion.

In the present investigation disturbances of water and salt metabolism were studied in dogs with experimental ascites produced by constricting the inferior vena cava above the liver and also in animals with toxic hepatitis but without ascites.

EXPERIMENTAL METHOD

Changes in the osmoregulatory function of the liver in experimental ascites were studied in 32 chronic experiments on 7 adult dogs. Special preparatory operations were performed. In the first stage, under morphine-ether anesthesia, fistulas of the stomach and urinary bladder were formed. From 10-12 days later, under endotracheal ether-oxygen anesthesia, thoracotomy was performed on the right side and the inferior vena cava constricted to half its diameter with a polyethylene ring. At the same time, at laparotomy, a polyethylene tube was introduced into the portal vein through its lateral branch. The end of the tube was brought out beneath the skin of the animal's back. The experiments were carried out 5-6 days later, when ascites was detected in the abdominal cavity. By introducing measured doses of water through the gastric fistula a steady diuresis was established, and against this background 5 ml of 3% NaCl solution was injected through the tube implanted into the portal vein. The solution was warmed to 38° and the injection lasted 20-30 sec. Before and after osmotic stimulation of the liver the diuresis and sodium excretion were studied by measuring 5-min samples of urine. In some experiments the renal filtration and reabsorption were studied relative to endogenous creatinine, the plasma sodium was determined, and from the results obtained the sodium load on the nephron and sodium reabsorption (ratio between sodium excreted and sodium filtered, expressed as a percentage) were calculated. Control data were taken from the work of E. A. Nikolenko and Ya. D. Finkinshtein [1], carried out in this laboratory. Toxic hepatitis was produced by injections of CCl_4 (0.2 ml/kg every other day for 2 months).

EXPERIMENTAL RESULTS AND DISCUSSION

Injection of 3% NaCl solution into the portal circulation of healthy intact dogs produced a marked antidiuretic reaction starting 5-10 min after injection of the osmotic stimulus. The mean duration of oliguria was 61.2±2.8 min, and the diuresis fell to 61.2±5.4% of its initial level (Table 1). The fall in diuresis took place mainly as the result of an increase in tubular reabsorption of free water, for in 30% of the experiments no change was found in glomerular filtration during the reaction, and in the remaining experiments a decrease in filtration by 10-18 ml/min/m^2 was observed during the first 5 min. In most experiments on healthy dogs the decrease in diuresis was accompanied by an increase in sodium excretion (Fig. 1). Sodium excretion developed a little after the beginning of oliguria: the latent period was 20-40 min and the duration of the sodium-excretory response 40-60 min. The level of sodium excretion reached 100-400% of its initial

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TABLE 1. Effect of Intraportal Injection of 3% Sodium Chloride on Diuresis in Healthy Dogs and in Dogs with Toxic Hepatitis and Experimental Ascites

Series of experiments	Latent period (in min)	Duration of oliguria (in min), M±m	Depth of fall of diuresis (in % of initial), M±m
Control	5-10	54.2±2.8	61.2±5.4
Toxic hepatitis	5-10	41.3±4.3	66.2±2.9
Ascites	5-10	47.0±3.2	49.0±3.9

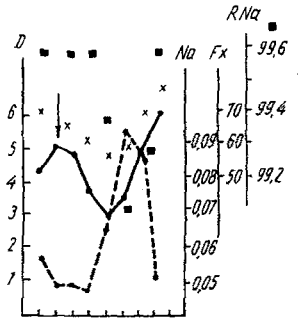

Fig. 1

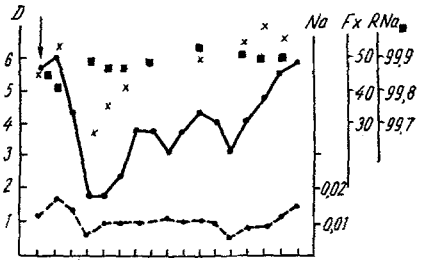

Fig. 2

Fig. 1. Changes in diuresis and sodium excretion following intraportal injection of sodium chloride (control experiment). Abscissa, time marker (5 min), ordinate, on the left: 5-min diuresis (in ml/m^2), on the right: quantity of sodium excreted in 5 min (in meq), glomerular filtration (Fx in ml/min/m^2), tubular reabsorption of sodium (RNa) expressed as a percentage of sodium load on nephron. Continuous curve shows change in diuresis, broken line shows change in sodium excretion. Arrow indicates time of injection of solution.

Fig. 2. Change in diuresis and sodium excretion following intraportal injection of sodium chloride (experiment during ascites). Legend as in Fig. 1.

value. As a rule sodium excretion took place as the result of a decrease in the tubular reabsorption of sodium with a relatively constant sodium load on the nephron.

In the experiments of series II the state of the osmoregulatory function of the liver was studied in toxic hepatitis. In response to intraportal injection of 3% NaCl solution an antidiuretic reaction was obtained in all 11 experiments, its duration and depth not significantly different from the control values ($t < 3$). Just as in the healthy animals, in most experiments (8 of 11) a well-marked sodium-excretory response was obtained.

In the experiments of series III on dogs with experimental ascites, osmotic stimulation of the liver produced an antidiuretic response in 28 of 32 experiments. The results obtained in this series were practically indistinguishable from those of the experiments of series I and II (Table 1). Just as in the control series of experiments, the antidiuretic response took place mainly as the result of an increase in tubular reabsorption of water. In most experiments with ascites no increase was found in the sodium excretion during the antidiuretic response (Fig. 2). A very slight increase in sodium excretion was observed in only 4 experiments (Fig. 3). A study of sodium excretion, the sodium load on the nephron, and the tubular reabsorption of sodium showed that in ascites the tubular reabsorption of sodium was unchanged in most experiments.

The course of the antidiuretic component of the complex osmoregulatory reflex in all three series of experiments thus showed no essential difference. Conversely, the sodium-excretory component of the response was absent in dogs with experimental ascites, although not significantly changes in dogs with toxic hepatitis.

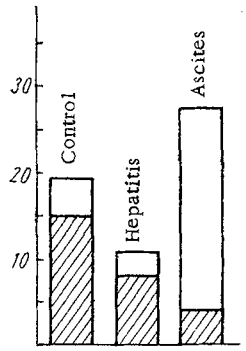

Fig. 3. Frequency of increase in sodium excretion in response to osmotic stimulation of liver of healthy dogs, dogs with toxic hepatitis, and dogs with experimental ascites. Ordinate, number of experiments. Shaded part of columns denotes experiments in which increased sodium excretion took place together with a decrease in diuresis.

It can be concluded from these results that the persistent inhibition of sodium excretion in ascites, despite the osmotic changes produced, is not connected with inhibition of vasopressin secretion, but with blocking of the sodium-excretory action of vasopressin, probably as a result of secondary hyperaldosteronism. The change in competitive aldosterone and vasopressin equilibrium developing as a result of this disturbs osmoregulatory processes which, in the presence of ascites, can take place only through a change in water excretion. With increased sodium retention, this leads to accumulation of sodium in the extracellular space, with subsequent retention of water.

LITERATURE CITED

1. E. A. Nikolenko and Ya. D. Finkinshtein, Fiziol. Zh. SSSR, No. 7, 884 (1964).
2. Ya. D. Finkinshtein, in: Current Problems in the Physiology and Pathology of the Kidneys and of Water and Salt Metabolism [in Russian], Moscow-Leningrad (1966), p. 29.