EFFECT OF HYALURONIDASE AND ITS NONSPECIFIC INHIBITORS (HEPARIN, PIPOLPHEN, ASCORBIC ACID) ON BILE SECRETION

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Intraperitoneal injection of hyaluronidase into rats reduced bile secretion and also reduced the excretion of potassium, sodium, and bile acids with the bile. After injection of nonspecific inhibitors of hyaluronidase, bile formation was increased and the potassium concentration in the bile was raised.

An important role in the reabsorption of water from the gall bladder is attributed to the hyaluronic acid–hyaluronidase system [2]. The writers have suggested that this system participates in the mechanisms of bile formation [1].

The results of an investigation into the role of the hyaluronic acid–hyaluronidase system in the mechanisms of the bile-forming function of the liver are described below.

EXPERIMENTAL METHOD

The experimental animals were 25 rats of both sexes weighing 200-250 g. Under urethane anesthesia (100 mg/100 g body weight) laparotomy was performed and a thin polyethylene catheter introduced into the common bile duct. The volume of bile formed was measured in hourly portions with an accuracy of up to 0.1 mg. After the first control hour of the experiment, the animals of the different series received intraperitoneal injections of testicular hyaluronidase (Reanal, 2500 units/100 g body weight, in physiological saline), heparin (100 units/100 g body weight), pipolphen (0.5 mg/100 g), and ascorbic acid (5.4 mg/100 g). Control animals received an injection of physiological saline. The content of bile acids in grams per liter was determined by the Scheer–Cooney method in hourly samples of bile, and the sodium and potassium concentrations (in meq/liter) were determined by flame photometry. The hyaluronidase activity of the bile was investigated by a viscosimetric method in the total volume of bile obtained during 5 h of the experiment.

EXPERIMENTAL RESULTS

Fluctuations in the volume of bile formed during the 5 h of observation on the control animals were negligible. Secretion of bile acids increased with time to reach a maximum at the 3rd hour of the experiment ($P < 0.02$). The potassium and sodium concentrations in the bile were not substantially changed throughout the experiment.

The volume of bile formed fell during the 1st hour after injection of hyaluronidase by 20.4% ($P < 0.06$), and the initial value was not restored before the end of the 4th hour of the experiment. Excretion of cholates fell progressively: during the 3rd hour after injection of hyaluronidase it was 42% below the initial level ($P < 0.01$). The excretion of potassium with the bile fell by 19.2% ($P < 0.01$) in the 1st hour after injection of hyaluronidase and remained at this level until the end of the experiment. No significant changes in sodium excretion were observed (Fig. 1).

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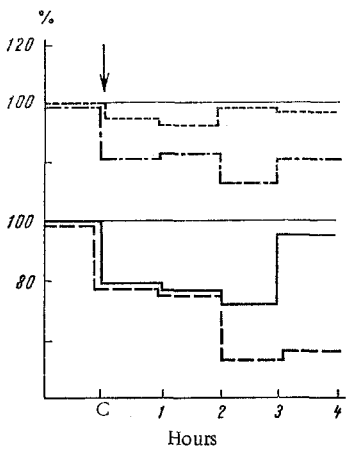

Fig. 1.

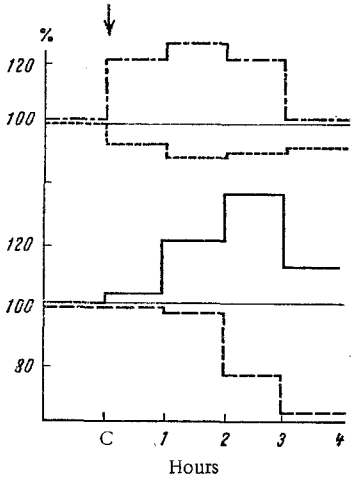

Fig. 2.

Fig. 1. Changes in bile formation and in the secretion of bile acids, potassium, and sodium following intraperitoneal injection of hyaluronidase into rats. Arrow denotes time of injection of solution after control (C) hour of the experiment. Abscissa, time of experiment (in h); ordinate, from top to bottom: excretion of potassium, sodium, and bile acids, volume of bile formed (in % of control hour of experiment).

Fig. 2. Effect of ascorbic acid on bile-forming function of rat liver. Legend as in Fig. 1.

Administration of the hyaluronidase inhibitors (heparin, ascorbic acid, and pipolphen) caused similar changes in bile secretion. The secretion of bile rose to reach a maximum at various times after injection depending on the type of inhibitor given. For instance, after injection of ascorbic acid (Fig. 2), bile secretion during the 3rd hour of the experiment was 36.9% higher than initially ($P < 0.01$), while after injection of pipolphen, the secretion of bile during the 5th hour of the experiment was increased by 52.2% ($P < 0.01$). Heparin increased bile secretion by 7% ($P < 0.05$) during the 2nd hour and by 20.5% during the 3rd hour of the experiment. Bile secretion returned to normal during the 4th hour after injection of heparin and ascorbic acid, and during the 6th hour of the experiment after injection of pipolphen.

Hyaluronidase inhibitors depressed the secretion of cholates. For instance, after injection of pipolphen the concentration of bile acids in the bile at the 3rd hour of the experiment was 36.5% below, and at the 4th hour 46.8% below ($P < 0.02$) the initial level. Similar changes in secretion of cholates were observed after injection of heparin and ascorbic acid. The excretion of potassium with the bile after injection of pipolphen rose by 42.1% ($P < 0.02$) during the 4th hour of the experiment, and by 39.4% ($P < 0.01$) during the 2nd hour, and after injection of ascorbic acid by 26.5% ($P < 0.05$), also during the 2nd hour. Excretion of sodium with the bile after injection of pipolphen was reduced by 9.1% ($P < 0.05$) during the 3rd hour, injection of heparin by 14.3% ($P < 0.02$) during the 3rd hour, and after injection of ascorbic acid by 10.4% ($P < 0.01$), during the 2nd hour of the experiment. All the hyaluronidase inhibitors thus caused an increase in the excretion of potassium and a decrease in the secretion of sodium with the bile.

The hyaluronidase activity of the bile after injection of hyaluronidase was higher than after injection of physiological saline or of hyaluronidase inhibitors. The writers consider that this demonstrates the possibility of penetration of exogenous hyaluronidase into the biliary tract. In this way hyaluronidase inhibits the secretion of bile and reduces its potassium concentration; heparin, pipolphen, and ascorbic acid, although different in nature and chemical structure, possess the property of stimulating choleresis and increasing the excretion of potassium. It can be postulated that the action of the enzyme is connected with stimulation of the reabsorption of water and potassium from the biliary tract, and that inhibitors depress these processes. The injected hyaluronidase evidently penetrates into the biliary tract, increasing the hyaluronidase activity of the bile, and thereby increasing the permeability of the wall of the bile ducts;

this ultimately brings about more effective reabsorption. Hyaluronidase inhibitors in all probability exert their action by depressing the permeability of the biliary tract and inhibiting the reabsorption of water and potassium. Processes of excretion of bile acids by hepatocytes are evidently depressed by the action of both hyaluronidase and its inhibitors, since the excretion of cholates was reduced during all hours of the experiment.

LITERATURE CITED

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