ROLE OF INTESTINAL HORMONES IN THE PATHOGENESIS OF EXPERIMENTAL PANCREATITIS

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UDC 616.37-002-092.9-07:616.37-008.6-092:
616.342-008.6:577.175.73

The course of disturbances of secretory reactions of the pancreas in response to adequate stimulation by intestinal hormones was studied in acute experiments on dogs with preinduced pancreatitis. Activity of combined preparations of intestinal hormones obtained from the duodenal mucosa was found in the acute period of the disease in these dogs. In chronic experiments an increased rate of acid formation in the stomach and a change in the pH of the duodenal contents toward the acid side in pancreatitis were found in chronic experiments. It is concluded that intestinal hormones play an important pathogenetic role in the mechanism of disturbances of the external secretory activity of the pancreas in pancreatitis.

KEY WORDS: pancreas; experimental pancreatitis.

The secretin test, used in the differential diagnosis of diseases of the pancreas, is based on changes in the reactivity of the pancreas under pathological conditions to "exogenous" secretin [1, 5-7, 9-11]. To discover whether these changes reflect general changes in the reactivity of the body during pancreatitis or whether they are directly related to the pathogenesis of the disturbances of external secretory activity of the pancreas, the investigation whose results are given in this paper was undertaken.

EXPERIMENTAL METHOD

Experiments were carried out on 19 dogs. Acute pancreatitis was induced by injecting the dogs' own bile into the pancreatic duct in a volume of 0.5 ml/kg body weight. To study the responses of the pancreas to "exogenous" intestinal hormones and also for biological standardization, a combined preparation of intestinal hormones (CPIH) obtained in the laboratory by means of a standard technology [2], but without the final stages of purification, was used.

In consequence of the technology of preparation and according to the results of biological standardization tests on rabbits, the CPIH contained several intestinal hormones (secretin, pancreozymin-cholecystokinin) and a certain quantity of biologically inactive denatured protein. The preparation was obtained in sufficient quantity for all the series of experiments from the duodenal mucosa of healthy dogs. To determine changes in the activity of the intestinal hormones in pancreatitis, samples of CPIH were obtained by the same technology from the duodenal mucosa of dogs killed at different times after the beginning of the disease.

To study changes in the reactivity of the pancreas to "endogenous" secretin, responses to intraduodenal injection of 20 ml of 0.3% HCl, the physiological stimulus causing an increase in the secretin concentration in the portal blood and in the general circulation [8], were studied.

There were three series of experiments. In series I the pancreatic duct of dogs in which pancreatitis had previously been induced was cannulated 3, 10, 20, and 30 days after the beginning of the disease, under urethane anesthesia, and the pure secretion in response to the above stimuli (CPIH, 2 mg/kg intravenously, or 20 ml of 0.3% HCl solution intraduodenally) was subject to quantitative and qualitative investigation. In the experiments of series II activity of CPIH samples obtained from the duodenal mucosa of dogs with pancreatitis was compared by biological standardization tests with the activity of samples obtained from healthy dogs. In series III observations were made in chronic experiments on seven dogs on the secretory activity of the stomach and the pH of the duodenal contents in the course of development of pancreatitis.

**EXPERIMENTAL RESULTS**

The volume of pancreatic secretion in response to intravenous injection of CPIH was much less than the control at all times of the disease. The concentration and hourly secretion of bicarbonates and pancreatic enzymes (trypsin, amylase, lipase) also were significantly below the control values (P < 0.05). After intraduodenal injection of HCl solutions secretory reactions of the pancreas were completely absent on the third day from the beginning of the disease. Later they reappeared but remained low in all their parameters.

Some special features of the disturbances of enzyme-secreting activity of the pancreas were noted depending on the type of the stimulus and the stage of the disease.

A characteristic feature of the responses to CPIH was a gradual decrease in the concentration and hourly rate of secretion of the corresponding enzymes. For trypsin the value of these indices was minimal on the 20th day of the disease, but for amylase on the 10th day. In the third week of the disease the changes in activity and hourly secretion of the various enzymes showed a form of reciprocity: the lowest indices of concentration and quantity of trypsin secreted on the 20th day corresponded to the highest values of these indices for amylase and lipase. Later, on the 30th day, indices characterizing trypsin secretion increased, and this coincided with their lowest values for the other two enzymes (Fig. 1, graph 1).

The dynamics of responses to intraduodenal injection of HCl solutions was characteristically different; the concentrations and, in particular, the gross rates of secretion of enzymes during the experiment increased for all enzymes relatively steadily until the 30th day (Fig. 1, graph 2). Figure 1 clearly shows that on the