ACTION OF PARENTERALLY ADMINISTERED CASEIN HYDROLYSATE ON EXOCRINE FUNCTION OF THE PANCREAS

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Experiments on dogs with a chronic fistula of the pancreatic duct have shown that casein hydrolysate, obtained by acid hydrolysis, when injected into the blood stream produces intensive secretion of pancreatic juice. The juice secreted under these conditions is relatively poor in enzymes and total protein. By contrast, fibrin hydrolysate and several other hydrolysates obtained from blood are unable to excite intensive secretion of pancreatic juice. The suggestion is made that casein hydrolysate contains some molecular fragments which are converted in the body into a peptide with secretin-like activity.

A number of investigations into the effect of nitrogenous substances on gastric function have been described in the literature. Under certain conditions, products of protein hydrolysis and pure amino acids can evoke gastric secretion [4, 9, 13, 14]. It has also been shown [1, 2] that protein hydrolysates such as hydrolysin L-103 and amino peptide-2, when injected intravenously, although they evoke gastric secretion, do so only very slightly.

The effect of protein hydrolysates on pancreatic activity has not yet been explained. In view of the importance of this problem, the investigation described below was carried out.

EXPERIMENTAL

Experiments were carried out on 6 dogs with a chronic fistula of the pancreatic duct as described by Fomina [11]. The resting secretion was determined in fasting dogs, after which the animals were injected with protein hydrolysates by intravenous drip (50-70 drops/min, total volume during experiment 250-350 ml). In most experiments the total time of administration was about 4 h, but in some experiments about 2 h.

The following substances were given: a) casein hydrolysate (TsOLIPK) obtained by acid hydrolysis (composition and physiological characteristics are given in [3, 5, 10]); b) casein hydrolysate obtained by enzymic hydrolysis (Fluka and Buchs); c) fibrin hydrolysate [6, 7]; d) hydrolysin L-103 [8]; and e) aminokrovin [12].* In control experiments, instead of the hydrolysates a 0.9% solution of sodium chloride was injected.

The principal enzymes, total protein, pH, and titratable alkalinity were determined in the pancreatic juice.

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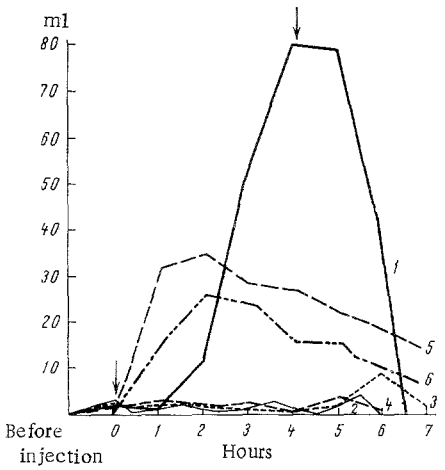

Fig. 1. Secretion of pancreatic juice in dog with chronic fistula of pancreatic duct following parenteral injection of casein hydrolysate (1), fibrin hydrolysate (2), aminokrovin (3), 0.9% sodium chloride solution (4), and after feeding one-third of daily ration (5) and 100 g meat (6). Arrows indicate beginning and end of administration, which in this case took 4 h.

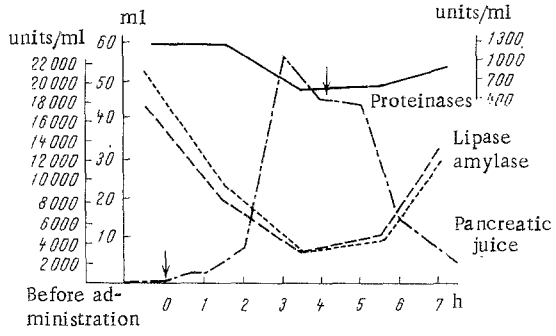

Fig. 2. Secretion of enzymes in pancreatic juice following parenteral administration of casein hydrolysate.

EXPERIMENTAL RESULTS

The study of the effect of the above-mentioned protein hydrolysates showed that casein hydrolysate (TsOLIPK), unlike the other substances tested, has a well marked ability to stimulate the exocrine function of the pancreas. The secretion of pancreatic juice evoked by this hydrolysate was so intensive that it exceeded the secretion evoked by a mixed food stimulus (Fig. 1). In all dogs the secretion of pancreatic juice was more intensive after injection of casein hydrolysate than after feeding with one-third of the total diet, and even more intensive than after administration of 100 g meat.

In the period of intensive secretion, the volume of juice secreted per hour was 2-3 times greater than the volume secreted after feeding with one-third of the daily ration.

Under the influence of casein hydrolysate, secretion was stimulated 30 min-2 h after its administration began. Secretion reached a maximum after 3-4 h, regardless of whether injection of the hydrolysate was complete after 2 or 4 h. Accordingly, when the injection of casein hydrolysate occupied only 2 h, the most intensive secretion occurred principally after the end of injection of the preparation, during the subsequent 2 h. If, however, the injection of hydrolysate continued for 6 h, increased secretion began after the same time interval but it continued longer, and the total volume of secretion was greater.

The enzyme content of the juice secreted in response to injection of casein hydrolysate, on the other hand, was at a low level. Compared with the initial period, the concentration of enzymes in the juice was reduced by several times (Fig. 2), the decrease in concentration of lipase and amylase being greater, and that in proteinases in general being smaller. The total protein content in the juice also showed a decrease; the pH of the juice and titratable alkalinity, on the other hand, showed a slight increase.

A study of the enzyme composition of the secretion suggests that casein hydrolysate causes the secretion of a pancreatic juice with low enzyme content, a characteristic feature also of the action of secretion.

Casein hydrolysate obtained by enzymic hydrolysis also appreciably stimulated pancreatic secretion, but to a much lesser degree than the acid hydrolysate.

The other nitrogenous substances which were studied had either no effect whatever or only a slight action on the exocrine function of the pancreas. In particular, following administration of hydrolysin L-103 and aminokrovin, some increase in secretion was often observed at one of the latter hours of the experiment (the 5th or 6th). This may be associated with excretory processes in the digestive system. In this case also, however, the volume of juice per hour was incomparably smaller than during the intensive secretion evoked by casein hydrolysate (TsOLIPK).

The mechanism of the effect of casein hydrolysate on the exocrine activity of the pancreas has not yet been explained. It can only be postulated that during hydrolysis of casein, peptide fragments resembling secretin are formed, and under the influence of enzymic processes in the body, these are subsequently converted into a peptide with secretin-like activity. However, further confirmation of this hypothesis is necessary.

All that can be taken for granted at present is that a sharp difference exists between the ability of the various protein hydrolysates used for parenteral feeding to stimulate the exocrine activity of the pancreas. Whereas some evoke a very intensive secretion of pancreatic juice (acid casein hydrolysate), others have no such action whatever or evoke only very slight secretion. This fact enables a differential approach to be made to the problem of selection of substances for parenteral feeding, depending on the state of the digestive system. In those stages (or forms) of diseases when the proximal part of the intestine and pancreas must be spared, preparations not stimulating pancreatic secretion should evidently be used. Conversely, in cases when it is desirable to stimulate the function of this part of the digestive system, preparations stimulating the exocrine activity of the pancreas should be given.

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