

EFFECT OF PARENTERALLY INJECTED PROTEIN HYDROLYZATES ON HUMAN PANCREATIC EXOCRINE FUNCTION

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Parenteral injection of casein hydrolyzate (TsOLIPK* brand) in man causes intensive pancreatic secretion and a corresponding sharp increase in volume of duodenal juice. Under the same conditions aminopeptide induces the secretion of only one-half to one-third the volume of juice. Both hydrolyzates stimulate enzyme secretion in the pancreas. This applies in particular to casein hydrolyzate, as a result of which not only is the volume of juice increased, but also the quantity of pancreatic enzymes secreted in unit time.

A previous paper described how casein hydrolyzate, obtained by acid hydrolysis, when injected into the blood stream is an active stimulant of pancreatic exocrine activity [3, 10, 11]. Several other protein hydrolyzates (aminopeptide, aminokrovin, fibrinosol) do not exert such a powerful action on the pancreas. The difference between the action of these different nitrogen-containing operations on digestive function may have a direct bearing on the planning of parenteral feeding in clinical practice.

This problem has been studied only in experiments on dogs. It was therefore decided that a corresponding investigation should be carried out on man with the object, in particular, of discovering to what extent this particular property of casein hydrolyzate is exhibited relative to the human pancreas.

EXPERIMENTAL METHOD

Observations were made on ten adult persons with a healthy digestive system. The method of duodenal catheterization was used. The saliva was collected in a separate vessel during catheterization and, in addition, as much gastric juice as possible was siphoned off.

The duodenal juice was collected in small portions in test tubes kept on ice. Only pure portions with the characteristic color and weakly alkaline reaction, cooled over measured time intervals, were tested for their enzyme content. Enzymes were determined by the usual methods employed in the Laboratory of Physiology and Pathology of Digestion [3]. Portions of juice for testing for their bicarbonate content were collected beneath a layer of oil, and the back-titration method was used [13]. Bicarbonate and lipase were determined not more than 2.5 h after the end of catheterization.

Protein hydrolyzates were injected intravenously by the drip method in volumes of 350-400 ml.

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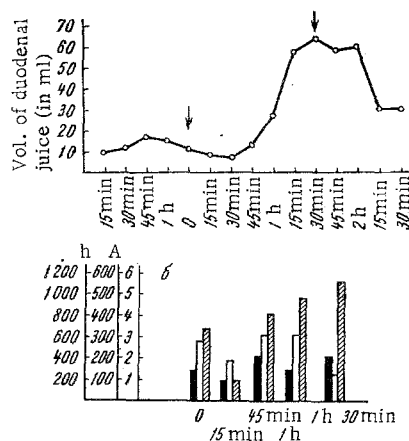


Fig. 1

Fig. 1. Increase in volume of duodenal juice (a) and of its content of pancreatic enzymes (b) in man under the influence of casein hydrolyzate. Here and in Fig. 2, arrows indicate beginning and end of parenteral injection of casein hydrolyzate. Black columns represent lipase (L), unshaded columns amylase (A), shaded columns total proteinases (P). Content of pancreatic enzymes given in units/ml.

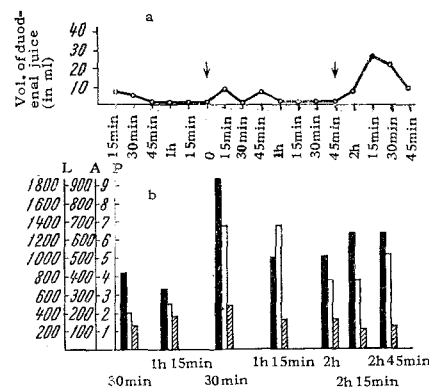


Fig. 2

Fig. 2. Changes in volume of duodenal juice (a) and in its content of pancreatic enzymes (b) in man after parenteral injection of aminopeptide.

EXPERIMENTAL RESULTS

Injection of casein hydrolyzate (TsOLIPK) led after a short time to intensive secretion of duodenal juice. The high content of specific pancreatic products in this juice and the comparatively low concentration of bile components indicated that it consisted mainly of pancreatic juice secreted at an increased rate.

The results of a typical experiment are given in Fig. 1. Immediately after introduction of the catheter into the duodenum a slight increase in the secretion of juice was observed. This was probably due to stimulation of gastric secretion by the catheter, and through the secretion mechanism this in turn caused stimulation of pancreatic secretion. However, this increased secretion soon ended and a low level was established. Against this background the administration of the protein hydrolyzates began.

The secretion of juice was again increased 1-1.75 h after the beginning of injection of casein hydrolyzate. The rate of secretion reached a maximum after 15-30 min, when it was four to eight times higher than the background level, after which it gradually diminished (Fig. 1). Stimulation proceeded at an increased rate usually for 1-1.5 h.

This secretory response of the human pancreas to injection of casein hydrolyzate was very similar to the response previously described experimentally in dogs [3, 10].

The concentration of bicarbonate in the duodenal juice secreted under the influence of casein hydrolyzate in man varies usually between 8 and 27 meq/liter. The content of pancreatic enzymes (lipase, amylase, total proteinases) was at the normal level for duodenal juice. Characteristically it was maintained at this same level, or even higher, during the period of intensive secretion induced by the hydrolyzate. By contrast with the secretion induced by secretin, in the present case no dilution of the enzymes with liquid juice was observed, and the quantity of enzymes secreted per unit time was significantly increased.

In the example given (Fig. 1), the concentration of enzymes in the first portion of duodenal juice was, as usual, quite high. After 15 min it was established at a comparatively low level characteristic of secretion induced by the secretin mechanism. The enzyme concentration subsequently rose under the influence of casein hydrolyzate and remained high (especially the concentration of proteinases), despite the very considerable increase in the volume of juice. The secretion of enzymes per unit time also was sharply increased during this period.

Casein hydrolyzate thus stimulates not only the secretion of juice, but also the secretion of enzymes in the pancreas.

In the intensity of juice secretion the observed response of the pancreas resembled that to injection of purified preparations of secretin into the bloodstream. According to published reports [15], in response to injection of secretin in man an average of 117 ml duodenal juice is secreted during the first 30 min. Recently the secretion of a somewhat larger volume (mean 282 ml in men during the 1st hour) has been demonstrated in the case of almost maximal secretion induced by injection of pure natural secretin [14]. In response to administration of old, less active preparations, in most cases less than 100 ml was secreted in 30 min [13]. In the present experiments, at the height of secretion under the influence of casein hydrolyzate, most frequently 110-122 ml was produced in 30 min. However, the bicarbonate concentration in this duodenal juice was much lower than in that obtained in response to secretin, as several investigations have shown [13, 14, 16].

Another protein hydrolyzate, aminopeptide, was also used for comparison. Injection of aminopeptide into the bloodstream in man led to a marked increase in the secretion of duodenal juice (Fig. 2). The action of aminopeptide began to appear, as a rule, somewhat later (after 1 h 30 min-2 h 13 min) than the action of casein hydrolyzate (1 h-1 h 45 min). So far as the composition of the juice is concerned, there were no significant differences, and in particular, its bicarbonate concentration was 7-29 meq/liter. Aminopeptide also stimulated the secretion of enzymes in the pancreas.

However, the intensity of secretion of juice in this case was much less than that induced by casein hydrolyzate. For example, the maximal secretion of juice 15 min after administration of aminopeptide was only one-half to one-third that obtained in response to casein hydrolyzate. A similar ratio was found in all the experiments except one.

The results of an investigation on dogs showed that aminopeptide evokes from seven to ten times less intensive pancreatic secretion than casein hydrolyzate [11]. The other hydrolyzates mentioned above, and a solution of pure amino acid, also had the same weak action as aminopeptide. Their effect is probably associated with their ability to induce some degree of gastric secretion [1], and this through the secretin mechanism leads to the secretion of pancreatic juice. Casein hydrolyzate evidently contains a specific agent of peptide nature, which, by some as yet imperfectly understood mechanism, has a powerful action on pancreatic exocrine function.

In man also, casein hydrolyzate thus produces a much stronger secretion of pancreatic juice than aminopeptide.

These results are a further argument in support of the need for a selective approach to the choice of agents for parenteral feeding, making allowance for the state of the digestive system.

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