# MECHANISMS OF EFFICIENCY OF MONO- AND POLYENZIME PREPARATIONS IN GASTROENTEROLOGY

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Keywords: enzymes, mechanisms of action, the hydrolysis of nutrients, diseases of the digestive system, the digestive conveyor

Physiological functions and implemented processes are natural processes that A.M. Ugolev defined as "As manufacturing processes, the natural process is the study of laws and principles of effective operation of various types, on the principles of effective interaction of different activities." One of those is digestion process. A key role in it performs enteral hydrolysis of nutrient pancreatic enzyme of the digestion-type cavity [10]. Over a day pancreas secretes 1.5-2.5 l secretion (up to 4.7-5.0 ml/min.), PH 7,5-8,8. Juice contains 2.0-3.5 g / l of total protein and 20 mg of enzyme protein are released in 1 hour. A set of enzymes contained in the juice, in a few isoforms of each, hydrolyzes all major nutrients. Excessive secretion of pancreatic enzymes hydrolyzing their regarding nutrients is a myth, as in the natural conditions their correlation in the duodenal chyme is regulated by itself by recurrent inhibition of pancreatic enzymes secretion unrelated to substrates [7]. Entering the duodenum pancreatic secretion and its components (enzymes and bicarbonates) are pluripotent. They have not only a digestive role, but also the signal one. The latest role is in modulation of exototic activity of the pancreas on the principle of negative feedback and the evacuation of the gastroduodenal complex, which is important in the systemic organization of the digestive process. [5]

Therefore exototic pancreatic insufficiency or severe secretion retardation causes not only direct maldigestion, but maldigestion, mediated by the digestive disorders of regulatory pipeline.

Consequently, the replacement enzyme therapy replaces not only the deficit exototic hydrolases and mediated by this maldigestion, but also corrects the functional gastro coordination. This emphasizes the legitimacy of a natural enzyme treatment technology approval, argues the use of enzyme preparations in the gastro-feeding, the presence of hydrolases in specific nutritional formulas [2, 3].

The presence of hydrolases in nutrient mixtures is important in the presence of nutrients in their composition polymers as proper intestinal hydrolases are oligo-, tri-and dipeptidase, disaccharidases. So what are the main aspects of this technology? First of all, it is the catalyst filling capacity of enteric contents substitution exototic reduction of pancreatic enzyme capacity, resulting in elimination of maldigestion. It becomes clear that the dose of exogenous enzyme preparations received should coincide with the composition and quantity of food taken in the nutrients and nutrient mixtures.

This correspondence is established individually, usually depending on exototic pancreatic insufficiency of a patient's diet and the enzymatic activity of the enzyme preparations received.

That is, during a vicarious admission of enzyme preparations natural digestive process should be adequately guaranteed on the level of enzymatic depolymerization of food nutrients and nutrient mixtures, as well as absorption of the products of their hydrolysis.

The achievement of this substitutional effect in vivo is not an analogy derived in vitro of nutrients depolymerization.

Digestive conveyor is realized in the time and space, i.e. the digestion of nutrients topography hydrolysis has a great role, of the exposure time for these enzymes, removal of the medium of its enzymatic reaction products that slow down the hydrolysis of nutrients which provides the suction of the hydrolysis products. In the distribution of hydrolysis and absorption in the digestive tract crucial role is played by its motor activity, and the activity of more than three dozen sphincters.

A striking manifestation of the digestive conveyor organization is gastroduodenal complex of evacuation operations, loading the food in portions of the stomach contents of the basic chemical reactor of the digestive system – the small intestine. The food forms different properties of stomach contents, the portions of different rate being transformed into the duodenum, then with varying speed and nature of the proximal-distal passage. Ceteris paribus carbohydrate foods leave the stomach more quickly, protein more slowly and fat even more slowly[5, 6]. Antroduodenal complex does antegrade and retragradnoe movement of its food content [5, 6].

The recent is the characteristic of the evacuation of stomach fat food that is subjected to emulsification and lipolysis in antroduodenalnoy cavity by means of bile, gastric and pancreatic lipases. This is the main component of the process of the delayed distal transit antroduodenal fat content. This localization of lipolysis is essential for intestinal digestion as triglycerides reduce the speed of cavity and wall hydrolysis of dipeptides and disaccharides. [9] Therefore, the priority of lipid hydrolysis is evident in the technology of polisubstrat intestinal digestion [6, 10].

As a result of our research, the evacuation of food gastric contents into the duodenum slows down with the duodenal ulcer, chronic gastritis, cirrhosis, cholecystitis, chronic colitis, chronic pancreatitis [5]. For different kinds of test breakfast this slowdown is expressed in different degrees, which is the cause of violation of differentiation evacuation process for which a healthy person has typical maximum speed of carbohydrate evacuation, the protein is lower and the lowest is of fat test breakfast. With chronic pancreatitis, gastric emptying of a carbohydrate and protein breakfast slows down and speeds up fat. The explanation is that the lipid slows the evacuation of the products of their hydrolysis, and pancreatic insufficiency of ekzosekret conditions of their formation is ruined.

Clearly, this leads to not only lipid maldigestion, but carbohydrates and proteins as well. Admission of pancreatin with the test breakfasts hastened their evacuation, and to some extent restored the characteristic norms differentiative speed gastric emptying of different types of nutrients. [7] Evacuation activities of the gastroduodenal complex is a multiparameter physiological process [6]. The speed of food contents evacuation from the stomach is differentiated depending on many factors, generally, defined as a non-

invasive method, and reflects the efficiency of the digestive process in the stomach and small intestine, in the first approximation may characterize it. Therefore, it seems that the success of the correction of maldigestion lies in replacement enzyme therapy, as assessed by many clinical and laboratory parameters that can be objectively assessed by the recovery rate of food evacuation of gastric contents.

An individual dose can be defined in this technology, recommended by the enzyme preparation in enzyme replacement ekzosekret pancreatic insufficiency, common for many pathological conditions [6].

In any case, such a technological method may be an initial step in determining the recommended dose of a particular enzyme preparation for the ongoing comprehensive treatment.

Ekzosekret potential of the digestive glands reduction leads to the secretion of the remaining functioning mass glandulocytes, and it may be one of the contributing causes of cancer pathology.

Under these conditions enzyme therapy acts not only as a replacement of hydrolysis nutrients, but as a function of residual stress-reducing cancer pool glandulocytes, as exogenous hydrolases reduce its activity on the principle of negative ekzosekret feedback.

This gland secretion inhibitory effect is important as a medical component of a replacement enzyme therapy.

Recurrent inhibition of pancreatic secretion was studied adequately in experiments on laboratory animals and in clinical observations [7].

Pancreatic autosekret, sodium, active and zymogen pancreatic enzymes administration reduce ekzosekret of intraduodenal. Proteases and their zymogens are considered as basic pancreatic secretion inhibitors. Depending on their doses they act as selective or generalized inhibitors: small monoferment doses selectively reduce the ekzosekret flow rate injected into the cavity of the duodenum enzyme, large monoferment doses having a generalized inhibitory effect, that is, they reduce the ekzosekret flow rate not only introduced, but other pancreatic enzymes as well [7 ].

The lowest thresholds are in duodenal proteases and their zymogens, a higher threshold is in amylase and even higher threshold is in chemosensory pancreatic lipase [7]. And for proteinase chemosensory the threshold is lowest in the lining of the initial part of the duodenum, the threshold for amylase is not only higher, but has a more distal minimum value, and the highest threshold among the three has hydrolases lipase fairly evenly, with mild proximal-distal gradient being distributed over the whole duodenum [7].

Introduction of pancreatic enzymes and autosekret of pancreatic jejunum and ileum has no inhibitory effect characteristic on the secretion of glands.

Therefore, exogenous pancreatic enzyme preparations should simulate the natural action of the technology throughout the duodenal mucosa. However, if orally taken pancreatin is not protected against the inhibitory effect of hydrochloric acid in the stomach, it will lose its inhibitory and digestive activity, lose its medicinal effects.

In this regard, orally ingestible formulations of pancreatin have an acid shell. And this principle is saved until you a proper quantity of acidresistant drugs is created. It is important that food contents of the stomach go into the duodenum together with exogenous pancreatin and was effective in its initial part.

This has been achieved in the technology of acidresistant microcapsules with a diameter of 1.0-1.2 mm, enclosed in a capsule, dissolved in the acidic funcorporeal contents of the stomach, where the microcapsules with pancreatine begin to mix with the food contents.

This mixture is mostly expressed in the antral part of the stomach, the contents of moves ante-and retrograde with powerful contractions. The prepared mixture in the form of a small bolus at the open pyloric sphincter in a coordinated human-induced duodenal motility moves into the duodenum, which begins in the oral enteric digestion of exogenous and endogenous pancreatic enzymes.

The mucosa of the duodenum responds to them, providing the effect of ekzosekret activity of the pancreas reducing. Thus, both components are provided with enzyme replacement.

Polyenzyme duodenal instillation give summed generalized inhibitory effect of pancreatic secretion.

Enzyme production rates are reduced by reducing the amount of secretion and less pronounced decrease in activity (concentration) of the enzyme in secret. According to the same principle hydrocarbons secretion is inhibited with intraduodenal administration of enzymes and bicarbonate solution.

There is a direct relationship of generalized inhibition of pancreatic secretion from the duodenal instillation dose of sodium and hydrolases (as well as zymogens). Species and organ belonging of the hydrolase in the inhibition of secretion is immaterial, important kind of enzyme activity. For example, human salivary a-amilaza causes selective inhibition of the secretion of experimental dogs' pancreatic amylase.

It is well known that pancreatin raw materials can be pancreas of pigs and cattle. In general, the mucous membrane of the duodenum is represented by chemoreceptor field, it distributes neuroceptors and enterinotsity, stimulation of which excites or inhibits somehow modulates the secretory activity of exocrine pancreatic cell and duktucrine pancreas.

This is a general principle of substantial coordination not only of somatic, but also visceral functions.

Chemosensory thresholds of pancreatic secretion return inhibition in duodenal mucosa change.

According to our data, patients with duodenitis have a threshold of secretion inhibition of the introduction of pancreatin drastically reduced. The threshold is increased with patients who are losing pancreatic secretion through the fistula. Patients after surgery pancreatoduodenectomy intraunal instillation of pancreatin gave almost no inhibition of secretion of cultured pancreatic cancer [7], due to overactivity of chemosensors enzyme predominantly in a resected duodenum.

In the postoperate gastroduodenal hypokinesia and delaying gastric emptying there are several mechanisms to blame, including conjugate ekzosekret deficiency of pancreatic enzymes, hormones duodenal [4] and the excitation of proteinase-activated receptor PAR [11, 12, 13, 14, 15].

Operating duodenal injury releases duodenal regulatory peptides that enhance pancreatic ekzosekrets that along with endosekrets pancreatic enzymes and hypertripsinemy is the cause of postoperative acute pancreatitis [8].

The results of experimental and traditional clinical developments on the return of inhibition of pancreatic secretion allowed to use its principles in surgical gastroenterology.

Intraduodenal probe instillation of trypsin solution at a dose of 0.1-0.3 mg/kg of patient's weight immediately after surgery or intraoperative duodenal probe position in post-operative period, depending on the tryptic activity of sera to patient allowed to achieve a stable and early relief from hyperfermentemia with most patients with edematous pancreatitis, necrotizing pancreatitis with increased secretory activity of the pancreas, contributed to relief of the clinical manifestations of the disease, reduce the effects of endogenous intoxication, normalizing the metabolic status of patients, the incidence of acute post-operative complications, the average of postoperative bed-days, the cost of prevention. No less effective was the use of postoperative enteric microsphere of polyenzyme drugs (Creon 10000/25000) [1].

The blockade of proteases (and other hydrolases) releasing duodenal cholecystokinin and secretin is the main mechanism of recurrent inhibition of pancreatic secretion.

Under natural conditions, cholecystokinin acts as a paracrine stimulator of kapsaitsinsensitive vagal afferents through which the evacuation of reflex inhibition and stimulation of gastroduodenal complex glandulocytes pancreas is carried out, but by reducing the incentive effects of duodenal contents of limited reduced rate of gastric emptying, pancreatic secretion is reduced [7].

Though releasing cholecystokinin and its concentration in the blood in vivo increases, it doesn't reach the threshold level of exocrine pancreatic cell receptor themselves [7].

Other mechanisms of recurrent ekzosekretion inhibition of pancreatic cancer have been revealed[6].

Ekzosekretion activity of the pancreas is characterized by mobility, including the urgency of the return and generalized selective inhibition of secretion. This property is typical not only for braking, but also for stimulating enzymes adapted for the secretory process [7].

Based on the classical view of the inertia of enzyme synthesis of exocrine pancreatic cell such phenomenology requires explanation. Secret gland consists of two pools. Initially allocated makes deposited to the gland and its stimulation of blood components, including hydrolytic enzymes, a second pool is this newly synthesized enzyme component provided through relatively long latency period. Therefore, recurrent inhibition of secretion urgently arisen is provided by the first reduction of the secretory pool, that is, the mechanism is not anabolic, but transport.

Due to the fact that the return secretion inhibition is controllable not only due to secretion volume, but also by its composition, which is evidenced by the possibility of selective inhibition of enzyme emission, it provides a mechanism for selectively inhibiting the transport of pancreatic enzymes in the ekzosekret parallel gradual reduction in ductal secretion of water and electrolytes. Secretion inhibition of components transport of secret of ductal system of the pancreas with its depositing and valve units involved has been reduced.

This possibility of urgent partial inhibition of glands secretion in the regions has been shown by us in the experiments on dogs with isolated secretory organ regions in situ [7] and formed a scientific paradigm of modular morphological and functional organization of the secretory activity of the pancreas (diploma at the opening number 256 dating 10.09.2004. reg. number 309).

The overall effectiveness of enzyme ekzosekret pancreatic insufficiency, which is a characteristic of a number of gastrointestinal (and other) disease states, happens due to the fact that active therapeutic reception simulates natural technology.