

Evidence-based pancreatology 2017/2018 (review of the results of studies on chronic pancreatitis and exocrine pancreatic insufficiency)

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Facts are a thousand times more important than words.

IP Pavlov [2]

Modern pancreatology, like all medicine, must be based on the results of evidence-based research. The path to truth in medicine lies through highly predictive research. This review is devoted to the data of modern evidence-based studies in the field of pancreatic pathology, which continues a similar review published in 2017 [1].

The highest level of evidence is a meta-analysis. In 2017 and in the beginning of 2018 published results of 22 new meta-analyses in the field of pancreatology. Most of them include randomized clinical trials comparing various surgical methods of treatment and those dedicated to prostate cancer. We were interested in research on the pathogenesis, course, diagnosis and treatment of chronic pancreatitis (CP), so we searched literature data among English-language publications published in 2017-2018. for the following key words: CP, substitution enzyme therapy (SPT), preparations in the form of a minimosphere, use in humans. Search carried out at the most major and known electronic bases Data : AdisInsight: Safety Reports, Allied & Complementary Medicine TM, Analytical Abstracts, BIOSIS Previews®, Embase®, EMCare®, International Pharmaceutical Abstracts, MEDLINE®, PubMed, ToxFile®.

It turned out that the evidence-based research in the field of pancreatology in recent years is divided into the following areas:

- proteomic studies — the search for new serological markers of pancreatitis and fibrosis of the prostate;
- improvement of methods of visualization of the pancreas;
- experimental studies with the study of new genetic factors predictors of prostate diseases, including diabetes mellitus, various risks of development of CP and exocrine pancreartic insufficiency (EPI).

Let us present the results of the studies that interested us, published for the indicated period of time, depending on the direction studied: the pathogenetic mechanisms of the onset of CP and EPI, new ways of diagnosing and treating these conditions.

Pathogenetic mechanisms

Extremely interesting for understanding the pathogenesis of CP are the results of a meta-analysis of the incidence and role of the syndrome of excessive bacterial growth (SIBR) in CP [27]. The authors of this work performed a meta-analysis and systematic review, trying to establish a relationship between the occurrence of SIBR and the symptoms of CP, as well as the nutritional status of patients. Based on the results of 9 studies (n = 336), the incidence of SIBD in CP was 36% (95% confidence interval (CI) 17-60%). The risk of SIBR in the presence of CP increased 4.1 times in comparison with the control (95% CI 1.6-10.4). A clear relationship between SIBR and the symptoms of CP is not documented, but it is established that the correction of SIBR contributed to an improvement in the clinical state of patients with CP.

A systematic review has been devoted to this problem, revealing the potential role of the microbiota of the digestive tract in the onset of the pathology of the prostate [18]. The authors analyzed 2833 articles published during the period 1940-2017. It turns out that patients with CP are characterized by quantitative and qualitative changes in the composition of the intestinal microbioma: a decrease in the number of *Bifidobacterium* and *Lactobacillus* and an increase in the number of *Enterobacteriaceae*. The presence of concomitant diseases affected the composition of the microbiota: in patients with CP without diabetes mellitus, the number of *Bacteroidetes* decreased, and the number of *Bifidobacteria* increased in the absence of VIN. Only one study recorded an increase in the number of *Enterococcus* and a decrease in the *Bifidobacterium* population in acute

pancreatitis. For pancreatic cancer, a decrease in the number of *Neisseria elongate*, *Streptococcus mitis* and an increase in the number of *Porphyromonas gingivalis* and *Granulicatella adiacens* are characteristic. The data obtained require further analysis to determine further tactics and possible ways of correcting these changes.

A large number of works devoted to the genetic aspects of prostate diseases, in particular, CP, are still published. Particular attention is paid to the mutation of the carboxyl-esterlipase gene [23]. This enzyme hydrolyses in the duodenum fats, cholesterol esters and fat-soluble vitamins. Some mutations are associated with exo-and endocrine pancreatic insufficiency, steatosis of the prostate.

VK Singh et al. (2017) performed a systematic review of the literature on the risk of occurrence of HPAI in various diseases [12]. EPI is one of the most important causes of digestive disorders and malabsorption, it may be a consequence of the disease of the prostate (primary EPI) or a secondary impairment of the exocrine function of the prostate in the initial disturbance of the work of other organs (secondary EPI). In addition to cystic fibrosis and CP, EPI develops in pancreatic cancer, certain metabolic diseases (diabetes mellitus), impaired hormonal stimulation of exocrine pancreatic function (celiac disease) and inflammatory bowel diseases. EPI occurs after surgical interventions on the digestive tract (47-100%), it is diagnosed in the majority of patients with prostate cancer (66-92%), diabetes mellitus of the 1st (26-57%) and the 2nd (20-36%) type, celiac disease (80%). The frequency of EPI in inflammatory bowel diseases ranges from 14% to 74%. The authors emphasized the urgency of conducting evidence-based clinical trials to assess the efficacy and safety of ZTT in various diseases associated with HPV.

Diagnostics

Clinical Features

One of Population analyzes (with an average follow-up of 10 years) were devoted to the study of the natural course of CP [17]. The average age of diagnosis of CP was 56 years; while this disease was more often diagnosed in men (56%). Despite the fact that the overwhelming majority of patients (76%) complained of severe abdominal pain, only 33% of patients needed invasive intervention: endoscopic and surgical interventions were performed in 23% and 11%, respectively. When comparing the characteristics of the flow of alcoholic and

nonalcoholic CP, it turned out that abdominal pain was more likely ($p < 0.05$) to be more troubling for patients who abused alcohol (87% vs 65%, respectively), they had a recurring course of acute pancreatitis (44% vs 23 %), frequent formation of pseudocysts (41% vs 16%), high total developmental rate of exocrine insufficiency (60% vs 21%) and a high incidence of hospitalizations during the year after diagnosis of CP (0.79 vs 0.25). The total risk of developing diabetes mellitus, calcification of the prostate, performing surgical interventions and the overall survival rate for alcoholic CP were comparable to those in non-alcoholic CP.

A large population study on the etiology, clinic, and efficacy of CP treatment ($n = 521$) in North America was conducted by J. Romagnuolo et al. (2016) [4]. Almost half of the examined patients were female (45%). The alcohol etiology of CP was completely untypical for women compared with men (30% vs 58.5%, respectively, $p < 0.05$), the females more often suffered from idiopathic (32% vs 18%), obstructive (12% vs 2, 4%), genetically conditioned (12.8% vs 7.3%) CP. Other characteristics (peculiarities of abdominal pain syndrome, morphological data, severity of exocrine and endocrine pancreatic insufficiency, incidence of disability due to CP, and the effectiveness of different treatment methods) did not have significant gender differences. Sphincterotomy was more often performed in women than in men (biliary: 33% vs 24%, pancreatic: 38% vs 28%, $p < 0.05$), while the stronger sex was more likely to undergo surgery for cyst / pseudocyst of the pancreas 6.6% vs 2.6%, respectively, $p = 0.02$).

Instrumental diagnostics

A number of studies evaluating the informativity of various diagnostic techniques in the pathology of the prostate. The study of HC Oh et al. (2017) [13] is devoted to the diagnostic value of the decrease in the activity of amylase and lipase in the diagnosis of CP. In accordance with the design of the study, patients with noncalcifying ($n = 99$) and calcifying ($n = 112$) CP, as well as practically healthy persons ($n = 170$) were examined. In patients with noncalciferating CP, the average concentration of blood amylase was 34.0 U / l (24.5-49.0 U / l), blood lipids — 19.0 U / l (9.0-30.0 U / l), in patients with calcifying CP, respectively, 30.0 Unit / l (20.0-40.8 U / l) and 10.0 U / l (3.0-19.0 U / l), while in healthy individuals the values of these indicators were 47.0 U / l (39.8-55.3 U / l) and 25.0 U / l (18.0-35.0 U / l), respectively. The borderline level below which the

non-calcifying CP can be differentiated from the norm is defined as 40 U / l for amylase and 20 U / L for lipase; to distinguish calcifying CP from a normal state it is possible at a level of amylase and lipase below 38 U / l and 15 U / l, respectively. Positive and negative predictive values of low concentrations of these enzymes were 37.4% and 88.8%, respectively; 66.1%, and 70.9%.

The results of a meta-analysis and systematic review comparing the informativeness of endosonography and magnetic resonance cholangiopancreatography in idiopathic acute pancreatitis are presented [5]. Analysis of 34 studies ($n = 2338$) showed that the informativity of endosonography in determining the etiology of the disease is 64%, and cholangiopancreatography — 34% ($p < 0.001$). Comparing the diagnostic value of these techniques in different subgroups (depending on the etiology of pancreatitis), the authors of the study established that in acute biliary pancreatitis and CP, endosonography ($p < 0.001$) becomes more important, and pancreas divisum — magnetic resonance cholangiopancreatography ($p < 0.001$).

An attempt to link the data of endosonography and elastography of the prostate with the severity of CP was undertaken in a randomized study, which is necessary to determine the criteria for the different stages of prostate fibrosis, similar to the criteria used to diagnose liver fibrosis [16]. Elastography of the pancreas and liver was performed by 52 patients with CP and 42 healthy volunteers. It is proved that in CP, the density of the prostate is much higher than that of healthy individuals (4.3 ± 2.4 kPa vs 2.8 ± 1.1 kPa, respectively, $p = 0.001$) (Fig. 1). A more significant increase in the density of the gland was recorded in patients with long-lasting CP, taking analgesics, as well as in patients with reduced body weight.

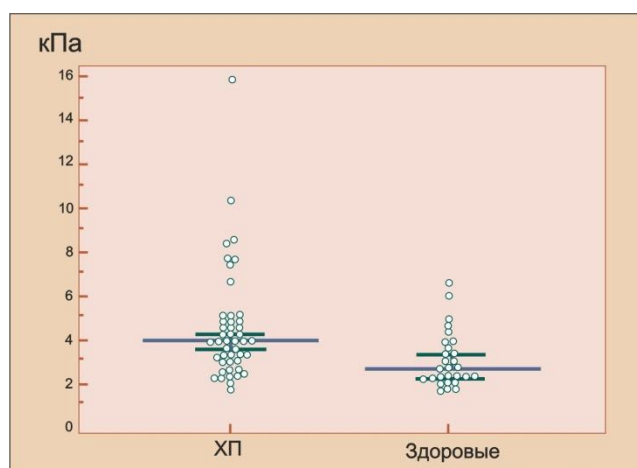


Fig. 1. Pancreas density in patients with CP and healthy individuals
(according to R. Pozzi et al., 2017 [16]).

In addition, the results published earlier by J. Iglesias-Garcia et al. (2013) [21]: a linear relationship between the number of endosonographic criteria of CP and a deformation index representing the ratio of the density of the patient's prostate tissue to that of a healthy person (norm) is fixed (figure 2); The increase in the strain index from a questionable to a definite CP is shown in accordance with the classification of M-ANNHEIM [25] (Fig. 3).

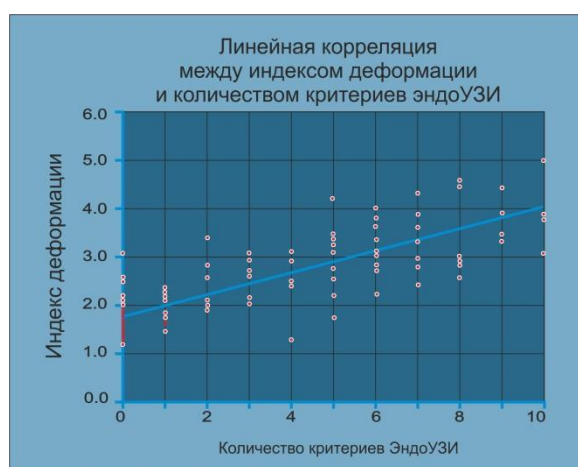


Fig. 2. Linear correlation between the number of endosonographic criteria of CP and deformation index (according to R. Pozzi et al., 2017 [16]).

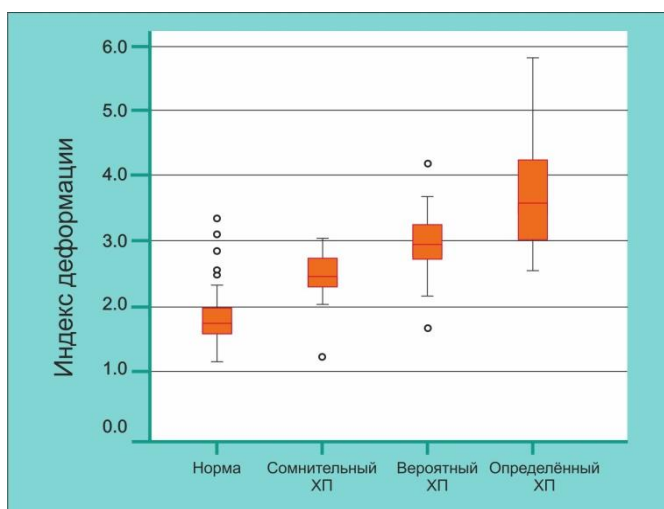


Fig. 3. An increase in the strain index from a questionable to a definite CP
(according to R. Pozzi et al., 2017 [16]).

Extremely important are the results of the meta-analysis and systematic review devoted to the analysis of the relationship between CP and RV cancer [11]. The results of 13 randomized trials were studied. The probability of occurrence of prostate cancer in patients with CP was 16.16% (95% CI 12.59-20.73) for patients with confirmed prostate cancer, which was detected within 2 years after the diagnosis of CP. The risk of developing pancreatic cancer in patients with CP decreased with increasing follow-up to 5 years — 7.90 (95% CI 4.26-14.66) and reached the minimum values for a 9-year follow-up period of 3.53 (95% CI 1, 69-7.38). Consequently, patients with CP require a thorough screening of the prostate cancer for at least 5 years after the diagnosis of CP.

A systematic review and meta-analysis again assessed the diagnostic value of various imaging methods in the diagnosis of CP [6]. Meta-analysis is based on the results of 43 studies conducted with the participation of patients with CP (n = 3460). The sensitivity of endoscopic retrograde cholangiopancreatography was evaluated in 82% (95% CI 76-87%), it exceeded the same value of routine sonography — 67% (95% CI 53-78%, p = 0.018). The sensitivity of endosonography, magnetic resonance imaging and computed tomography was 81% (95% CI 70-89%), 78% (95% CI 69-85%) and 75% (95% CI 66-83%), respectively; these indicators were not statistically different from each other. Comparison of specificity indicators showed comparability of the studies: endosonography — 90% (95% CI 82-95%), retrograde cholangiopancreatography — 94% (95% CI 87-98%), computed tomography — 91% (95% CI 81-96%), magnetic resonance imaging — 96% (95% CI 90-98%), transabdominal sonography — 98% (95% CI 89-100%). The choice of the method of visualization should be carried out taking into account the degree of invasiveness of the study, its availability in a particular medical institution, the cost, as well as the experience of the doctor.

Treatment

In 2017, the first unified European clinical guidelines for the diagnosis and treatment of CP were published, which are the result of a long 3-year work of European experts, including leading Ukrainian specialists [28]. This document details all aspects of the diagnosis and treatment of CP.

CFT

In our opinion, the most important for practicing gastroenterologists are the nuances of carrying out PTA with exocrine insufficiency of the prostate (EPI). Given the importance of this issue, we will repeat the provisions corresponding to this aspect from our article published last year [28].

- *Question 4.2-1* : What are the indications for the appointment of OPT in CP?
Position 4.2-1: Substitution therapy is indicated for CP with EPI in the presence of clinical or laboratory signs of malabsorption. An appropriate nutritional status study is recommended to identify signs of malabsorption (*the level of evidence is 1A, the degree of agreement of the experts is strong*).
- *Question 4.2-2*: Which enzymes are the drugs of choice?
Position 4.2-2: Enteric coated microspheres or minimocrosses with a size of less than 2 mm are the drugs of choice for VNPW. Micro- or minitabets measuring 2.2-2.5 mm can also be effective, but scientific evidence of their effectiveness in CP is limited. Comparative clinical studies of various enzyme preparations are not available (*level of evidence is IV, the degree of agreement of experts is strong*).
Comments. The effectiveness of pancreatic enzyme preparations depends on several factors: 1) mixing with food; 2) evacuation from the stomach with food; 3) mixing with duodenal chyme and bile acids; 4) rapid release of enzymes in the duodenum. It has been shown that minimocrosses with a diameter of 1.0-1.2 mm are evacuated from the stomach simultaneously with food and have a higher therapeutic efficiency compared to microspheres 1.8-2.0 mm in size, which, nevertheless, work satisfactorily.
- *Question 4.2-3* : How should I prescribe enzyme preparations?
Regulation 4.2-3: Enzyme preparations should be distributed between basic and intermediate meals (*the level of evidence is 1A, the degree of agreement of experts is strong*).
- *Question 4.2-4*: What is the optimal dose of enzyme preparations for HPV

caused by CP?

Position 4.2-4: The minimum dose of lipase is 40 000-50 000 units for the main meal and half the dose for intermediate meals (*level of evidence is IA, the degree of agreement of experts is strong*). The most recent and well-methodologically constructed RCTs demonstrated the effectiveness of the ZPT EPI with the use of an enteric-coated minimosphere at a dose of 40,000 to 80,000 units of lipase per basic meal and half the dose for each intermediate meal per snack.

- *Question 4-2.5 :* How to assess the effectiveness of the ZPT of EPI?

Position 4-2.5: The effectiveness of ZTFTA can be objectively judged by alleviating the symptoms associated with maldigestion (for example, steatorrhea, weight loss, flatulence), and normalizing the nutritional status of patients. In patients who have not responded to treatment, it may be useful to use functional studies of the prostate (determining the fat absorption factor or ¹³ C-mixed triglycerides) in parallel with the use of enzyme preparations. *level of evidence — IV; the degree of consensus of experts is strong*). Comments. Despite the fact that the disappearance of clinical symptoms of malabsorption is usually considered the most important criterion for the success of the UPP of the VLPW, which is associated with an improvement in the quality of life, later studies have demonstrated that symptom relief is not always associated with normalization of nutritional status. The concept of controlling the normalization of nutritional parameters (both anthropometric and biochemical) as an optimal way of evaluating the effectiveness of the ZPT of the VNPW is confirmed.

Of course, the minimosphere enzyme preparation Creon, which for several decades reserves the right to be the "gold standard" of the CFT all over the world, has all the necessary qualities and advantages.

A number of high-level studies carried out in 2017, was devoted to the review of the effectiveness of the ZPT at EPI. Interesting data were obtained in one randomized trial, during which patients with chronic circulatory failure (n = 104) and healthy subjects (n = 20) were monitored. The frequency of changes in the parameters of the fecal elastase test, the relationship between EPI and the degree of

decrease in appetite, and the trophological status were studied. A positive correlation was found between the results of the questionnaire conducted to assess the appetite expression (questionnaire-appetite) and fecal elastase-1 (FE-1) (Figure 4).

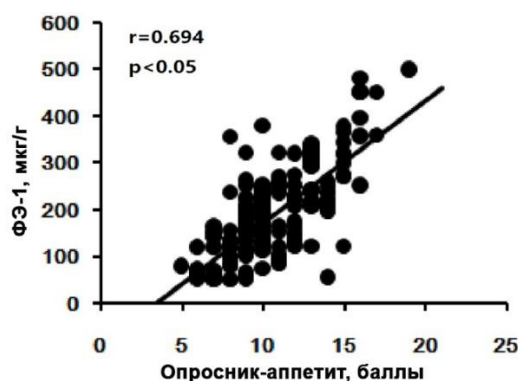


Fig. 4. Correlation between the results of questionnaires intended for assessing appetite and FE-1 (according to T. Xia et al., 2017 [29]).

Patients with reduced PE-1 concentration were given Creon 10 000 2 capsules 3 times / day for a month. Such treatment contributed to a significant improvement in appetite, an increase in albumin and prealbumin in the blood serum (Figure 5).

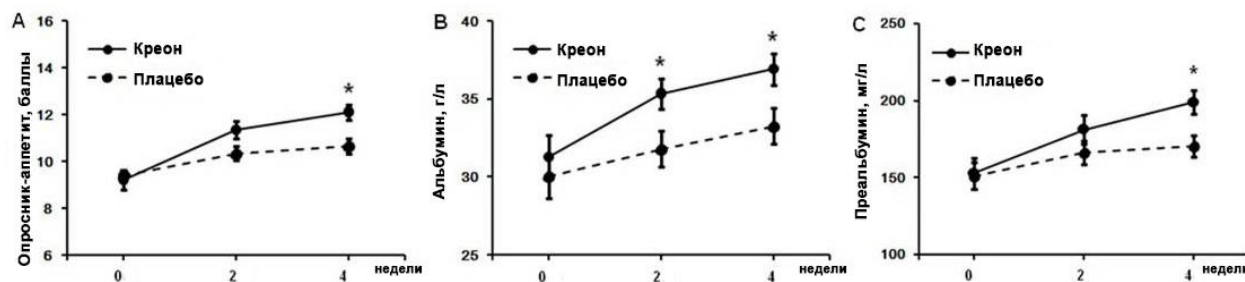


Fig. 5. Influence of Creon's administration on patients with chronic circulatory failure and low level of FE-1 on the studied parameters (according to T. Xia et al., 2017 [29]).

The authors of the study summarized that a decrease in appetite in case of chronic circulatory insufficiency is partially associated with EPI, and Kreon's substitution therapy improves appetite. These results suggest the presence of a possible pathogenetic link between a decrease in appetite and the development of

EPI with chronic circulatory failure. Further studies are needed to determine the possible pathogenetic mechanisms.

A randomized controlled study at the Queen Elizabeth Central Hospital in Miami, USA, was devoted to the study of the efficacy and safety of ZTT in children aged 6-60 months with severe malnutrition ($n = 90$) [15]. All children received standard treatment; in addition, some small patients were assigned a 28-day AFT. Weight gain in children receiving enzyme preparations did not exceed that in the control group ($15.3 \pm 11.3\%$ vs $13.7 \pm 9.0\%$, respectively, $p = 0.56$). The mortality rate in the group of children who were on the AFT was significantly lower than in the control group (18.6% vs 37.8% , respectively, $p < 0.05$). Children who received PTA, more often ($p = 0.02$) were discharged from the hospital, in contrast to patients who were on standard therapy.

VK Singh (2017) analyzed the Cochrane review of 13 randomized trials on the efficacy and safety of CFT in cystic fibrosis [26]. Overwhelming majority of patients with cystic fibrosis (85-90%) are born with EPI or acquire it in early childhood, and need lifelong PTA to minimize maldigestion and malabsorption. Most often for PF use pancreatin preparations. Of great importance is the presence of an enteric coating that prevents the inactivation of enzymes in the acidic environment of the stomach and dissolves in the duodenum, ensuring the release of enzymes in a "safe" medium with a pH of 5.0-5.5. The enzyme preparation should have an optimal particle size that will ensure its uniform mixing with food and simultaneous intake with chyme from the stomach to the duodenum, which is possible only with the use of microspheres and minimocrosses of pancreatin. In the Cochrane review, that minimally enteric-coated microcosms exert a greater influence on the clinical symptoms of HPN as compared to drugs that do not have an acid-resistant coating. Enzyme preparations should be taken with food. There are three potential strategies for the World Climate Program. At present, the optimal strategy has not yet been developed, in part because there are many factors that influence the physiological secretion of the prostate, including age, sex, and nutrition. Dosing pancreatin, based on the fat content in food (500-4000 units of lipase per gram of fat) seems logical, but for most patients it is quite difficult. A possible method of dosing may be to select a dose of pancreatin taking into account the patient's weight (500-2500 units / kg for the main meal and half the dose for intermediate meals in patients older than the baby). The latter strategy is

based on the appointment of a fixed dose of pancreatin. Taking into account the fact that about 480 000-960 000 units of lipase, and 5-10% of the total volume of lipase is required to prevent malabsorption, then 50 000-100 000 units of lipase should be prescribed for the main meal.

Among the new enzyme preparations of non-animal origin, which have a great clinical potential, Lipromazu, which is a combination of bacterial lipase, fungal protease and amylase, should be specially emphasized. The efficacy of Lipromadase in cystic fibrosis is indicated in randomized, placebo-controlled trials [10, 24] (Figure 6), but the drug has not yet been approved by the FDA.

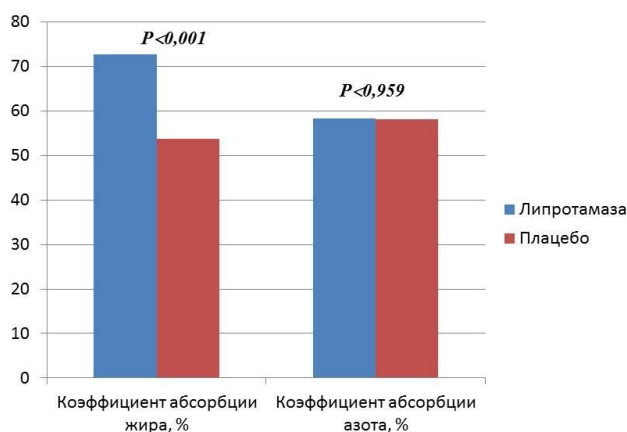


Fig. 6. Effect of Liprotamase on fat and nitrogen absorption coefficients for cystic fibrosis (according to JE Heubi et al., 2016 [24]).

Meta-analysis and systematic review, which is of great importance for practical activities, confirmed the effectiveness of PFT in pancreatin in CP [8]. Analyzing the results of 17 randomized trials ($n = 511$), the authors demonstrated a significant increase in the fat absorption coefficient in the dynamics of pancreatin treatment compared with placebo. The efficacy of the treatment was improved by using the optimal doses (40,000-50,000 units of lipase per basic meal and 20,000-25,000 units of lipase per meal) of pancreatin. Moreover, a further increase in the dose of the enzyme preparation did not have a significant effect on the fat absorption coefficient. The effectiveness of PPT increased with the use of acid-resistant drugs (with enteric coating), reception of an enzyme preparation during a meal, as well as simultaneous administration of proton pump inhibitors.

T. Saito et al. (2017) conducted a prospective cohort study examining the effectiveness of OPT in unresectable prostate cancer [22]. Patients (n = 91) were randomized for standard chemotherapy (n = 45) and additional pancreatin (n = 46) at a dose of 48,000 units of lipase per meal at the time of chemotherapy. Prior to the appointment of SPT, the status of the exocrine function of the prostate gland was assessed by means of a test with benzoyl-tyrosyl-paraaminobenzoic acid (PABC test or bentiramine test). The values of the PABC test were reduced in 94% of patients randomized to pancrelipase. The initial and final values of nutritional markers, their successive changes (defined as the ratio of marker values at week 16 to the initial indications) in the dynamics of treatment were analyzed. Consecutive changes in body mass index in the pancrelipase group compared with the traditional therapy group were 1.01 vs 0.95, respectively ($p < 0.001$), serum albumin — 1.03 vs 0.97 ($p = 0.131$). The authors concluded about the high prevalence of exocrine pancreatic insufficiency in patients with unresectable prostate cancer and the potential effectiveness of ZPT in correcting the nutritional status during chemotherapy.

Another multi-center, open-label, randomized controlled trial, presented by S. Tomotaka et al. (2017), analyzed the effectiveness of ZPT in unresectable prostate cancer [14]. Patients (n = 88) were equally divided into the main and control groups. Patients making up the main group were given pancreatin at a dose of 48,000 units of lipase per basic meal during chemotherapy; patients of the control group received standard chemotherapy. Before the study, all patients underwent a PABC test. The primary endpoint was a change in nutritional status after 8 weeks (mass index body, serum albumin, total serum cholesterol). As secondary endpoints, overall survival and other trophological markers were used after 8 and 16 weeks of therapy. The values of the PBA test were reduced in 90% of cases. The researchers did not detect significant differences in the values of trophological markers after 8 and 16 weeks of therapy, i.e. In this study, the appointment of SPT did not affect the achievement of the primary endpoint. The median overall survival in the pancreatin group was 21.0 months, while in the control group, the indicator was 14.5 months ($p = 0.078$). Thus, the results of this study did not confirm the optimistic data of the previous prospective study. Of course, further study of the effectiveness of OPT in prostate cancer involving more patients is needed.

Not only the CFT

An important conclusion about the possibility of arresting pain in CP by prescribing proton pump inhibitors is made in a prospective randomized trial performed by AK Pujahari et al. (2017) [20]. Patients (n = 137) were divided into 2 groups: control (traditional treatment of pancreatic pain by analgesics) and basic (60 mg omeprazole 2 times / day for 1 year). Within two weeks, the pain syndrome was stopped in 68.1% and 96.96% of the patients in the control and main group, respectively. After 1 year of therapy, it was found that patients who received omeprazole were more likely to gain weight (95%) than patients in the control group (69.5%). In the omeprazole group, the resolution of all pseudocysts of the prostate gland is noted; undesirable phenomena with omeprazole therapy are not fixed.

Surgical methods of treatment

In the retrospective study (n = 168), the prognostic factors of the effectiveness of therapy, including the long-term effectiveness of endoscopic treatment of CP, were studied [19]. The average duration of follow-up after the intervention was 10 months; endoscopic treatment in 83% of cases contributed to a decrease in the intensity of the pain syndrome. Young age (up to 40 years) is recognized as a reliable factor that increases the effectiveness of endoscopic treatment, then smoking was associated with the worst results of therapy. The need for hospitalization after the intervention was more likely to occur in smokers and patients with alcoholic CP.

The problem of the effectiveness of treatment of pancreatic pain in CP was studied in meta-analysis and a systematic review based on the results of 16 studies (n = 1498) [7]. Direct relief or relief of pain after endoscopic treatment was recorded in 88% of cases (95% CI 81.0-94%). Long-term effectiveness of endoscopic therapy was 67% (95% CI 58-76%), and the probability of complications of endoscopic treatment (mainly acute pancreatitis, occlusion or stent migration) was 7.85%.

In a study by J. Cornman-Homonoff et al. (2017) [3] proved the feasibility of blockade of the solar plexus and neurolysis for the relief of pancreatic pain. The blockade of the solar plexus is a minimally invasive manipulation that effectively

reduces pain, improves the function of the pancreas and reduces dependence on opiates, and improves the quality of life. The probability of complications is low enough. Scientists summarized that the blockade of the solar plexus and neurolysis can be used to relieve pancreatic pain in the early stages of the disease.

A population-based study of the quality of life of patients who underwent pancreatoduodenectomy five years ago for various indications (n = 245, 157 of them had no malignant pathology) were performed by pancreatologists of the United States and Great Britain [9]. Diabetes mellitus was diagnosed in 10.6% of patients; 50.4% of patients took enzyme preparations, 54.6% of participants — antacids. Using the questionnaire for assessing the quality of life EORTC QLQ-C30, the researchers recorded a higher quality of life in patients who underwent pancreatoduodenectomy compared with controls (78.7 vs 69.7, $p < 0.001$). The parameters of physical and role functioning in patients who underwent surgery (86.7 and 86.3, respectively) significantly exceeded those in the control group (77.9 and 74.1, respectively, $p < 0.001$ in all cases). Additional statistical processing (linear regression, correction for socio-economic data) did not reveal significant differences in the studied parameters depending on the nature (benign or malignant) of the underlying disease. The intake of pancrelipase (-6.8, $p = 0.035$) or antacids (-6.3, $p = 0.044$) was associated with lower social indicators.

Mobile app

In 2017, the European Club of Pancreatologists released an application containing the "Unified European Clinical Recommendations for Diagnosis and Treatment of CP," which is available for both Android and IOS (Apple). In order to download this application to your phone, it's enough to do three simple steps:

1. go to the App Store (Apple) or Google Play (Android);
2. type in the search box "pancreatitis";
3. Select the free UEG application and download it to your phone / tablet.

Using this application, practical doctors can at any time get easy and quick access to the provisions of the current European guidelines for the treatment of CP and apply them in their clinical practice.

Summarizing, we emphasize that the development of innovative diagnostic methods and genetic screening will provide early diagnosis of CP and reduce the risk of functional failure of the pancreas. Improvement of clinical recommendations based on the results of evidence-based studies is the most correct way to improve diagnosis and treatment in pancreatology, which, however, does not exclude, but implies the need for practical experience of the doctor. As Pavlov said: "If there are no ideas in your head, you will not see the facts" [2].

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Evidence-based pancreatology 2017/2018 (review of the results of studies on chronic pancreatitis and exocrine pancreatic insufficiency)

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The article provides an overview of the European recommendations on the diagnosis and treatment of chronic pancreatitis. The results of evidence-based research related to the epidemiology, course of chronic pancreatitis, assessment of the informative value of various imaging techniques, treatment of pancreatic insufficiency upon chronic pancreatitis, cystic fibrosis, pancreatic cancer are analyzed. A conclusion is drawn about the need for further carrying out of evidence-based studies.