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THE EFFECTIVENESS OF SYSTEMIC ENZYME THERAPY IN COMPLEX TREATMENT CHRONIC PANCREATITIS IN OLD AGE

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Abstract

Relevance. The variety of functional changes in internal organs characteristicofgeriatricage necessitates the search for drugs that can exert a multifaceted effect on various links in the pathogenesis of chronic pancreatitis (CP) in comorbidity with the most common diseases of the elderly. Purpose. Investigation of the effectiveness of the inclusion of a systemic enzyme therapy drug in the complex treatment of chronic pancreatitis in elderly patients. **Materials and methods.** We examined 77 patients with CP over the age of 66 years, the average age (71.3 ± 1.4) g. Group I of patients with CP (23 patients) - took aconventional therapeutic complex (MC) for three months: pantoprazole 40 mg on an empty stomach according to requirement, continuous enzyme replacement therapy with pure pancreatin in an adequate dose with each meal, prokinetics / or antispasmodics if necessary. Group II consisted of 34 patients with CP (MC + W), in addition to LK, the drug of systemic enzyme therapy (SET) Wobenzym, 5 tablets, was taken. three times a day for three months. The control group consisted of 20 patients without signs of pathology of the digestive system.

The parameters of lipid metabolism were determined by the enzymatic-colorimetric method. The assessment of the depth of exocrine pancreatic insufficiency (PI) was determined by the level of fecal α-elastase (FαE) by enzyme-linked immunosorbentassay using standard BIOSERVELASTASE 1-ELISA kits. Statistical analysis was performed using Excel and the statistical package Statistica v. 5.0. **Results**. Additional inclusion of the drug SET (Wobenzym) in the generally accepted MC promoted a significant improvement in lipid profile parameters in elderly patients with CP, as well as a reliable correction of the excretory function of the P by the level of FαE (from the level of moderate to mild insufficiency). **Conclusions.** 1) The inclusion of Wobenzym in the general treatment complex contributed toa decrease in the levels of TC, βLP, TG and LDLP by 15.4%, 19.8%, 32.0% and 33.9%, respectively ($p < 0.001$), as well as an increase in the level of HDLP by 21.7% and a decrease in AF (by 41.3%) ($p < 0.001$); 2) under the influence of treatment with the use of Wobenzym, a significant increase in the level of FαE (by 42.6%) was found relative to this indicator to treatment ($p < 0.001$), which significantly exceeded the results (by 15.8%) in the MC group, which were not statistically significant ($p > 0.05$).

Key words: chronic pancreatitis; enzyme therapy; exocrine insufficiency; lipid metabolism

Introduction. The course of chronic pancreatitis (CP), like other most common nosologies, depends on age and physiological changes inherent in it. Attempts to distribute by age groups are toacertain extent determined by the average life expectancy of a person, the changes in which directly depend on the period of onset of the senility. The population of Ukraine, which is a global tendency, is “getting older”, therefore it is important to include in the treatment approaches toany pathology, including CP, the prophylacticaspect related to the age aggravating features. It is known that the most significant changes indicative of senility are observed in middle age and are associated with the physiological characteristics of the organism.

After 45 years, due to disturbances in the central mechanisms of regulation of endocrine functions of the hypothalamus-pituitary-gonads system, negative shifts occur in regulatory mechanisms that change complex neuroendocrine relationships and lead with age to the development of dystrophicand degenerative processes in all tissues and body systems is in the process of aging, gradually adapting these systems to new age-related changes in existence. Therefore, the period of life of patients who have CP, after 65 years of age, it is very important to include additional means and techniques in order to prevent the effect on

aging organs. In addition, elderly patients with CP are characterized by the presence of polymorbidconditions, among which atherosclerosis and cardiovascular diseases occupy a leading position, and is acomplicating factor of atherosclerosis, microcirculatory changes, chronic ischemiaof the pancreas (P) and adjacent organs with loss of basic functions [8]. Often the first marker of loss of functions and aging is the formation of dyslipidemia, which is often inherent in CP, which leads to the complication of its clinical course. There is evidence of recent years: the age of dyslipidemia is "younger",and even people younger than 55 years old without morbid obesity, diabetes mellitus (DM) and arterial hypertension show echocardiographic signs of early diastolic dysfunction of the left ventricle. Therefore, dyslipid disorders in CP are often important to diagnose and control.

It is also known that P is one of the first organs that, in the presence of prolonged ischemia, responds with a decrease in functional activity, which manifests itself as both minor structural changes and significant degeneration of the gland, which leads to severe functional failure [1, 2]. Many experts believe that P has great compensatory properties, therefore, for a long time, progressive exocrine insufficiency (PEI) clinically manifests itself only as amalabsorption syndrome, and a violation of pancreatic secretion is manifestedonly in severe damage to the gland. However, achieving control over the state of functional ability of P is an extremely important way of not only enzyme replacement therapy, butother additional means. This motivates clinicians and scientists to search for drugs, to have a multifaceted effect on various links in the pathogenesis of CP in comorbidity with dyslipidemia, atherosclerosis, cardiovascular disorders, the formation of insulin resistance and DM [9].

Among the additional possibilities for enhancing the complex treatment of CP,attention was drawn to intracellular enzymes, which are specific proteins that significantly accelerate chemical processes in living organisms. During the administration of systemic enzyme therapy (SET) drugs, they enter the vascular system from the small intestine and provide a therapeutic effect due toa direct effect on the immune system, hemostasis and rheological properties of the blood. The following effects are inherent in SET drugs: immunomodulatory, protipal, fibrinolytic, antiplatelet, hypocoagulant, anti-edematous [7]. The capabilities of SET are provided due to its ability to remove immune complexes from the bloodstream and membrane deposits from tissues, as well as to eliminate detritus, protein and toxiccomponents formed during an acute and / or chronic inflammatory process from the focus of inflammation. The anti-inflammatory effect of SET is due to the improvement in the breakdown of fibrin, which is released. Considering the above, I consider it appropriate

toconducta study on the possibilities of the influence of SET on some pathogenetic links of CP in elderly patients.

Aim of the study: to study the effectiveness of the inclusion of a systemic enzyme therapeuticagent in the complex treatment of chronic pancreatitis in the elderly.

Materials and methods: On the basis of the "Odessa Regional Clinical Medical Center", 77 patients with CP over 66 years old were examined. The average age is (71.3 ± 1.4) years. The source of information was “Medical records of an outpatient patient” and “Medical records of an inpatient patient” of patients with CP during 2014-2020. The diagnosis of "chronic pancreatitis" bulov is established on the basis of the clinical protocol according to the Order of the Ministry of Health of Ukraine No. 638 dated 09/10/2014.

Criteria included in the examination: patients over 66 years of age with an established diagnosis of CP in the phase of complete and incomplete remission and taking intoaccount the concomitant pathology without exacerbation.

Exclusion criteria: blood diseases, oncological diseases, acute infectious diseases during the last 3 months, exacerbation of chronic pathology, the state of decompensationof vital organs, patients with diabetes on insulin therapy.

I group of patients with CP (23 patients) - took a generally accepted treatment complex (MC) for three months: pantoprazole 40 mg on an empty stomach on demand, continuous enzyme replacement therapy (CERT) with a preparation of pure pancreatin in an adequate dose with each meal, prokinetics / or antispasmodics as needed.

Group II consisted of 34 patients with CP (MC + W), who took, in addition to TC, the drug SET Wobenzym, 5 tablets each three times a day for three months.

The control group consisted of 20 patients without signs of pathology of the digestive system, comparable in age, gender, social and medical status.

Patients of the study groups were under outpatient care and adhered to the recommendations for normotrophic nutrition.

Using the enzymatic-colorimetric method, lipid metabolism parameters (total cholesterol (TC), high and low density lipoproteins (HDLPand LDLP), β-lipoproteins (β-LP), triglycerides (TG), atherogeniccoefficient (CA) were determined. carried out according to the latest clinical guidelines [4].

Evaluation of exocrine insufficiency of the pancreas was determined by the level of fecal α-elastase (FαE) by enzyme immunoassay using standard kits from BIOSERV-ELASTASE1-ELISA. The level of FαE > 200 mkg / g indicated the absence of pancreatic

insufficiency. Level from 150 to 200 mkg / g - moderate (moderate pancreatic insufficiency), FαE level> 100 mkg / g - severe pancreatic insufficiency [10].

Statistical evaluation was carried out in accordance with state standards and settings using biomedical statistics using Excel [5] and the statistical package Statistica 5.0 [6]. Parametric Student's and F-Fisher's tests for related and unrelated samples were used tocompare them after checking the homogeneity of variances using the Bartlett test. The deviation between the means was compared and the strength of the relationship between the variations in indicators was assessed by the value of the Pearson[3] sample correlation coefficient, the difference from the zero value of which was considered significant at $p < 0.05$.

Results and their discussion. Among 77 patients with CP, 26 were men (33.7%), women - 51 (66.3%). The rather large difference in terms of gender can be explained by the fact that it is a sample of older people [11], the life expectancy of women is longer than that of men, and also that men pay less attention to their state of health, so women patients are a lot more often in outpatient observation.

Acomparativean alysis of the treatment outcomes was carried out in the study groups according to the effect on the parameters of the lipid profile. According to the table 1, stated that all patients in both groups had lipid metabolism disorders in the direction of arteriosclerosis in all parameters, which were typical for their age and an existing accompanying pathology.

In the first group of MC there was a tendency to improve the lipid profile parameters ($p_2>0.05$) against the background of an improvement in general well-being after treatment, but the mean values of all parameters were nevertheless in the zone of atherosclerotic changes. A significant decrease (14.6%) only occurred in group I after treatment ($p_2<0.05$) in the TG content, but this content was in the triglyceridemia zone.

In group I found a slight improvement in lipid profile by 2.40; 4.15; 1.5; 3.50 and 1.40%, respectively, on the content of TCH, βLP, LDLP, HDLP and KA, but the results were not statistically significant ($p>0.05$). The study showed that the additional inclusion of Wobenzyme in MC according to the proposed scheme helped to reduce the levels of TCH, βLP, TG and LDLP by 15.4%, 19.8%, 32.0% and 33.9%, respectively. Significantly, the inclusion of SET in the treatment course contributed toan increase in the level of HDLP by 21.7% and a decrease in AF (by 41.3%) almost the upper limit of normal ($p < 0.001$).

The effectiveness of the proposed program of treatment of patients with CP of the elderly with the inclusion of Wobenzym also on the functional ability of the Pon the indicator of FαE (data in table 2).

Table 1 - Dynamics of lipid metabolism in elderly patients with CP in comparison groups according to treatment complexes

Indicator lipidograms	Control (n=20)	MC (I group, n=23)		MC+W (IIgroup, n=34)	
		Before healing	After healing	Before healing	After healing
GC, mmol/L	5,06±0,17	6,62±0,14 p_1<0,001	6,46±0,12 p_2>0,05	6,14±0,17 p_1<0,01	5,19±0,20 p_2<0,01 p_3<0,001
βLP, од	51,11±2,44	72,15±2,37 p_1<0,01	69,14±2,28 p_2>0,05	65,06±3,55 p_1<0,01	52,17±2,43 p_2<0,001 p_3<0,01
TG, mmol/L	1,95±0,03	3,48±0,12 p_1<0,001	2,97±0,09 p_2<0,05	3,62±0,37 p_1<0,01	2,46±0,33 p_2<0,05 p_3<0,05
LDLP, mmol/L	2,61±0,11	4,24±0,17 p_1<0,001	4,18±0,14 p_2>0,05	3,45±0,13 p_1<0,01	2,28±0,17 p_2<0,01 p_3<0,01
HDLP, mmol/L	1,82±0,03	1,59±0,06 p_1<0,01	1,64±0,07 p_2>0,05	1,43±0,01	1,74±0,06 p_2<0,01 p_3>0,05
AF	2,38±0,31	4,31±0,34 p_1<0,001	4,25±0,33 p_2>0,05	3,44±0,22	2,02±0,18 p_2<0,001 p_3<0,01
Notes: 1. p_1 – the difference between such indicators relative to the control group; 2. p_2 – the difference between such indicators relative to their group to treatment; 3. p_3 - the difference between such indicators relative to the MC group					

Table 2 - Comparative analysis of the effectiveness of treatment programs for exocrine insufficiency of the pancreas software in CP in elderly patients

Comparisongroups	Index FαE, мкг/г	
	Before healing	After healing
MC (I група, n=23)	124,17±7,76 p_1<0,001	143,87±3,24 p_2>0,05
MC+B(II група, n=34)	118,56±8,21 p_1<0,001	169,16±5,12 p_2<0,001 p_3<0,01
Control (n=20)	271,2±3,12	
Notes: 1. p_1 – the difference between such indicators relative to the control group; 2. p_2 – the difference of such indicators in relation to their group before treatment; 3. p_3 - the difference between such indicators relative to the MC group;		

Under the influence of treatment, a statistically significant increase in the level of FαE (42.6%) was found in patients of group II relative to this indicator before treatment (p

<0.001). The rate of FαE in group I after the proposed treatment increased compared to baseline by 15.8% and amounted to (143,87±3,24), but was not statistically significant (p> 0,05).

Thus, under the influence of complex treatment with additional inclusion of Wobenzyme in elderly patients with CP there was a significantly more significant improvement in lipid metabolism parameters compared with MC, which contributed to the improvement of general well-being of patients. In addition, there was an increase in the level of FαE, which is a marker of the restoration of the excretory function of P to the level of EXI P mild, which allows us to expect not only improvement of digestive processes, but also optimization of trophological status.

Conclusions:

1) Additional inclusion in the conventional treatment complex of systemic enzyme therapy (Wobenzym) contributed to the probable improvement of lipid profile parameters in patients with CP of the elderly, as well as significant correction of excretory function of the P by the level of fecal α-elastase (from mild to moderate);

2) the inclusion of Wobenzyme in MC contributed to a decrease in the levels of TCH, βLP, TG and LDLP by 15.4%, 19.8%, 32.0% and 33.9%, respectively (p <0.001), as well as an increase in the level of HDLP by 21 , 7% and a decrease in spacecraft (41.3%) almost to the upper limit of normal (p <0,001);

3) under the influence of treatment with Wobenzym, a significant increase in the level of fecal α-elastase (by 42.6%) relative to this indicator before treatment (p <0.001), which significantly exceeded the results (by 15.8%) in the group of MC, which were not statistically significant (p> 0.05), which proved the feasibility of using systemic enzyme therapy in the treatment of elderly patients with CP.

There is no conflict of interest. Participation of the authors: concept and design of the study – L.S. Babinets. Material handling and writing of the text – N. A. Shevchenko. Statistical data processing - N. A. Shevchenko.

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