

Treatment of Patients with Chronic Pancreatitis against the Background of Hypothyroidism

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Relevance. The activity of the pancreas (PG) is under the regulatory influence of thyroid hormones[1,3,18]. When the thyroid gland is removed, pancreatic atrophy is observed, and the use of thyroid hormones leads to restoration of pancreatic mass[2,3,19,20]. On the other hand, in patients with acute edematous pancreatitis, 72 hours after hospitalization, a decrease in the level of triiodothyronine, characteristic of hypothyroidism, is shown, but without clinical manifestations of the latter[4,5]. A decrease in the content of triiodothyronine and thyroxine was noted in patients with chronic pancreatitis[6,7,23]. According to the literature data, the close relationship between the thyroid gland and the pancreas is obvious, but the features of the course and treatment of chronic pancreatitis (CP) in patients with hypothyroidism remain insufficiently studied[8,9,10]. In this work, the task is to determine pathogenetically substantiated therapy for patients with CP with concomitant hypothyroidism[21,22,24].

Materials and research methods: To solve this problem, 52 patients with CP with concomitant hypothyroidism were examined, of which 27 (51.9%) patients with subclinical hypothyroidism, 14 (26.9%) - 1st degree of severity, 7 (13.5%) - 2nd degree of severity, 4 (7.7%) - 3rd degree of severity[23,24,25]. There were 2 men, 50 women, aged from 20 to 62 years[25,26,27]. In the verification of hypothyroidism, in addition to anamnestic and physical data, the results of modern laboratory and instrumental studies are used[28,29,30,31]. The levels of TSH (thyroid-stimulating hormone), fT4 (free thyroxine), and Ab-TPO (antibodies to thyroid peroxidase) were studied using the immunochemiluminescent method. Echography of the pancreas and thyroid gland was performed using a Symens SV 70 device (USA), taking into account their structure, echogenicity of the parenchyma, size and contours. The endocrine function of the pancreas was studied by insulin levels, C-peptide by immunochemiluminescent method and blood glucose by enzymatic method. The content of amylase in the blood was studied using an enzymatic test on an ASCA AG2 analyzer, lipase - using a kinetic-colorimetric method on a Humalyzer 2000 analyzer[6,8,9,10]. The content of trypsin in feces was determined by an enzymatic method with a 1% NaHCO₄ reagent. The results of scatological studies were assessed. Depending on the treatment option, patients were divided into two groups comparable by gender, age and severity of the disease[11]. Patients in the observation group (21 people) received complex therapy, including levothyroxine (25-100 mcg/day), Creon 1 capsule (10,000 units) per day and mildronate 250 mg 2 times a day. Combined pharmacotherapy with drugs selected in this way, as can be expected in advance, will make it possible to complement the replacement effects of levothyroxine and Creon with the intracellular anabolic effect of mildronate[32,33]. Patients in

the comparison group (31 people) received only levothyroxine for treatment. The course of treatment lasted from 1 to 2 months. The results of special studies of patients were compared with the indicators of the control group, which consisted of 27 practically healthy individuals aged 25 to 42 years[34,35,36].

Research results and discussion: As shown in table. 1, in patients the level of fT4 decreases and TSH secretion increases[12,13]. Researchers have previously noted a decrease in the level of thyroid hormones in hypothyroidism[14,15]. An increase in the level of TSH and a decrease in the content of fT4 occurs according to the principle of a feedback, negative connection between the pituitary gland and the thyroid gland. During the therapy, a restoration of thyroid hormone levels was noted in both groups[16,17].

Table 1. Dynamics of thyroid hormone levels during therapy

Indicators	TSH (μIU/ml)		St T4 (pm/l)	
	Before treatment	After treatment	Before treatment	After treatment
Observation group n=21	18.75± 5.84*	2.51± 0.22**	9.71± 0.74*	15.1± 0.4**
Comparison group n=31	27.08± 8.89*	2.37± 0.27**	10.78± 0.63*	15.98±0.9**
Control group n=27	2.02±0.2		15.51±0.54	

*Note: hereinafter * - reliability in relation to the control group; ** - reliability of changes in relation to the initial level.*

One of the leading symptoms of pancreatic damage is abdominal pain of varying intensity. In the observation group, 7 (33.3%) patients complained of moderate pain in the left hypochondrium, pain in the epigastric region - 3 (14.3%), pain in the right hypochondrium - 2 (9.5%), 2 (9.5%) of patients had shingles pain. In the comparison group, 10 (32.3%) patients noted pain in the left hypochondrium, pain in the epigastric region - 5 (16.1%), pain in the right hypochondrium - 2 (6.4%), girdling pain was observed in 1 (3.2%) patient.

In the observation group, bloating was noted in 15 (71.4%) patients, in the comparison group - in 17 (54.8%), nausea - in 7 (33.4%) and 8 (25.8%) patients, respectively. , bitterness in the mouth - in 2 (9.5%) and 3 (9.8%) patients, respectively; rumbling in the abdomen - in 9 (48.9%) patients in the observation group and in 12 (38.7%) patients in the comparison group. In the observation group, pain decreased on days 1-2 in all patients, pain completely disappeared in all observed patients on days 2-3. In the comparison group, pain decreased in patients on day 3, and completely disappeared on days 5-6 of treatment[10,11,12].

Dyspeptic symptoms in the observation group disappeared in most patients on days 4-5 of treatment. Thus, bloating decreased in 46.7% of patients on the 3rd day of treatment, and disappeared in 53.3% of patients on the 4-5th day of treatment. Nausea and bitterness in the mouth disappeared in all patients on days 2-3 of treatment; Rumbling in the abdomen decreased in 77.8% of patients on days 3-4 of treatment, and completely disappeared in 88.9% of patients on days 5-6. In the comparison group, bloating decreased in 50% of patients on days 6-7 of treatment, and disappeared on days 10-11 in 62.5% of patients; nausea decreased in 60% of patients on days 3-4 and disappeared in all patients on day 7 of treatment; bitterness in the mouth decreased in all patients on the 3-4th day of treatment, disappeared in all patients on the 6-7th day; Rumbling in the abdomen decreased in the examined patients on days 5-6 of treatment, and disappeared in all patients on days 8-9 of treatment.

General clinical symptoms (fatigue, drowsiness, decreased performance, depressed mood, dizziness, headache) during treatment in the observation group decreased after 2 weeks in 16

(76.2%) patients, in the comparison group - in 9 (29%) . In the observation group, 18 (85.7%) patients noted an improvement in general well-being, and in the comparison group - 14 (45.2%) patients.

When assessing the exocrine and endocrine functions of the pancreas (Table 2), in patients in the observation group and the comparison group before treatment, an increase in amylase levels was noted in relation to the control group. After treatment, a significant decrease in amylase was observed in the observation group; in the comparison group, its level only tended to decrease. In both groups of patients, no significant changes were noted in the lipase content either in relation to the control group or in the dynamics of the treatment.

Table 2. Dynamics of indicators of exocrine and endocrine functions of the pancreas during treatment

Indicators	Study period	Observation group (n=21)	Comparison group (n=31)	Control group (n=27)
Amylase (mmol/l)	Before treatment	149.8±10.2*	147.3±8.1*	123.4±4.7
	After treatment	120.6±7.4**	135.2±7.1	
Lipase (units/l)	Before treatment	15.2±0.6	15.4±0.5	15.0±0.3
	After treatment	15.4±0.3	15.6±0.7	
C-peptide (nm/l)	Before treatment	1572±63.2*	1682±42.8	1835b8±55.2
	After treatment	1775±54.3**	1789±55.4	
Insulin (µIU/ml)	Before treatment	16.6±0.9	16.4±0.5	15.8±0.4
	After treatment	16.3±0.6	16.3±0.7	

The level of C-peptide in both groups of patients was reduced relative to the control group (Table 2). Against the background of complex treatment carried out in the observation group, a significant increase in the level of C-peptide was noted. In the comparison group, after treatment, the level of C-peptide increased slightly compared to the initial value. In both groups of patients, there was a tendency to increase insulin levels in the blood; After treatment, no significant changes were noted in its levels.

In the dynamics of the treatment, there were significant changes in glucose levels both in the observation group (before treatment 5.07±0.12 mmol/l, after treatment 5.09±0.09 mmol/l) and in the comparison group (before treatment 5.12±0.1 mmol/l, after treatment – 5.06±0.79 mmol/l) not noted.

During a scatological study before treatment, the predominance of mushy stool, with the presence of neutral fat, soaps and muscle fibers in it, was noted in 9 (42.8%) patients in the observation group, in 12 (38.7%) patients in the comparison group; formed stool with the presence of neutral fat in it was detected in 10 (47.6%) patients in the observation group and in 12 (38.7%) patients in the comparison group. After treatment, mushy stool containing neutral fat and muscle fibers persisted only in patients in the comparison group in 16.5% of cases. The level of trypsin in feces before treatment was reduced in the observation group in 10 (47.6%) patients and in the comparison group in 12 (38.7%); after treatment in the observation group, the level of trypsin in feces was restored in all patients, in the comparison group - in 4 (12.9%) patients.

Changes in the functional state of the pancreas in hypothyroidism are associated with the initiation of uncontrolled processes of free radical oxidation associated with thyroxine deficiency. In addition, with sudden changes in the activity of thyroid hormones, hemodynamics suffer to one degree or another, including in the pancreas. Against this background, there is a decrease in exocrine secretion and disruption of trophic processes in the pancreas. In patients, the level of C-peptide, which is a precursor to insulin, decreases[].

The use of levothyroxine, mildronate and Creon as part of complex therapy promotes faster relief of pain and dyspeptic symptoms in the patient. A positive clinical effect is achieved, as

established in the work, with an improvement in the functional state of the pancreas. Previously Podorozhny A.A. noted that in patients with exocrine insufficiency of the pancreas and deficiency of thyroid hormones, exogenous administration of the latter stimulates the ductular and acinar apparatus of the organ. During treatment, there is an increase in the level of C-peptide in the blood, probably due to the antioxidant activity of both the thyroid hormones themselves and mildronate.

Conclusion. The results of the observations showed that the complex use of levothyroxine, mildronate and Creon for chronic pancreatitis with concomitant hypothyroidism is pathogenetically determined and clinically effective. Under the influence of treatment, the secretion of hormones of the thyroid system is restored in patients and the functional state of the pancreas improves.

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