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FEATURES AND PRINCIPLES OF TREATMENT OF CHRONIC PANCREATITIS IN CHILDREN WITH ATOPIC DERMATITIS.

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Summary. This study found that among children with atopic dermatitis (AtD) among diseases of the gastrointestinal tract (GIT), chronic pancreatitis (CP) is most common (52.9%). A high positive correlation was found between the clinical signs of atopic dermatitis (the intensity of the rash) and the abdominal pain observed with CP (r = + 0.9), while abdominal pain was also associated with symptoms such as itchy skin and abnormal sleep (r = +0.7 and r = + 0.83). In AtD, there was a high negative correlation between an increase in the SCORAD index and a decrease in the amount of elastase (r = -0.82), as well as an increase in IgE and a decrease in the amount of elastase (r = -0.9). The use of enzyme preparations (in age-specific dosages) in complex treatment in children with AtD corrects pancreatic insufficiency; leads to the normalization of digestion, as a result of which there is a prolongation of the remission of AtD by 2.2 times.

Keywords: atopic dermatitis, children, gastrointestinal tract, chronic pancreatitis, elastase, enzyme preparations.

Relevance of the study. In recent years, atopic dermatitis (AtD) has become one of the most pressing problems among allergic diseases in the world. Allergic dermatitis accounts for 40-60% of all allergic diseases [8,11]. In our country, as in developed countries [6], in recent years several scientific studies have been conducted in the study of clinical and laboratory changes in the gastrointestinal tract in cystic fibrosis and atopic dermatitis, including exocrine insufficiency [1,2,10]. According to modern theories, chronic pancreatitis observed in atopic dermatitis is accompanied by pancreatic insufficiency, resulting in irreversible morphological changes in the parenchyma of the pancreas [3,4]. This, in turn, leads to impaired exocrine and endocrine function of the pancreas [5,7]. Against the background of atopic dermatitis, the risk group for the development of gastrointestinal dysfunction includes children with a combined genetic predisposition to gastroenterological and allergic diseases [5, 9]. The role of the pancreas in the course of AtD in children shows the importance and necessity of developing new new treatments. The aim of the study was to improve the principles of early detection, diagnosis and treatment of risk factors that

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cause clinical laboratory changes in the gastrointestinal tract in children with atopic dermatitis.

Materials and methods of research. 386 children with atopic dermatitis aged 6 months to 18 years treated at the multidisciplinary clinic of the Tashkent Medical Academy in 2017-2020 were included in the study (for retrospective and prospective follow-up). The study used general clinical, laboratory-instrumental, allergological, immunological and statistical research methods.

Results and discussions. To address the above objectives, 386 children with AtD from 6 months to 18 years of age were divided into three groups based on the classification adopted by the Russian Association of Clinical Immunologists and Allergists (2002). Infants with atopic dermatitis (children under 2 years of age) - 167 (43.6%), children with atopic dermatitis (2 to 12 years) - 134 (34.7%) and adolescents with atopic dermatitis (12 to 18 years) 85 (22.0%) of the sick children were different, with an average age of 6.2 ± 1.3. The results showed that AtD was 1.2 times more common in girls than in boys when distributed by sex in all groups, according to the literature, the predisposition to the disease was determined in girls. Retrospectively analyzed sick children were divided into groups according to the condition of the gastrointestinal tract (GIT). In atopic dermatitis, 331 children (85.7%) had clinical and laboratory changes in GIT, and 55 children (14.2%) did not have clinical and laboratory changes in GIT. According to the data obtained, the observation of clinical and laboratory changes in GIT in patients diagnosed with AtD has been increasing from year to year.

For example, in 2017, 29 patients (68.4%) with clinical- GIT laboratory changes in AtD, while by 2020 the number of applications was 137 (86.1%).

The nature of nutrition, which is one of the factors influencing the development of clinical and laboratory changes in the gastrointestinal tract, was studied, taking into account the composition, type and order of daily meals of patients in the group.

While 69.6% of infants with AtD were found to be switched to early artificial feeding, the transition to family table meals was found to be early, while children (64.9%) and adolescents with AtD (82.3%) were found to be mostly non-compliant. According to the nature of the diet, the predominance of high-consumption products, ie sweets, mainly in infants AtD (73.6%) ($r > 0.05$), the predominance of fatty foods (69.4%) ($r < 0.001$), the predominance of sharp, spicy foods in adolescents AtD - (64.7%) was observed. Children were found to have AtD observed in 103 (76.8%) cases of excessive consumption of meat ($r < 0.001$).

However, the frequency of AtD feeding in adolescents was lower than in children of other ages ($r < 0.001$).

One of the factors contributing to the development of the disease in children was hereditary predisposition, which was reported to be high in both groups (84% and 86.4%). Diseases of the gastrointestinal tract were found to be 2.4 times more common in the parents of the first group of children (49.3% vs. 20.3%, $r < 0.001$).

The identified GIT diseases of patients with AtD in the analysis were distributed as follows: 52.9% - chronic SP, 24.5% - chronic gastritis, 22.9% - chronic cholecystitis, 20.5% - intestinal syndrome, 15.6% - chronic gastroduodenitis, 15.5% had gallstone

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disease, 8.4% had ulcer disease, and more than 50% of these patients were diagnosed with 2 and 3 gastrointestinal tract at the same time. It is noteworthy that in the diagnosis of chronic pancreatitis, the most common form of in pagastrointestinal tract tients with AtD (52.9%), the cases of external and internal secretory insufficiency, which are critical in the treatment and management of patients, were not reflected. A study of children suspected of having atopic dermatitis showed that all of those examined complained of an itchy rash that spread to the skin within 6-12 months. The presence of pruritic rashes in the last 12 months of AtD was 2 times more common in the first group of children (infants AtD) than in children and adolescents (76.0%; 34.3% and 51.7%, respectively) (r> 0.05). However, the location of typical rashes below the knee, on the wrist surfaces, on the skin of the palms, around the neck, eyes, and ears was predominant in the examined adolescents 81.1%.

AtD was observed in more children and adolescents with complete disappearance of AtD rash at the end of 12 months, complete clinical remission periods with no evening discomfort and itching (61.1% and 62.3%). Sleep disturbances less than once a week as a result of severe itching were observed in more infants 60.4%, more than 1 time per week was observed mainly in children and adolescents AtD. Gastroenterological complaints were detected in 78.2% of children and adolescents with AtD. Most often, sick children were disturbed by complaints such as a feeling of heaviness in the abdominal area (52.9%), pain in the epigastric area (47.4%), belching (29.7%) and heartburn (18.2%). Occasionally, children and adolescents also complained of vomiting (32.1%), constipation (29.5%), or diarrhea (18.4%). In order to study the most common pancreatic insufficiency (52.9%) in children with atopic dermatitis, 120 patients with AtD were included in the in-depth study. Since 52.5% of the patients with CP in the study were children aged 2 to 12 years, the treatment plan was conducted in patients of the same age. In the process of determining pancreatic elastase in children with AtD at this stage of the study, the presence of external secretory insufficiency in patients with concomitant chronic pancreatitis and their indicators were compared with the absence of chronic pancreatitis in AtD and healthy children (Table 1).

Table 1.

Analysis of the amount of pancreatic elastase in the feces of patients with AtDli

Groups	**Elastase (mkg)**	**The norm**
There is an ATD CP n=70	150,9±0,56**	CP severe levels: <100mkg CP moderate severity: 100-200mkg Dosage: 200-500 mcg Increase: 500-700 mcg Significant increase:> 700
There is no AtD CP n=30	280,4±0,23*	
Healthy children n=20	367,7±0,31	

Note: r <0.001 relative to healthy children.

In the children in our study, elastase levels ranged from small numbers to normal. In children with pancreatic insufficiency (WPI) with AtD, the amount of pancreatic elastase ranged from <100 mcg to 230 mcg. The amount of pancreatic elastase did not show a significant difference (p = 0.001) (p = 0.001) from children

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with WPI iency and healthy children with AtD WPI deficiency (497 mcg from the 209 mcg interval).

We found a weak correlation correlation (r = + 0.21) between the SCORAD index and the amount of pancreatic elastase, which indicates the severity of AtD in children whose ChP was not detected. In patients with ChP, a strong negative correlation was observed (r = -0.82). This means that the heavier the AtD (the higher the SCORAD index), the heavier the ChP (the amount of elastase decreases to moderate to severe). In the course of the study, the following factors leading to the development of ChP were identified in the analysis of AtD patients. Among all gastroenterological complaints observed in patients, we distinguished those specific to ChP: pain in the left subcostal space (74.1%), nausea (61.6%), flatulence, flatulence, with varying degrees of intensity, caused by eating disorders decreased appetite (70.8%), increased number of stools containing undigested food particles, lack of body mass gain.

Specific changes were noted in all groups in the diagnosis of ChP in children with AtD, as well as pancreas laboratory tests, as well as ultrasound examination (UTT), which allows a complete analysis of the state of pancreas. UTT results showed varying degrees of unevenness and changes in the exogenousness of the pancreas parenchyma in 62.9% of patients with AtD in the study. The increase in pediatric AtD pancreas pancreas was higher than in adolescent and infant AtD (61.9%; 46.1% and 32.5%, respectively) (r <0.001). Changes in the homogeneous distribution of exosignal signals and exchange of dense areas in adolescents were more pronounced than in other infants AtD, and it was found that they were more prone to changes from major spectral changes - outflow tract enlargement, increased pancreas density. The study also analyzed the characteristics and causes of abdominal pain, which is one of the main symptoms of ChP, especially exocrine insufficiency. The nature of the pain is constant, exacerbated after consuming large amounts of fatty foods, and a decrease in the intensity and duration of pain is observed in the exacerbation of functional insufficiency.

When studying the peripheral blood parameters of children, no significant changes in peripheral blood were observed in both groups of patients, except for the number of eosinophils during the period of disease progression. The number of eosinophils was slightly higher in patients with AtD ChP (7.1 ± 0.2) than in patients without ChP (6.5 ± 0.31 *), but eosinophils in healthy children (1.31 ± 0.12 **) an increase in the number of patients in both groups (5.4; 4.5, respectively) was observed (r <0.001). In patients with AtD ChP, total IgE averaged 406.9 XB / ml in the range of 102–1514 XB / ml. In patients without AtD ChP, this figure averaged 377.2 XB / ml in the range of 93.5–1059 XB / ml. Both groups made a reliable difference (p = 0.0001) from the control group in terms of total IgE content (healthy group averaged 45.6 XB / ml, range 17.2 - 87.1 XB / ml). The highest total IgE was found in patients with AtD ChP, which was 8.9 times higher than in healthy children.

In our opinion, this is because the allergic process in patients with AtD ChP is more severe than in patients without AtD ChP. Specific allergological examinations were performed in 50 children with AtD-confirmed. Diagnostically significant

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concentrations of allergen-specific IgE in the serum of patients with AtD ChP were detected in 81.5%.

Diagnostically significant concentrations of allergen-specific IgE in the serum of patients without AtD ChP were detected in 52.3%. It should be noted that 75.5% of children with AtD ChP were sensitive to serum-specific IgE, mainly food allergens, which was 35% in the comparison group. The study found that the higher the SCORAD index associated with the severity of the disease in patients with AtD ChP, the lower the pancreatic elastase (Fig. 1). The analysis between the SCORAD index and the pancreatic elastase index showed a strong negative correlation correlation (r = -0.82).

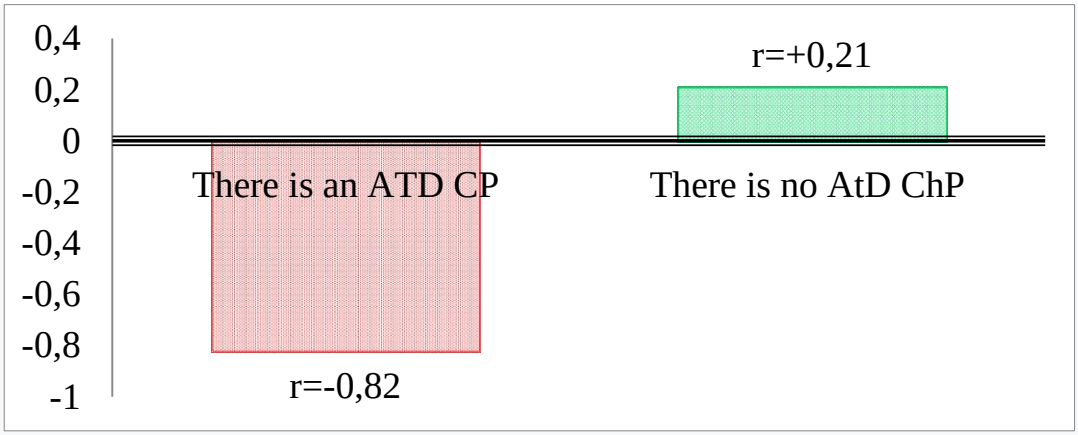

Figure 1. AtD SCORAD index and correlation with pancreatic elastase

A strong negative correlation correlation was also found between pancreatic elastase index in fecal and total IgE (r = -0.9). Therefore, the level of pancreatic elastase in the feces can be assessed as a prognostic criterion for the onset and outcome of AtD.

Patients with AtD ChP were divided into 2 groups (primary and control) depending on the type of treatment. Thirty patients in the control group (who have AtD ChP) were given basic therapy to treat atopic dermatitis (hypoallergenic regimen, antihistamines, topical glucocorticosteroids, symptomatic treatment).

The main group consisted of 43 children (who have AtD ChP), and they were given enzyme preparations (creon) to correct pancreatic insufficiency in addition to basic treatment. The average dose of creon was given 1 capsule (10,000 units of lipase) 3 times a day for 4 weeks. The effectiveness of treatment was assessed through the study of the main symptoms of digestive disorders (abdominal pain, irregular stools, nausea, flatulence), as well as coprology (dynamics of creatorrhea and steatorrhea). During the administration of basic therapy + enzyme drugs in the main group of patients with ChP deficiency: abdominal pain disappeared in 79.1% of patients, and in the control group of patients - 16.6%; unstable stools decreased in the main group of patients to 65.1% and 11.6%, respectively, in the control group of patients this sign was maintained in high percentages. Coprologic examination revealed type 1 steatorrhea (presence of neutral fat in the stool) in 35 (87.5%) children, creatorrhea - 8 (20%), indigestible tissue - 31 (77.5%), amylorea - 34 (85%), Decreased elastase value was detected in 31 (77.5%) children. Loss of neutral

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fat in coprologic examination, normalization of elastase levels is a marker of the effectiveness of enzymatic treatment.

It should be noted that in 16 (40%) of the main group of children we observed, steatorrhea disappeared by the 14th day of enzyme treatment, and by 4 weeks of treatment, it disappeared in almost all patients. Against the background of complex treatment with enzyme therapy in the main group of patients, in parallel with the regression of abdominal, dyspeptic and coprology syndromes, positive dynamics of skin symptoms were observed: lesion area according to the SCORAD index, hyperemia and infiltration, itching decreased (Table 2). Significant improvement in skin syndrome was observed in 72.5% of children, moderate improvement in 20.0%, ineffectiveness was observed in 7.5% of patients compared to the treated measures, which requires a more in-depth study of the causes of the pathological process. In a coprologic examination of children in the control group, steatorrhea persisted in 90% of patients by day 14 of the disease, and creatorrhea persisted in 40% of patients. On the 28th day of the disease, these figures were significantly higher than in the main group.

Table 2.

Evaluation of patients according to the SCORAD index

The severity of the disease in the patients on examination	**The main group n=40**		**Control group n=30**	
	Before treatment	From the case Then	Before treatment	From the case then
SCORAD index (in points)	39,6±0,5	12,5±1,6**	38,2±0,3	21,5±0,9*

Note: r <0.001 relative to healthy children.

Regression of abdominal, dyspeptic, and coprology syndromes was almost non-existent in the control group, with positive dynamics of skin-induced symptoms observed in only 21.4% of patients: skin lesions, hyperemia and infiltration, and pruritus remained high. Significant improvement in skin syndrome was observed in 19.5% of children, with an average improvement in 10.0%, and 70.5% of patients did not respond effectively to baseline treatment measures.

In the children in our study, elastase levels ranged from small numbers to normal before treatment. The amount of pancreatic elastase in children with pancreas deficiency with AtD ranged from <100 mcg to 530 mcg before treatment. The amount of elastase in the stool was found to be reduced in 77.5% of patients before treatment.

Table 3.

Analysis of the amount of pancreatic elastase in the feces of patients with ATD after treatment

Groups	**Elastase content (mkg)**		
	Before treatment	**14 days after treatment**	**28 days after treatment**
The main group n=40	170,9±0,56**	270,5±0,34**	340,7±0,68***

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Control group n=30	180,4±0,23*	220,4±0,62*	250,4±0,81*
Healthy children n=20	367,7±0,31		

Note: r <0.001 relative to healthy children.

Normalization of fecal elastase levels was observed in 15 patients on the 14th day of treatment and in 30 patients on the 28th day of treatment. This indicates that the amount of enzyme drug is adequately selected and highly active. Against the background of complex treatment with enzyme therapy in the main group of patients, the amount of elastase in the feces increased by 1.5 times on 14 days of treatment (Table 3). On day 28 of treatment, however, in the control group of patients, this figure was close to that of healthy children (340.7 ± 0.68; 367.7 ± 0.31, respectively). The results showed that the amount of elastase in the control group of patients remained significantly lower than in healthy children on days 14 and 28 of basal treatment (220.4 ± 0.62; 250.4 ± 0.81, respectively).

Conclusions. Among children with atopic dermatitis, gastrointestinal tract: chronic pancreatitis (52.9%) was detected in large numbers. AtD high positive correlation was found between clinical signs of AtD (rash intensity) and abdominal pain (r = + 0.9), but was also associated with symptoms such as abdominal pain, itchy skin, and sleep loss (r = + 0.7 and r = + 0.83).

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