The American Journal of Medical Sciences and Pharmaceutical Research
(ISSN – 2689-1026)
Published: March 31, 2021 | **Pages:** 132-140
Doi: https://doi.org/10.37547/TAJMSPR/Volume03Issue03-19

IMPACT FACTOR
2021: 5. 64
OCLC - 1121105510

Diagnosisand Therapy Of Pancreatic Dysfunction In Atopic Dermatitis In Children

Khalmatova Barnoturdixodjayevna
Professor, Head Of The Department Of Children's Diseases №1, Tashkent Medical Academy, Tashkent, Uzbekistan

Mirrakhimova Maktuba Khabibullayevna
Docent,Dsc, Department Of Children's Diseases №1, Tashkent Medical Academy, Tashkent, Uzbekistan

Nishonboyeva Nilufar Yunusjanovna
Assistant, First Faculty Of Children's Diseases, Tashkent Medical Academy, Tashkent, Uzbekistan

ABSTRACT

Most of allergic diseases are caused by allergic skin lesions.The aim of the study was to assess the effectiveness of the enzyme agents in the correction of pancreatic insufficiency in children with atopic dermatitis.As a result of the study clinical and laboratory markers of relative pancreatic insufficiency were identified in 69.7% of the patients, who required the prescription of enzyme agents. The results also showed that in 92.5% of patients the correction of exocrine function disorders to a certain extent affects the regression of dermal manifestations. In the scatological tests the loss of neutral fat, normalization of the amount of elastase in feces serve to be a marker of the effectiveness of the enzymatic therapy.

KEYWORDS

Atopic dermatitis, children, IgE, pancreatic dysfunction, elastase, diagnosis, treatment.

INTRODUCTION

High prevalence rate of allergic diseases among children, no decreasing tendency in morbidity rate cause constant serious dispute during the last decades and can be explained by insufficient efficacy of therapeutic methods used in pediatric practice every day

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[4,6,7,20].According to official data, there is not only continuos growth of allergic diseases prevalence among children, but the age of allergic diseases in every fourth or fifth also become younger[8,9,11].

Most part of allergic diseases are allergic lesions of skin [7,14,15].Genetically determined chronic inflammatory immune pathologic (in most cases based on mechanisms linked with IgE) atopic dermatitis (AD) characterized by typical start in childhood, age-specific clinical morphological features, recurrent progression, and itching, takes the first place among allergic dermatoses in children. AD is characterized by polymorphism of clinical symptoms, tendency for chronic proceeding, wave-like progression, various stages and terms of incomplete remission, and plenty of causing factors [16]. Combination of triggers such as food allergy, stressful conditions, changes in microbiom, changes in micro ecology of the environment, anatomical physiological predisposition of child's organism serve the basis of AD etiopathogenesis [19].

AD takes a leading position among pediatric dermal pathologies (20-50% of children with dermatoses); that increases the interest of pediatricians and family doctors in the rise of efficacy of the pathology treatment. Besides that, all allergic pathologies, particularly AD, are characterized by development of associate pathologic alterations in organs and systems,which makes duly adequate correction of the pathology an object of interest not only for allergists, but also for otolaryngologists, ophthalmologists, endocrinologists, and other specialists [16,18].

One of the specialists taking the most active part in AD therapy is children's gastroenterologist. It is not a secret that, a lot of alterations in skin and the stage of these alterations are linked to gastrointestinal (GI) pathologies; and 52% of patients with AD have some of those symptoms[6,10]. It is known that, surface of small intestine contacts alien substances 10 times more often than respiratory epithelium and 300 times more often than skin. In digestive system there are several barriers manifested by physiological, anatomical, and immunologic factors. These barriers prevent the entrance of food antigens into organism and they are responsible for immunity. Taking into account age-specific anatomical and physiological characteristics of gastrointestinal tract, most cases of barrier failure occur in childhood [1,6,11,16,18].

Functional disorders in digestive system lead to absorption of incompletely split food components, particularly proteins, and increase of organism sensitivity to various allergens. A great amount of antigens coming from intestine cause dysfunction of pancreas[4,6]. Besides that, allergens entering a body of a child with predisposition for allergy initiate a cascade of immunologic and biochemical processes, which in its turn leads to rise of several biologically active substances in blood (histamine, serotonin, acetylcholine, heparin, and others) causing blood circulation disorders in various organs.One of the organs suffering almost in any allergic process is pancreas[19].

Unfortunately, in most cases of AD therapy pediatritians are limited by local and pharmaceutical methods suppressing histamine, without paying enough attention to gastrointestinal pathologies. Correction of pancreatic failure (PF) has a great importance in the therapy of allergic skin diseases as well as correction of secondary secretion[6,18].

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Clinical manifestations ofPFin children include stomachache, change in appetite (low or lack of appetite), nausea, belching, flatulence, rumbling, and unstable stool.

Intensity and expression of these manifestations are linked with the stage of pancreatic lesion.Direct and indirect test methods are used to determine pancreatic exocrine dysfunction. Direct methods are based on direct definition of enzyme activity in duodenal juice and splitting degree of certain substrates in gastrointestinal tract under influence of pancreatic enzymes. Direct methods requiring application of duodenal probing are not used in pediatric practice, as these methods take a long time, these are considered to be invasive methods, and have uncertain interpretation of the results. Indirect methods are not very accurate but easy to use in everyday practice.

Nowadays coprologic test is considered to be the most widely used method in PF diagnosis due to its simplicity and being non-invasive. Increase of neutral fat amount indicates lipolytic dysfunction in pancreas; increase of muscular fibers indicates disorders in proteolytic processes; and increase of starch amount is indicator of disorders in amylase function (first of all pancreatic, as amylase in the composition of saliva also effects digestion of starch).

Correct and accurate coprogram is considered to be a very descriptive method and in the majority of cases it is enough for primary differential diagnosis and monitoring of a patient's total health status. These days fecal lipid profile is considered to be more accurate, but more difficult and more expensive direct method [1,3,5,12].

Nowadays golden standard methods of PFdiagnosis include definition of constant amount of pancreatic elastase-1 in feces in distal parts of intestine. Normal amount of it in feces is over 200 mkg/mL, while lower values indicate PF. Test results are not affected by patient's nutrition and administration of pancreatic enzymes[2,18]. However, decrease of fecal elastase-1 amount indicate mild and severe PF, which is rarely observed in childhood. That is why that method cannot exclude additional methods for definition of pancreatic exocrine function (coprogram or the best one lipid profile) from the practice, as only these methods provide assessment of adequacy of replacement therapy and dose of the medicine [1,11,13,17].

New methods of ultra sound diagnosis including ultra sound imaging of pancreas after meal and definition of blood flow amount in superior mesenterial artery before and after the meal can also provide much information[2].

That method is used for definition of fasting condition of pancreas in children in the morning, its countor, structure, echogenicity, pathologic inclusions, condition of the main pancreatic duct, and measurement of linear sizes of pancreas before and after meal (in 90 minutes after test breakfast). Increase less than 5% (decrease) is considered to be a sign of chronic pancreatitis, up to 5-15% indicate reactive alterations in pancreas, and above 15% indicates normal reaction after meal.

From the modern point of view effective PF treatment, based on decrease of pancreatic enzymes secretion or their inactivation by means of various endogenic factors, requires replacement therapy with enzyme agents (EA). For the provision of normal digestion in duodenum of healthy person there should be

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5-10% of enzymes amount produced at the maximal stimulation of pancreas.

The objectiveof the study was assessment of Mezim Forte 10 000 enzyme agent micro tablets efficacy in PF correction in children with AD.

Inclusion criteria were: age from 3 to 6 years old; AD and PF confirmeddiagnoses; parents' concent to participation in the study; ability of a child to cooperate well during the term of the study.

Exclusion criteria were the following: high sensitivity to enzyme agents in the history; acute diseases which could affect the results of the study; participation in any other clinical trial.

MATERIALS AND RESEARCH METHODS

Forty children with AD-like dermal syndromes proceeding together with PF at the age from 3 to 6 years old were enrolled to the study. Symptoms of allergic skin lesions included eruthema, papula, macula, lischenoid popular polymorphic rash, itching, and lichenification. Besides clinical tests, we determined IgE amount, coprogram (in the beginning and at the end of the study), pancreatic elastase, and ultra sound imaging of abdominal organs.Definition of pancreatic elastase level is simple, non-invasive method for the assessment of pancreatic function, which allows evaluation of pancreatic exocrine failure (sensitivity 90-100%, specificity 93-98%). Sensitivity of the method is low in cases of latent pancreatic failure, but in mild and severe cases it reaches 100%. Pancreatic elastase is a specific protein secreted by pancreas. It is secreted to duodenum and participates in digestion. Deficit of that protein leads to certain physiological disorders. Definition of pancreatic elastase-1 in feces is used for the assessment of pancreatic capacity to produce digestive enzymes (its exocrine function).

Together with AD therapy all the children participating in the study were prescribed Mezim Forte 10 000 polyenzyme agents for correction of pancreatic exocrine failure. Its day dose was calculated on the basis of lipase amount (1000 B lipase per 1kg of a child's weight), in other words, 2 micro tablets per a kilo a day divided to the times of taking meal. The tablets were administered with every meal (3-4 times a day) for 2 weeks.

At the same time with individual approach to diet, the criteria for the choice of adequate dosage and term of the agent intake included normalization of the number of defecations and feces characteristics, disappearance of neutral fat in coprogram and normalization of its other parameters, rise of appetite, and disappearance of dyspeptic and pain syndromes.

Efficacy of enzyme therapy was assessed on the basis of expression of basic symptoms of indigestion (stomachache, lack of appetite, flatulence, disorders in defecation, nausea) and results of scatological tests.

Digital data were processed using mathematical methods of medical statistics with calculation of mean values (M) and average deviation (m) of the studied parameters.

RESULTS OF THE STUDY

The studied group of children included 40 children aged from 3 to 6 years old, among which there were 19 (47.5 %) boys and 21(52.5 %) girls. According to the duration of the disease the children were classified as follows:

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1–3 years22 children (55%), more than3 years 18 children (45%). All the children applied to hospital within incomplete remission period of earlier diagnosed AD; among them there were10 (25%) children with erythematous squamous type, 19 (47.5%) with lichenification and erythematous squamous type, and 11 (27.5%) with lichenoid one. Thirty (75%) of the patients had limited pathologic process, 9 (22.5%) had spread and 1 (2.5%) had diffusive process. In the studied group of children there was a reliable prevalence of mild AD; 29 (72.5%) patients had 3-4 relapses a year.Light form of the pathology was observed in9 patients, while severe one in 2 (22.5 and5%, respectively). According to the history data, frequent relapses of the disease were linked with foci of infection, gastrointestinal symptoms, and violation of hypoallergic diet. At the time of application to hospital all the patients had average rise of serum IgE up to 560 IU/mL.

From all gastrointestinal complaints of the patients we isolated those relevant to PF such as pain in the left subcostal area of various intensity accompanied by indigestion, nausea, belching, flatulence, low appetite, feces with particles of indigested food, deficit of weight gain(Table 1).

Table 1

PF clinical symptoms in children with AD (n=40)

Symptoms	n (%)
Stomachache	40(100%)
Nausea	22 (55%)
Belching	21 (52.5%)
Flatulence	19 (47.5)
Low appetite	29 (72.5%)
Unstable stool	23 (57.5%)
Body weight deficit	12 (30%)

Objective checking showed painful palpation of pancreas projection points(Meyo-Robson, Kach, Kerte) in all (100%) patients.Scatological tests showed 1-type steatorrhea (neutral fat in feces) in 35 (87.5 %) children, creatorrhea in 8 (20 %), indigested cellulose in 31 (77.5 %), amylorrhea in 34 (85%), decrease of elastase in 31 (77.5 %) children (Table 3).

Ultra sound imaging on empty stomach showed insignificant enlargement of pancreas due to parenchyma swelling (mostly in caudal part) indicating absence of structural pathologies in 16 (40%) children. After verification of the clinical diagnosis and prescription of Mezim Forte 10 000 enzyme agent clinical symptoms were checked up every day; after discharge from the hospital the symptoms were checked once a week (Table 2). Scatological tests were performed at the 7th and 14th days of the therapy.

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Table 2

Changes in clinical symptoms with progression of the therapy

Symptoms	before therapy		3th day		7th day		14th day	
	abs.	%	abs.	%	abs.	%	abs.	%
Stomachache	40	100	31	77.5	19	47.5	2	5
Nausea	22	55	15	37.5	10	25	2	5
Belching	21	52.5	13	32.5	7	17.5	2	5
Flatulence	19	47.5	16	40	11	27.5	2	5
Low appetite	29	72.5	22	55	14	35	1	2.5
Unstable stool	23	57.5	19	47.5	12	30	1	2.5

As it is presented in Table 2, expression of abdominal pain syndrome decreased 3 folds by the 7th day of the therapy; by the 14th day it was bothering only 2 children($p < 0.01$). There was also a positive dynamic in the decrease of dyspeptic symptoms: flatulence and unstable stool frequency reliably diminished at the end of the first week of the therapy($p<0.05$) and disappeared almost in all the children by the end of the therapy($p < 0.01$).

Disappearance of neutral fat in scatological tests and normalization of elastase amount served to be markers of the therapy efficacy. It should be noted that, among the children enrolled in our study therapy with Mezim Forte eliminated steatorrhea in 16 (40%) by the 7th day, while at the second week of the therapy it disappeared almost in all patients. It was determined that fecal elastase diminished in 77.5% of the patients prior to the therapy. At the 7th day there were fifteen and at the 14th day 30 patients with normal elastase level. It proved that the enzyme agent was chosen adequately and it was highly effective.

Table 3

Scatological parameters dynamic in the process of the treatment

Parameter	before therapy		7th day		14th day	
	abs.	%	abs.	%	abs.	%
Steatorrhea	35	87.5	19	47.5	1	2.5
Creatorrhea	8	20	5	12.5	2	5
Amilorrhea	34	85	21	52.5	1	2.5
Elastase	31	77.5	16	40	1	2.5

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At the time of Mezim Forte 10 000 complex therapy together with regression of abdominal, dyspeptic, and coprologic syndromes we observed a positive dynamic in the expression of dermal manifestations such as diminishing of lesion area, hyperemia, infiltration, and itching. Significant improvement of dermal syndrome was observed in 72.5% of the children; 20.0% had mild improvement; in 7.5% of the patients therapy was not effective, which required further study of the factors causing pathologic process.

In the therapy of the patients with AD Mezim Forte 10 000 enzyme agent assisted disappearance of pain and dyspeptic syndromes and improvement of laboratory parameters indicating functional status of pancreas. The agent was accepted well by the patients; it did not cause unfavorable effects, that is why it can be recommended as a therapeutic agent for PF treatment in children with AD.

DISCUSSION

According to the modern notions, expression of AD dermal manifestations and intensity of pain are closely interrelated with exocrine function failure of pancreas based on decrease of pancreatic enzyme secretion or inactivation of these enzymes under the influence of various endogenic factors[6,15, 18, 20].

Results of our study showed that changes in coprogram were determined almost in all patients, which indicated mixed character of pancreatic lesion in AD.

Ultra sound imaging before and after meal showed insignificant enlargement of pancreas due to swelling of its parenchyma (mostly caudal part), indicating absence of structural pathologies in it. In the children enrolled in our study ultra sound characteristics of alterations in pancreas showed that clinical symptoms of PF appear much earlier than structural changes in it.

Results of the study showed presence of relative clinical and laboratory manifestations of PF in the patients, which required prescription of enzyme agents. A lot of researches showed high efficacy of micro tablet enzyme therapy of PF. These agents have high safety rates, so they can be used even for new-born children.

The obtained results showed that in the majority of the patients correction of exocrine function disorder of pancreas to certain extend effected regression of dermal symptoms. However, explanation of the mechanisms of these effects require particular study. Absence of improvement in dermal syndrome observed in 7.5% of the patients after enzyme therapy shows the need in further research for identification of the pathologic causing factors.

CONCLUSIONS

1. Eliminating pain and dyspeptic syndromes Mezim Forte 10 000 lead to PF positive dynamic and it is considered to be an effective therapeutic agent for the treatment of PF in children with AD.
2. Mezim Forte is well accepted by patients; it has no side effects and convenience in its administration makes it different from other enzyme agents: 2 micro tablets per 1 kg of body weight divided to the number of taking meal.
3. Two-weeks therapeutic course of Mezim Forte 10 000 is recommended for the therapy of PF in children with AD.

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4. Disappearance of neutral fat and normalization of fecal elastase in the results of scatological tests serve to be markers of the therapeutic efficacy.

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