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EFFICIENCY OF ENTEROSGEL IN CORRECTION OF SYSTEMIC ENDOTOXEMIA IN CHILDREN WITH ATOPIC DERMATITIS

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Children with atopic dermatitis have shown an increased plasma levels of endotoxin up to 0.140 ± 0.071 EU/ml ($p < 0.001$), and levels of endotoxin depend on the period of disease severity and activity of the skin process. The presence of systemic endotoxemia in this pathology is an indication for administration of drug Enterosgel (polymethylsiloxane polyhydrate) as a part of the complex antiallergic therapy. This leads to decrease of plasma endotoxin levels by 12 times from 0.142 to 0.012 EU/ml, decline of the acute period by 1.6 times (days) and reduction of the SCORAD index by 5 times. This method of therapy has shown a high efficiency and can be widely used in the treatment of atopic dermatitis.

Key words: *atopic dermatitis, endotoxin, Enterosgel*

Summary

Endotoxin aggression is developed with the expressed release of endotoxin (ET) in the bloodstream on the background of insufficient activity of excretory systems and is qualified as a universal mechanism involved in the pathogenesis of many infectious and non-infectious diseases [1]. Systemic endotoxemia can develop as a result of both inactive intestinal microbiota, constant permeability disorders of the intestinal mucous membranes, and pancreatic insufficiency, biliary duct insufficiency, depression of liver barrier function or reduced portal blood flow, etc [2]. ET presence affects immunocompetent blood cells and is one of the considerable stimulation factors of the immune system. Under physiological conditions, anti-endotoxin antibodies are released in response to ET presence [3]. In pathological endotoxemia a decline of adaptive capacity and body resistance takes place [4, 5]. It is also known that endotoxemia causes cellular hypoxia, metabolic disorders, activation of sympathetic nervous system, complement system, resulting in lysis of leukocytes and platelet aggregation with the release of biologically active substances - kinins, histamine, serotonin, causing "mediator chaos."

All of the above has allowed us to make an assumption about the importance of systemic endotoxemia and endotoxin aggression in atopic dermatitis (AD) in children.

Objective: to define level of systemic endotoxemia in children with AD and evaluate drug Enterosgel (polymethylsiloxane polyhydrate) in complex therapy of the pathology.

Material and Methods

The study involved 30 children with AD aged 10 to 17 who entered the main group. Clinical AD structure: children with erythematous-squamous form - 40% ($n = 12$), lichenoid form - 60% ($n = 18$). Activity of skin process of II degree was diagnosed in 12 patients (40%), III degree - in 18 patients (60%).

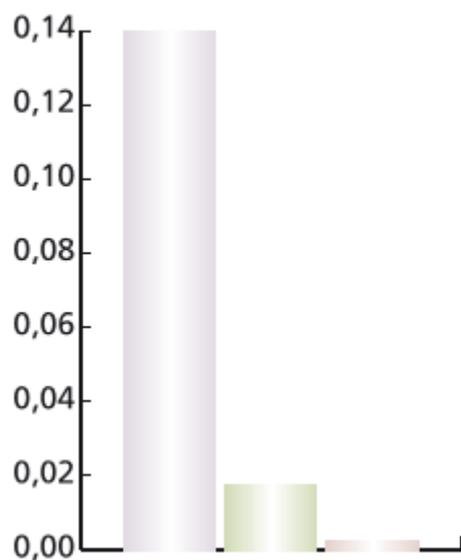
Moderate course of the disease was observed in 20 children (67%), severe – in 10 patients (33%). In 20 patients (67%) total serum immunoglobulin E (IgE) increased. Among children with increased total serum IgE its value up to 300 IU was marked in 5 patients (15%), more than 500 IU – in 26 children

(85%). Specific IgE to food allergens were detected in 18 patients (60%), domestic allergens - in 4-patients (13%), pollen - in 5 patients (16%). 21 patients (70%) experienced sensitization to all three allergen groups.

The control group consisted of 20 healthy children aged 10 to 17 years.

ET was determined by method of J. Levin, F.B. Bang. «LAL-test» (Limulus

Figure 1. Plasma endotoxin (EU/ml) in children depending on AD stage in comparison with healthy patients



1) Acute 2) Remission 3) Convalescence

Amebocyte Lysate), according to instructions of the manufacturer *Sigma* (USA). The results are expressed in international units (EU). Plasma sampled and stored in strictly apyrogenic conditions was the study material. We used a set of tubes containing 0.1 ml of the test plasma with ET solution of known concentration (0.5 EU / ml, 0.25 EU/ ml, 0.125 EU/ ml, 0.06 EU/ ml, 0.03 EU/ ml, 0.015 EU/ ml), and pure water. 0.1 mL preparation E-TOXATE[®] (Limulus Amebocyte Lysate) was added to each vial. After incubation in the thermostat for 1 hour at 37 ° C a test was conducted as follows: a tube sample was rotated by 180 ° and watched for signs of gel formation. A positive test result was formation of thick gel that maintained its form after rotation. All other results (liquid gel, increased viscosity, clean liquid) the results were considered negative. To determine ET level in the sample showing a positive result, it was diluted with pure water (2, 4, 6, 8, 10-fold, etc.) and each dilution was tested as the initial until negative result. ET level was determined by multiplying the value inverse to the largest dilution giving positive test by the lowest concentration of the standard ET solution giving the positive test. The results are expressed in EU/ ml.

To evaluate enterosorption effectiveness of Enterogel, the patients were divided into 2 groups. The study group included 16 children with AD treated with Enterogel in the complex therapy for 14 days at the following doses: children aged 10-4 years - 1 dessert spoon 3 times a day (30 g), over 14 years - 1 tablespoon 3 times per day (45 g). The comparison group included 14 children treated with traditional anti-allergic drug therapy without Enterogel.

Antiallergic therapy did not differ in both groups and included hypoallergenic diet, antihistamines, external anti-inflammatory drugs as well as medical and cosmetic skin care.

Results and discussion

Analysis of the data revealed (Fig. 1) that in children surveyed in the exacerbation period of AD, plasma ET concentration was 0.140 ± 0.071 EU/ ml, whereas in the control group it was 0.002 ± 0.001 EU/ ml ($p < 0.001$). In remission plasma ET decreased to 0.018 ± 0.014 EU/ ml ($p < 0.05$), while it exceeded ET level in the control group ($p < 0.001$).

In severe AD, endotoxemia levels were equal to 0.168 ± 0.079 EU/ ml, significantly exceeding the at moderate to severe course – 0.076 ± 0.023 EU/ ml ($p < 0.05$). In children with erythematous-squamous and lichenoid forms, endotoxemia indicators do not differ significantly and were 0.123 ± 0.118 EU/ ml and 0.124 ± 0.077 EU/ ml, respectively (see. Table)

The correlation analysis revealed the relationship of ET level with total IgE in the period of exacerbation and remission ($r = 0.56$ and $r = 0.42$, respectively) and the number of eosinophils in peripheral blood ($r = 0.43$ and $r = 0.39$, respectively).

Thus, in AD exacerbation of content of plasma ET exceeded those in the control group by nearly 60 times ($p < 0.001$), decreasing by 8 times in remission ($p < 0.05$). However, its performance did not reach values of the control group. Defined ET content in healthy children shows physiological endotoxemia.

The presence of systemic endotoxemia was an indication for enterosorption [6] and inclusion of drugs in the complex AD treatment providing sorption, and detoxification and cytoprotective action, as well as a positive effect on the intestinal microflora.

This drug with a complex mechanism of action was Enterosgel - enterosorbent with porous gel-like structure and consistency. The drug prevents damage of the GIT mucosa, restores mucosal damage and normalizes the microcirculation, resulting in improved ; activates restoration processes, creates conditions for the growth of normal intestinal microflora. Thanks to its gel-like consistency, the drug absorbs high-molecular-toxic substances (including bacterial toxins) and has protective properties. Enterosgel absorbs and neutralizes ET of gram-negative bacteria, forming a protective layer of gel-like particles on the mucous membrane, which protects the mucosa from chemical

Table ET values in the blood plasma depending on the course, form and AD activity degrees

AD features	ET (EU/ml)
Severe AD (n=10)	$0,168 \pm 0,079$
Moderate AD (n=20)	$0,076 \pm 0,023$
Erythematous-squamous form with lichenification (n=12)	$0,123 \pm 0,118$
Lichenoid form (n=18)	$0,124 \pm 0,077$

and physical effects. Considering the above, there are all indications for the drug Enterosgel in endotoxemia in AD in children.

On the background of the therapy (Fig. 2), there was a marked decline in ET plasma levels in the main group – by 12 times, from 0.142 EU/ ml to 0.012 EU / ml, while in the control group, it was only 6 times - from 0.139 EU/ ml to 0.023 EU/ ml, $p < 0.05$.

On the background of significant decrease of endotoxemia, in the main group of children overall therapeutic effect was 87.5% ($n = 14$). Meanwhile 10 patients (62.5%) had clinical improvement, and in 4 patients (25%) there has been a considerable improvement of the skin process. This was manifested by positive dynamics on the part of skin process, a decrease of SCORAD index (Scoring atopic dermatitis) by more than 2.5 times, and seizing, and improved quality of life (decreased intensity of itching,

improved night's sleep). Lack of effect was observed in 2 patients (12.5%). On the therapy background reduction of exacerbation period was marked as well as complete relief of morphological skin elements and clinical remission on average observed on the 12th day from the start of therapy. SCORAD index in the group decreased on average 5 times - from 50 to 10 points.

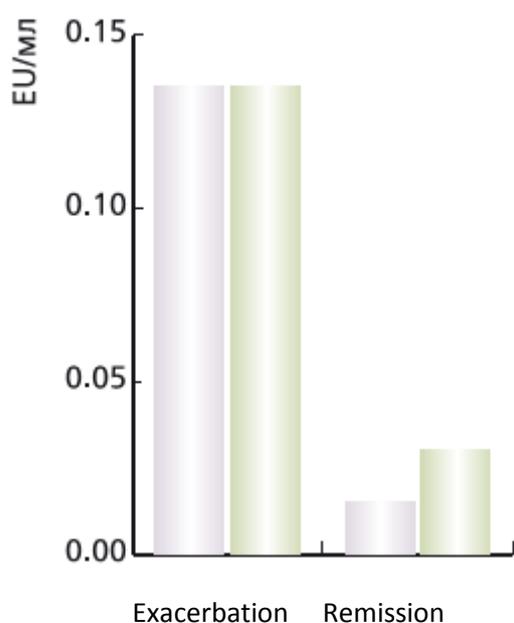
In the comparison group total therapeutic effect amounted to - 64.3% (n = 9). Thus, in 6 patients (42.9%) clinical convalescence was noted. In 3 patients (21.4%) took place a significant improvement of the skin process. The lack of effectiveness was noted in 5 patients (35.7%).

On the background of the therapy SCORAD index declined by an average of 3.3 times - from 50 to 15 points. Clinical remission was observed on the 20th day from the beginning of the therapy.

Conclusion

Thus, in children with AD system endotoxemia was established. Plasma ET in remission significantly decreased compared with exacerbation period, but did not achieve that of the control group (healthy). The content of plasma ET depends on severity of skin process. Presence of systemic endotoxemia is an indication for enterosorption

Figure 2. Endotoxemia dynamics in children with Ad depending on the therapy



Main group – Comparison group

Use of Enterosgel in the age-related dose in the complex antiallergic therapy lowers the level of plasma ET by 12 times - from 0.142 to 0.012 EU/ ml, with reducing exacerbation period - by 1.6 times (days) and reducing SCORAD index by 5 times.

This method of treatment has shown high efficiency and can be widely used in the treatment of atopic dermatitis in children and adolescents.

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