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THE IMPORTANCE OF ANTIMICROBIAL PEPTIDES IN THE MECHANISM OF DEVELOPMENT OF THE INFLAMMATORY PROCESS ON THE SKIN IN PATIENTS WITH ATOPIC DERMATITIS

Mavlyanova Sh.Z., Khakimov D.R., Khonkhodzhaev Sh.Sh

Republican Specialized Scientific and Practical Medical Center of Dermatovenereology and Cosmetology of the Ministry of Health of the Republic of Uzbekistan.

Mavlyanova Shakhnoza Zakirovna - Doctor of Medical Sciences, Professor, Head of the Scientific Laboratory of the Republican Specialized Scientific and Practical Medical Center for Dermatovenerology and Cosmetology, Ministry of Health of the Republic of Uzbekistan, tel: +998901885779 *.e-mail:* **shahnoza_m@mail.ru**

Khakimov Dilshod Rustamovich – PhD, researcher of the Republican Specialized Scientific and Practical Center for Dermatovenereology and Cosmetology of the Ministry of Health of the Republic of Uzbekistan, tel: +99890 910-30-60 ; *e-mail:* doctordilshod@mail.ru

Khonkhodzhaev Sherzod Shukhratovich - Researcher of the Republican Specialized Scientific and Practical Center for Dermatovenereology and Cosmetology of the Ministry of Health of the Republic of Uzbekistan, tel: +99890 188 76 65 *.e-mail:* sherzod105@mail.ru

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ABSTRACT

Polymorphism of clinical manifestations, multifactoriality, and the presence of immunogenetic mechanisms for the development of atopic dermatitis require a more in-depth approach to assessing the severity of the inflammatory process, both local (skin) and in the whole organism.

The purpose of the study was to assess the level of the antimicrobial peptide - cathelicidin - LL-37, taking into account local immunity and C-reactive protein in the clinical and morphological course of atopic dermatitis.

Material and research methods. 56 patients aged from 12 to 60 years were under observation. All patients underwent clinical (SCORAD index determination), immunological, microbiological, and statistical studies.

Research results. The results of an ELISA study of antimicrobial peptides LL-37 in blood serum showed an increase in the concentration of cathelicidin by 5.7 times against the background of hyperproduction of total IgE and C-reactive protein in the blood serum of patients with AD. It should be noted that with increasing age, the concentration of AMP LL-37 increased by 5.4 and 7.6 times, respectively, and were statistically significant ($P < 0.05$). The level of total IgE was increased by 2.6 and 3.8 times compared to the healthy control group and was statistically significant. Correlation analysis showed that the level of LL-37 was in direct significant correlation with C-reactive protein - $r = +0.8$ and total IgE - $r = +0.79$ ($P < 0.05$).

Conclusion: In patients with AD, an increase in the level of AMP cathelicidin LL-37 is induced by an infectious factor caused by staphylococcus spp, which contributes to an increase in the level of C-reactive protein and the development of lymphohistiocytic infiltration with the content of neutrophils in the skin biopsy, indicating the invasive-inflammatory nature of the skin pathological process in patients with blood pressure.

Key words: atopic dermatitis, clinic, antimicrobial peptides, C-reactive protein.

INTRODUCTION

In dermatological science, the study of the mechanisms of development of inflammatory processes in allergic skin diseases is one of the links in fundamental directions. [1,2,3,5-9]Polymorphism of clinical manifestations, multifactoriality, and the presence of immunogenetic mechanisms for the development of allergic dermatoses require a more in-depth approach to assessing the severity of the inflammatory process, both local (skin) and in the whole organism. [7,8,9]

In this direction, the assessment of antimicrobial peptides in the pathogenesis of inflammatory reactions of the skin in patients with atopic dermatitis is of great scientific and practical interest.

Cathelicidins are inducible peptides - LL-37 is an amphipathic, alpha-helical antimicrobial peptide. The production of antimicrobial peptides LL-37 is stimulated due to skin damage, inflammatory reactions and its infection with pathogenic microorganisms S.aureus, E.coli, Candida and the vaccine strain of variola virus. [5, 11,12]. Research has established the participation of antimicrobial peptides in inflammatory reactions and have a direct effect on the effector parts of the inflammatory process.

The purpose of the study was to assess the level of the antimicrobial peptide - cathelicidin - LL-37, taking into account local immunity and C-reactive protein in the clinical and morphological course of atopic dermatitis.

Material and research methods. 56 patients aged from 12 to 60 years were under observation. Among them, there were 32 females and 24 males. According to the age aspect, patients of young - active age - 19 - 40 years - 30 and 41-60 years - 26, respectively. All patients underwent clinical (SCORAD index determination), immunological, microbiological, and statistical studies. Clinical studies of the SCORAD index were determined using software diagnostics (Scoring of Atopic Dermatitis, 1993), which is calculated using the formula:

SCORAD = A/5 + 7B/2 + C, where A is the prevalence of rashes, B is the intensity of inflammation of the pathological process (erythema, edema, crusts, excoriation, lichenification, dry skin), C is the severity of subjective symptoms (itching and sleep disturbance) . As well as the clinical course, taking into account the duration of the disease, hereditary factors and seasonality of the disease. (DGU 17814)

The level of AMPs was determined in blood serum using commercial test systems (Human LL-37, ELISA Kit. ABBEXA. USA) by ELISA. The level of total IgE, C-reactive protein in blood serum was determined using commercial ELISA test systems "Vector-Best" (Novosibirsk). To conduct morphological studies, biopsies were fixed in 10% neutral formalin (pH-7.3), carried out with isopropyl wire, compacted in xylene-paraffin slurry, and embedded in paraffin blocks. Sections 3-4 microns thick were made on a microtome, applied to glass slides with an adhesive coating, and deparaffinized. Sections were stained with hematoxylin and eosin. Microscopic studies were carried out using an Eclipse E200 light microscope from Nikon (Japan) at a magnification of x180 and x400 times.

To evaluate the correlation analysis, we used the Pearson method. Statistical studies using variation analysis using Student's t-test (Excel-2010).

Research results. The results of software diagnostics of the severity of blood pressure in the examined patients revealed a mild degree of severity in 8 patients (14.3%), a moderate degree in 26 (46.4%) and a severe degree in 22, which amounted to 39.3% of cases. Taking into account

age, at a young age, moderate degree was more often diagnosed - in 14 out of 30 (46.6%) and 41-60 years - moderate and severe degree - in 12, respectively, which amounted to 46.2% of cases.

The results of an ELISA study of AMP LL-37 in blood serum showed an increase in the concentration in patients with blood pressure by 5.7 times compared with the indicators in the healthy control group and averaged 10.3+0.6 pg/ml (P <0.05). (Fig. 1) It should be noted that with increasing age, the concentration of AMP LL-37 increased by 5.4 and 7.6 times, respectively, and were statistically significant (P <0.05). The level of total IgE was increased by 2.6 and 3.8 times compared to the healthy control group and was statistically significant. (table 1)

Table 1. Indicators of LL-37, IgE, and C-reactive protein in blood serum in patients with AD, taking into account age indicators. (M+m)

Patients with AD	IgE	C-reactive protein	LL-37
19-40 y N=30	168,6±15,7*	11,5±0,6* **	9,8±0,4* **
41-60 y N=26	245±6,7* **	18,6±0,4* **	13,8±0,5***
Control group N=35	63,2 ± 1,4	4,6 ± 0,08	1,8± 0,04

Note: * - reliability indicator in relation to healthy individuals (P<0.05); ** - reliability indicator in relation to patients with blood pressure aged 12-18 years. (P<0.05)

It should be noted that against the background of an increase in the concentration of the antimicrobial peptide LL-37 and hyperproduction of total IgE, the level of C-reactive protein increased statistically significantly in all studied groups and averaged 11.5+0.6 mg/ml and 18.6+0. 4 mg/ml respectively. Moreover, correlation analysis showed that the level of LL-37 was in direct, significant correlation with C-reactive protein - r=+0.8 and total IgE - r=+0.79 (P<0.05).

This increase in the concentration of C-reactive protein, which is responsible for the acute phase of inflammation in patients with AD, in our opinion, is due to the infiltrative-inflammatory process, characterized by a high contamination of staphylococcus spp. on the skin in lesions characterized by the development of a syndrome of impaired resistance of microorganisms. (Table 2)

Table 2. Colonization patterns of Staphylococcus spp. in the examined patients (CFU/cm²)

group	St. aureus	St. epidermidis	St. saprophyticus	St. Haemoliticus
patients AD	96,3±0,8*	51,2±0,9*	46,1±1,4	48,2±0,4
Control group , N=72	3	6,6±0,4		

Note: * - reliability indicator in relation to the indicators of healthy individuals (P < 0.05)

As can be seen from the table, in the examined patients, increased colonization of staphylococcal flora was observed on the skin of the lesions, which was statistically significantly different from the indicators of the control healthy individuals (P <0.05).

Thus, in studies of patients with AD with high levels of antimicrobial peptides LL-37 and seeded St. Aureus in AD, the morphological picture is varied due to different clinical forms of AD (erythematous-squamous, erythematous-squamous form with lichenification, lichenoid, exudative, pruriginous). The general picture observed in the preparations: hyperkeratosis of varying degrees of severity, serous fluid in the stratum corneum containing neutrophils, sometimes bacterial colonies, thickening of the granular layer, uneven acanthosis, pronounced intercellular edema of the cells of the spinous layer, vacuolization of the cells of the basal layer. In the papillary layer of the dermis, swelling, dilation of the dermal capillaries were observed, around them there was lymphohistiocytic infiltration containing lymphocytes, neutrophils and from single to focal accumulation of eosinophils. In some sections there was a pronounced inflammatory picture: pronounced swelling of the papillary layers of the dermis and infiltration consisting mainly of neutrophils and eosinophils.

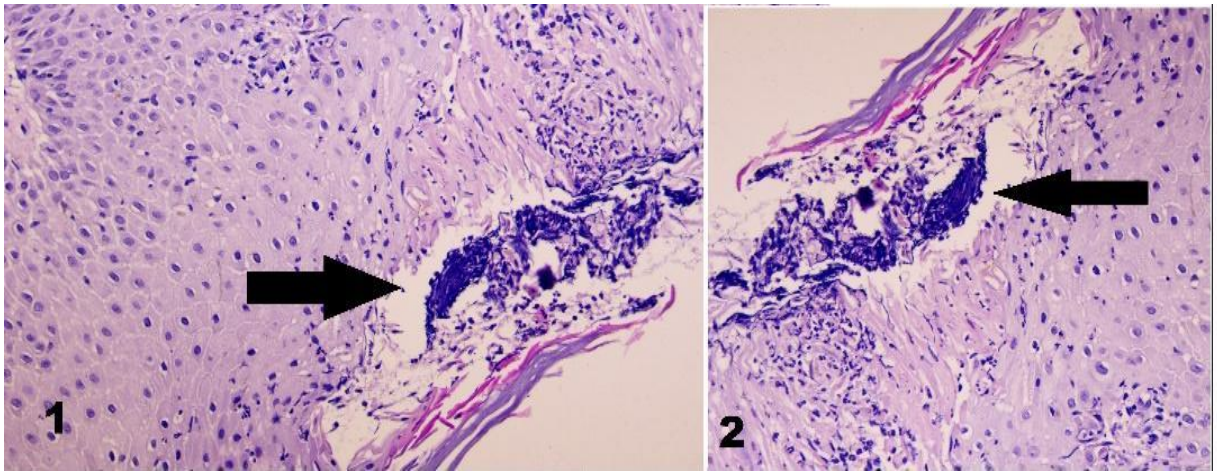

Fig.1. Pathomorphological picture of the skin AD cultured by St. Aureus. In photos 1-2: neutrophils and bacterial colonies in the stratum corneum of the epidermis (indicated by a black arrow)

Analysis of the results obtained indicates that in patients with AD, an increase in the level of AMP cathelicidin LL-37 is induced by an infectious factor caused by staphylococcus spp, which contributes to an increase in the level of C-reactive protein and the development of lymphohistiocytic infiltration with the content of neutrophils in the skin biopsy, indicating invasive-inflammatory the nature of the skin pathological process in patients with AD.

Conclusions:

1. The results of an ELISA study of antimicrobial peptides LL-37 in blood serum showed an increase in the concentration of cathelicidin by 5.7 times against the background of hyperproduction of total IgE and C-reactive protein in the blood serum of patients with AD.

2. In patients with AD, an increase in the level of AMP cathelicidin LL-37 is induced by an infectious factor caused by staphylococcus spp, which contributes to an increase in the level of C-reactive protein and the development of lymphohistiocytic infiltration with the content of neutrophils in the skin biopsy, indicating the invasive-inflammatory nature of the skin pathological process in patients with blood pressure.

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