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Original Article

The value of eosinophilic cationic protein in atopic dermatitis

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Abstract

Objective Till date, the search for diagnostic markers of atopic dermatitis (AD) is still active. Such investigations will assess not only the allergic inflammation, but also help controlling the severity of the disease.

Method To analyze diagnostic significance of eosinophilic cationic protein in AD patients, a number of 24 patients with AD and 10 practically healthy persons were examined. The patients in the main study group were distributed by age: 18-40 years (12 persons) and over 40 years (12 persons). All AD patients were tested for allergic inflammation makers. Statistical processing of the obtained results was carried out by the method of variational statistics using the Statistica 10.

Results With ageing, there was a tendency to a decreased number of AD extrinsic (high levels of IgE), instead the number of people with AD intrinsic increased (low levels of IgE) (OR = 2.92; 95% CI 1.83-4.65; p <0.001). In addition, both the forms of AD and the total serum IgE level were dependent on the age of the patients (OR = 5.72, 95% CI [2.52–13.94]; p <0.001). Simultaneously, when the severity of AD increased, ECP levels were increased significantly (OR = 4.26, 95% CI [2.01–9.05)].

Conclusion It is efficient to determine the level of ECP in AD, as an indicator for allergic inflammation. The levels of ECP increased with the severity of the disease. The level of ECP did not depend on the age of the patient and the form of AD.

Key words
Disturbance of the skin barrier, pathogenesis, inflammatory process.

Introduction

The incidence of atopic dermatitis has not significantly changed in recent decade, despite advances in treatment of the disease. According to epidemiological data, atopic dermatitis (AD) is a "worldwide phenomenon" that is affecting 20% of both children and adults around the world.[1] The literature's analysis shows that the "schematics" and the standard approaches towards management of patients with AD do not allow carrying through full necessary therapeutic and diagnostic measures. As a result of the absence of specific diagnostic laboratory markers of AD, the clinical diagnosis of the disease is based on the anamnestic data of the patient, specific clinical symptoms and the

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exclusion of other non-inflammatory skin diseases.[2]

The pathogenesis of AD is multifactorial and presumably depends on the interaction of genetic, immunological, environmental and infectious factors that lead to inflammation and the disturbance of the skin barrier, however, this issue continues to be studied.[3] The mechanism of disease's development distinguishes between IgE-mediated and non-IgE-mediated AD. Recent literature reports indicate that 10 to 45% of patients with endogenous (intrinsic AD) are characterized by low serum immunoglobulin E (IgE) and the absence of allergen-specific IgE. In addition, scientists believe that laboratory markers for the diagnosis and assessment of the severity of the disease are not enough for patients with AD.[4,5] Till this date, the search for diagnostic markers that will allow assessing not only allergic inflammatory process, but also control the severity of the disease is still going on. The back bone of modern mechanisms of development of AD is complemented by the association of the disease with the increased level of eosinophilic cationic protein (ECP).[6]

In allergic inflammatory processes, the release of eosinophils from the bone marrow increases, also their degranulation and ejection of cationic proteins take place. One of the major cationic proteins is the eosinophilic cationic protein. It is suspected that products of eosinophilc activation are meditators that conciliate late-phase allergic response and are responsible for hyperreactivity in atopy. It has been proven that eosinophilic cationic protein has a significant proinflammatory effect and plays a role in the development of subacute and chronic signs of allergy and is one of the markers of allergic inflammation. However, there are conflicting and limited data on the diagnostic value of ECP in AD.[7] Therefore, given the difficulty in assessing the activity of the allergic inflammation in patients with atopic dermatitis; especially in severe cases, in our opinion, it is relevant to study the clinical significance of eosinophilic cationic protein in this pathology. This study aims to analyze the diagnostic significance of eosinophilic cationic protein in AD patients.

Materials and Methods

The methodology of the study was based on the use of a systematic approach to the patients who addressed the hospital with complaints that are common for the patients with AD. According to the inclusion criteria, 24 patients were examined. The control group consisted of 10 healthy individuals. The patients in the main study group were divided by age: 18-40 years (12 people) with an average age of patients 31.3±2.1 years and older than 40 years (12 people) with an average age of patients 56.8±2.6 years. The mean age of the control group was 41.1±2.3 years.

The criteria for inclusion in the study were confirmed diagnosis of AD, age 18 and older and willingness to perform all the procedures that are provided by the design of this study. The diagnosis of AD was established on the basis of criteria formulated by J.M. Hanifin and G. Rajka.[8] All patients were analyzed for family and allergic history, objective examination data and laboratory diagnostic results. The SCORAD index was used to assess the severity of exacerbation of AD. All patients of AD were tested for markers of allergic inflammation, namely IgE and ESR in the serum. The statistical processing of the obtained results was carried out by the method of variational statistics using the statistical package of Microsoft Office 2010 and Statistica 10 program. The analysis of gender characteristics revealed that among the observed patients with AD, female persons prevailed, which amounted to 15 (62.5±3.96%)

persons.

Results and Discussion

In the study it was established that people living in civic areas were 2.5 times more likely to suffer from AD compared to village residents ($p < 0.01$). Among the patients with AD, civic residents accounted for 63.5±4.12% versus 37.5±4.11% of people living in the village. The analysis of seasonal features of exacerbation of AD revealed that the largest proportion of patients was registered in February–March, i.e. winter-spring period, which was 68.75±4.22% of cases compared to April–May that was spring period. Nevertheless, the number of patients in the spring period was 2 times less (31.25±4.21% of cases), ($p<0.05$).

In the study group of patients with AD, four people were diagnosed with a common form of chronic allergy (16.67±4.12%) cases. In the course of the study, the severity of BP in the subjects was evaluated with SCORAD index that ranged from 18.4 to 78.6 points, averaging 48.5±7.8 points. A moderate grade was predominant occurrence, mainly in 12 (50.0±4.44%) individuals with a mean SCORAD score of 33.5±6.4 points. Severe grade was determined in 9 (37.5±4.15%) subjects with a SCORAD index value of 68.62±4.5 points. Mild course of the disease occurred only in 3 (12.5±4.64%) patients with a mean SCORAD index of 16.2±3.8 points.

We did not find a significant difference in the severity of the disease depending on the age groups of the examined persons. In the process of our study, we analyzed the level of total IgE in the serum of the subjects. A significant difference was found between the mean serum IgE levels, which was 6.2 times higher in AD patients than in practically healthy people ($p<0.05$). It should be pointed out that in the majority of patients with AD (62.5±4.38%, 15 persons), an increased level of total IgE in serum was detected. However, 9 (37.5±4.37%) patients with AD had reference values for the level of total IgE in serum.

It should also be noted that concomitant allergic pathologies, mainly allergic rhinitis, conjunctivitis and bronchial asthma, was found in 7 (29.17±3.24%) patients with AD, with an increased levels of total IgE in the serum. Taking into account the literature data, that is the selection of clinical and pathogenetic variants of AD, such as extrinsic (ADe) and intrinsic (ADi) forms; we used the value of the total IgE level as a basis for isolation of pathogenetic variants of the disease. Notably, along with an increase in the age of patients, there was a tendency to a decrease in the number of persons with an extrinsic form of AD, although the number of persons with an intrinsic form of the disease increased. Thus, the extrinsic form of AD in the age group of 18-40 years old amounted to 84.8% of patients, while the number of such patients decreased in the age group of 40 years old and older. It is necessary to note that with increased age of the patients there was a tendency to decreased number of extrinsic forms of AD, in return the number of individuals with intrinsic form of the disease increased. Thus, the extrinsic form of AD in the group of 18-40 years was 84.8% of patients, inversely such patients decreased in the group over 40 years (78.4%), (OR = 2.92; 95% CI 1.83-4.65; $p<0.001$). The analysis of the disease course showed that moderate and severe course was 2.0 times more common among the surveyed than the mild stage. However, among patients with serum levels of IgE that did not go beyond the age limit, mild disease activity was reported 5.6 times more frequently than moderate and severe ($p < 0.05$).

Nevertheless, it must be noted that both the

forms of AD and the average level of total IgE in the serum rely on the age of the patients (OR=5.72, 95% CI [2.52–13.94]). Also with the age, the level of total IgE decreased and respectively, the frequency of extrinsic type of AD. So, it was determined that in the group of patients aged 18-40 years, the average level of total IgE (64.5±3.51 IU/ml) was significantly higher than this indicator in the surveyed persons over 40 years of age (24.3±4.34 IU/ml), ($p<0.05$). In this manner, it can be assumed that with the age, the sensitivity of total IgE, its importance and expediency in patients with AD are lost.

A higher direct assist of search for a sensitive marker of allergic inflammation in AD According to the literature it is known that eosinophil activation products are mediators that mediate the formation of an allergic response and are responsible for hyper reactivity in allergies.[7] Therefore, the next step in our study was to analyze ECP in the serum of the patients that were examined. We found that the average level of EC in the serum was 6.5 times higher in patients with AD, compared to results of absolute healthy people. In addition, an elevated serum ECP was detected in the vast majority of AD patients, namely 22 (91.67±2.38%). Whereas this indicator did not go beyond the reference values except in 2 (8.33±3.34%) persons with ADi form of the disease. It should also be noted that elevated total serum ECP levels occurred in all patients with extrinsic AD[9]. The mean serum ECP level in AD patients was 56.78±2.72 ng/ml, which was significantly higher than in AD patients (32.13±2.62 ng/ml), ($P <0.05$).

As well, in our study, it was found that as the severity of AD increased, the average serum ECP level also increased significantly (OR = 4.26, 95% CI [2.01–9.05)]. Thus, among those surveyed with a high mean levels of ECP in the blood serum, the severe course of the disease was more often, namely 4.0 times more (value of the SCORAD index of 54.9±5.4 points was established), than the moderate level (value of the SCORAD index of 33.9±5.1 points). ($p<0.05$). Yet, we did not report a mild course AD in patients with elevated total serum ECP. Howsoever, only two patients with ECP level not exceeding beyond the serum reference values had a mild disease score (SCORAD index score of 13.9±6.4 points ($p <0.05$)).

It is also important to note that the ECP level is positively correlated with the SCORAD score in individuals with both the ADe form ($r = 0.318$, $p=0.002$) and the ADi form of the disease ($r=0.471$, $p=0.002$). In the course of the study we did not find a significant difference in the value of ECP in serum depending on the age of the patient and form of the disease.[10,11] In the course of clinical examination of the subjects included in the study, the sensitivity and specificity of the ECP level in AD were determined. In consequence, we found that ECP, as a marker of allergic inflammation, had a high sensitivity (Se) of 91% and specificity (Sp=76.4%; LR+1.52, +PV=65%, -PV=26%).

Despite the long duration of AD problem studying, its etiology and pathogenesis are still questions that remain concerning the development of such chronic inflammation of skin. Our study aimed to evaluate both the value and level of ECP as a marker for adult allergic inflammation. It is revealed that clinical features of ADi are characterized by a mild degree of severity according to the SCORAD score and moderately pronounced activity of allergic inflammation, unlike the group of patients with ADe.

On the contrary, the mean value of ECP in blood serum in ADe was three times higher than in patients with ADi form of the disease. It should

be noted that the literature on ECP linkage with the severity by the SCORAD index is controversial and debatable. Also, according to the conducted research, in children aged 3-36 months, no correlation was found between both of studied indicators. Inversely, some scholars claim that there is a positive correlation between ESR and SCORAD in AD in both children and adults.

Conclusions

Thereby, our studies have shown that in patients with AD disease is accompanied by pronounced changes in indicators of allergic inflammation, especially ECP. This indicator can serve as a marker of allergic inflammation in AD in adults that depends on the severity of the disease. However, it does not depend on the age of patients and the pathogenetic form of the disease (ADe or ADi). In AD, the level of ECP is efficient as an indicator of allergic inflammation. The level of ECP increases as the severity of the disease does. The level of ECP did not depend on the age of the patient and the form of the disease.

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