

Evaluation of periostin level for predicting severity and chronicity of childhood atopic dermatitis

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Adv Dermatol Allergol 2019; XXXVI (5): 616–619

DOI: <https://doi.org/10.5114/ada.2018.79728>

Abstract

Introduction: Periostin has some effects on the pathogenesis of atopic dermatitis (AD) via release of pro-inflammatory cytokines and chemokines from activated keratinocytes and it is related to chronicity of skin lesions.

Aim: To evaluate the relationship between plasma periostin levels and severity and chronicity of AD in children.

Material and methods: The study population consisted of 29 children with atopic dermatitis without concomitant allergic disease such as asthma or allergic rhinitis and 31 healthy controls. Data of demographic features, serum eosinophil, total IgE and skin prick test results were collected through the patient's medical records. The severity of the disease was assessed by the SCORAD index. Serum periostin levels were measured with a human periostin ELISA kit.

Results: The mean ages of the AD patients and the control group participants were 80.7 ±52.8 and 90.3 ±41.6 months, respectively. Mean plasma periostin levels were 63.0 ±19.0 ng/ml in AD patients, and 23.6 ±7.3 in healthy controls, and there was a statistically significant difference between the two groups ($p = 0.001$). Plasma periostin level did not vary according to total IgE or serum eosinophil count ($p > 0.05$). Age of onset and duration of symptoms also were not correlated with plasma periostin levels. Although there was a positive relationship between plasma periostin level and the SCORAD index of patients, it was not statistically significant ($r = 0.19$, $p > 0.05$).

Conclusions: This study showed that plasma periostin levels were increased in children with atopic dermatitis. Periostin may have a partial role in the pathogenesis of atopic dermatitis, but it is not associated with severity or chronicity in children with atopic dermatitis.

Key words: atopic dermatitis, periostin, eczema, children.

Introduction

Periostin is an extracellular matrix (ECM) protein that belongs to the fasciclin family [1]. Periostin is expressed during ECM remodeling, mechanical stress, and post-injury tissue repair [2]. Many studies have revealed that periostin plays a role in various conditions such as allergic inflammation [3], cancer [4], fibro-proliferative disorders [5], myocardial infarction [6], and wound healing [7].

Atopic dermatitis (AD) is a chronic, pruritic, and relapsing inflammatory skin disease. It is accompanied by skin barrier dysfunction and dominant Th2 type inflammation [8, 9]. It was recently found that periostin plays an important role in amplifying allergic skin inflammation

by inducing Th2-type cytokines such as IL-4 and IL-13, which are related to the immune response [10, 11]. Additionally, periostin has some effects on the pathogenesis of AD via the release of proinflammatory cytokines and chemokines such as thymic stromal lymphopoietin (TSLP), IL-25, and IL-33 from activated keratinocytes [12]. Further, it is related to the chronicity of skin lesions [13].

Aim

The purpose of this study was to evaluate the serum periostin level and its association with the severity and chronicity of AD in children.

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Received: 19.09.2018, **accepted:** 15.10.2018.

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Material and methods

The study population consisted of 29 children with atopic dermatitis and 31 healthy children (control group) who were monitored at the Pediatric Allergy and Immunology outpatient clinics in the Sağlık Bilimleri University Okmeydanı Research and Training Hospital and Istanbul University, Istanbul Faculty of Medicine. The diagnosis of atopic dermatitis was made by a physician according to the Hanifin-Rajka criteria [14]. Children with atopic dermatitis had no concomitant allergic diseases such as asthma or allergic rhinitis. Data on demographic features such as age, gender, family history of atopy, age of onset and duration of symptoms, laboratory values of serum eosinophil, and total IgE and skin prick test results were collected through the patients' medical records. The severity of the disease was assessed by the SCORing Atopic Dermatitis (SCORAD) index [15].

Laboratory investigation

Venous blood samples from all patients were collected by antecubital venipuncture and dispensed directly into K3-EDTA tubes. The plasma separation was performed after centrifugation of the EDTA whole blood samples at 1500 g for 10 min. The plasma specimens were kept frozen at -80°C while they awaited analysis.

Biochemical analysis

The serum periostin levels were measured with the Human Periostin ELISA kit from Bioassay Technology Laboratory (Shanghai, China) according to the manufacturer's instructions.

Skin prick tests

The commercial allergen solutions manufactured by Stallergenes (Paris, France) were used for the skin prick

tests. Ten different aeroallergens were applied in the skin prick tests: *Alternaria*, *Aspergillus* mixture, birch, cat epithelia, cypress, *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, dog epithelia, grass pollen mixture, and weed pollen mixture. There were also six different food allergens: cocoa, egg white, egg yolk, milk, peanut, and wheat. The skin prick tests were considered positive if, after subtraction of the negative value, a wheal with a maximum diameter of at least three millimeters was present.

Ethical approval

The study was performed in accordance with good clinical practice and the tenets of the Declaration of Helsinki, and it was approved by the Ethical Committee of Istanbul Faculty of Medicine (2017/430). All study patients and their parents were given information about the study, and signed consent was obtained from the parents.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 19 (IBM, Armonk, NY, USA). The Shapiro-Wilk test was used to test distributions for normality. Parametric data are expressed as the mean \pm standard deviation (SD), and non-parametric data are expressed as the median and interquartile range (IQR). The Mann-Whitney *U* test or Student's *t*-test was used to calculate the differences in variables between groups. The correlation between 2 variables was assessed using the Spearman rank correlation coefficient or Spearman's test. Categorical data were evaluated using the χ^2 test; $p < 0.05$ was accepted as statistically significant.

Table 1. Demographic and clinical values of patients and controls

| Parameter | AD patients (n = 29) | Control group (n = 31) | P-value |
|---|-------------------------|---------------------------|---------|
| Age, mean \pm SD [months] | 80.7 \pm 52.8 | 90.3 \pm 41.6 | > 0.05 |
| Gender, M/F | 15/14 | 18/13 | > 0.05 |
| SCORAD, mean \pm SD | 35.1 \pm 12.6 | – | |
| Serum total IgE > 100 IU/l, n (%) | 34 (58) | ND | |
| Eosinophils > 4%, n (%) | 18 (62) | ND | |
| Atopy, n (%)* | 17 (59) | ND | |
| Food allergy, n (%) | 3 (10) | – | |
| Aeroallergen sensitivity, n (%) | 9 (31%) | ND | |
| Treatment, n (%): | | | |
| Emollient or moisturizer only | 9 (32) | – | |
| Topical steroid + emollient or moisturizer | 18 (62) | | |
| Topical calcineurin inhibitors + emollient or moisturizer | 2 (7) | | |

AD – atopic dermatitis, ND – not done. *Atopy: Patients with a serum IgE level > 100 IU/l and/or positive for at least one allergen in SPT.

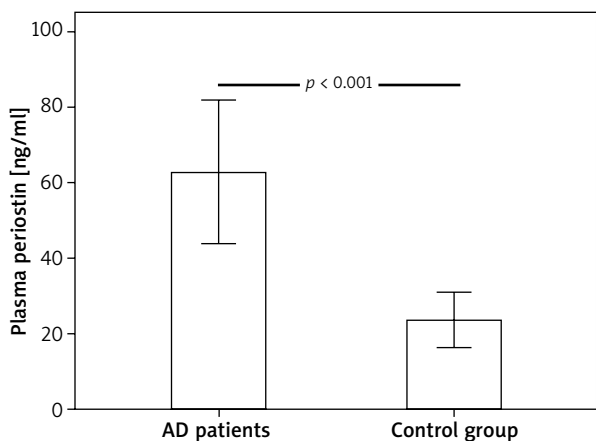


Figure 1. Serum periostin levels in study and control groups

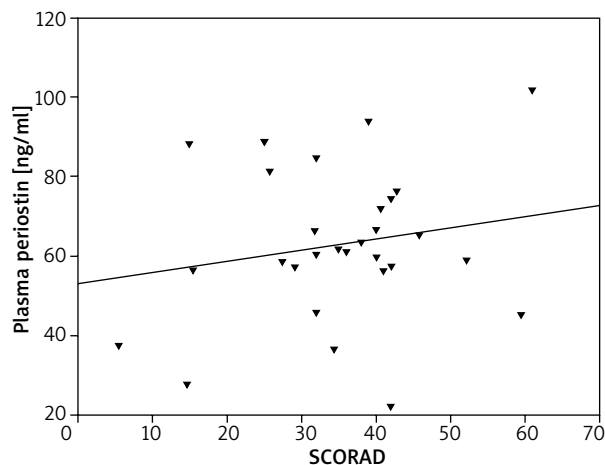


Figure 2. Scatter graph showing the plasma periostin levels and SCORAD relationship in patients with atopic dermatitis

Results

The study group consisted of 15 boys and 14 girls with AD, and the control group consisted of 18 boys and 13 girls. The mean ages (in months) of the AD patients and the control group participants were 80.7 ± 52.8 and 90.3 ± 41.6 , respectively. No significant differences in age or gender existed between the groups ($p > 0.05$). Some demographic and clinical features of the patients are shown in Table 1.

The mean plasma periostin levels were 63.0 ± 19.0 ng/ml in the AD patients and 23.6 ± 7.3 in the control patients. There was a statistically significant difference between the two groups ($p = 0.001$) (Figure 1). The plasma periostin levels did not vary according to gender and atopy. Additionally, the plasma periostin levels did not correlate with the serum total IgE or the serum eosinophil count ($p > 0.05$). Additionally, the age of onset and duration of symptoms did not correlate with the plasma periostin levels (data not shown). Although there was a positive relationship between the plasma periostin levels and the SCORAD index of patients, it was not statistically significant ($r = 0.19$, $p > 0.05$) (Figure 2).

Discussion

Atopic dermatitis is the most common inflammatory dermatological disorder. It is a chronic or chronically relapsing disease, and it is characterized by intense pruritus and dry skin [16]. Patients with AD have defective skin barrier functions and suffer increased transepithelial water loss. Dryness, when coupled with itching or scratching behaviors, is one of the main triggers of lichenification, which consists of epidermal hyperplasia and fibrosis [9]. Periostin, an ECM protein, was recently found to have a role in amplifying and maintaining skin inflammation

by keratinocyte activation, along with increasing the Th2-type immune response [17].

Increased levels of IL-13 in chronic skin lesions indicate its possible role in the proliferation and differentiation of keratinocytes and remodeling in AD. Similarly, IL-4 and IL-13-induced periostin production from airway epithelial cells reflects refractory eosinophilic inflammation and remodeling in asthma patients [18]. Using a mouse model of skin inflammation, Masuoka *et al.* demonstrated that periostin is a critical mediator for the amplification and persistence of allergic differentiation and proliferation of keratinocytes. Furthermore, Masuoka *et al.* also observed increased expression of periostin in the skin tissues of AD patients and its correlation with AD severity [12]. Data derived from a recent study performed on canine AD (cAD) suggested that IL-13, possibly derived from T helper 2 (Th2) cells, stimulates periostin production in both keratinocytes and fibroblasts. This study has been accepted as a spontaneous atopic animal model. The authors commented that periostin may play a role in the enhancement and chronicity of skin lesions via IL-25 [13].

In the present study, we determined that plasma periostin levels were significantly higher in children with AD than in healthy children. Previous studies also determined that children and adults with AD had increased serum periostin levels [9–11]. Correlations between plasma periostin levels and serum total IgE and blood eosinophil levels have been reported in some studies [9]. However, we did not find a relationship between plasma periostin level and serum total IgE and blood eosinophil level. This may be due to the non-specificity of IgE and eosinophils in allergic diseases.

Recent studies suggested that plasma periostin levels may have a role in the severity and chronicity of AD. Sung *et al.* found a significant relationship between the SCORAD index and plasma periostin levels [19]. How-

ever, their study group consisted primarily of patients with mild AD. In our study, there was no significant relationship between plasma periostin levels and severity of atopic dermatitis based on the SCORAD index. We think that the reason for this difference in the results is due to heterogeneity and the small sample size of the patients. For this reason, we cannot state a firm conclusion concerning this matter. The authors also reported higher plasma periostin levels in children with early onset of AD (< 2 years of age) compared to those with an AD onset age under 2 years. Based on this finding, the investigators suggested that serum periostin can be a biomarker of AD chronicity. We did not find any significant relationship between the plasma periostin levels and age at AD onset. Kou *et al.* [20] detected higher levels of serum periostin in patients with erythrodermic type AD and widespread type AD, as compared to patients with lesions that had not spread systemically. Uysal *et al.* reported significant correlations between plasma periostin levels and the duration of symptoms and the presence of atopy [21]. Our results contrast with these study results, and this difference may be associated with sample sizes, recruitment strategies and ELISA kit-specific changes.

As it has with asthma, biomarker-based endotyping in AD has engendered new hope for predicting prognoses and improved therapy outcomes. Various biomarkers such as TARC, TSLP, IL-31, and IL-33 have been investigated to evaluate the pathogenesis of AD and to predict severity and chronicity. TARC and TSLP were found to be related to AD severity and chronicity [21]. Our study has some limitations. The research was conducted with a small group of patients, and, unlike patients in other studies, ours were more likely to have moderate to severe atopic dermatitis.

Conclusions

Plasma periostin levels are higher in patients with atopic dermatitis. Periostin may play a partial role in the pathogenesis of atopic dermatitis. We cannot determine the potential of serum periostin as an indicator of the severity and chronicity of atopic dermatitis in childhood in contrast to previously published studies.

Conflict of interest

The authors declare no conflict of interest.

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