International Journal of Pediatric Otorhinolaryngology 93 (2017) 24–29

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: http://www.ijporlonline.com/

Serum periostin level is not associated with allergic rhinitis or allergic sensitization in Korean children

Dong Young Kim [a, 1], Jeong Hong Kim [a, b, 1], Keun-Hwa Lee [b], Seong-Chul Hong [b], Hye-Sook Lee [b], Ju Wan Kang [a, c, *]

[a] Department of Otorhinolaryngology, Jeju National University School of Medicine, Jeju, South Korea
[b] The Environmental Health Center (Atopic Dermatitis and Allergic Rhinitis), Jeju National University School of Medicine, Jeju, South Korea
[c] Department of Medicine, Yonsei University Graduate School, Seoul, South Korea

ARTICLE INFO

Article history:
Received 21 September 2016
Received in revised form
13 December 2016
Accepted 13 December 2016
Available online 19 December 2016

Keywords:
Periostin
Allergic rhinitis
Allergic sensitization
Children
Korean

ABSTRACT

Objectives: Periostin is a matricellular protein, synthesized in the airway epithelium and induced by interleukin (IL)-4 and IL-13. The significance of periostin as a biomarker of T helper type 2 cell (Th2)-induced airway inflammation, and as a measure of the response to Th2-targeted therapy, has recently been highlighted. We explored the relationship between serum periostin and allergic rhinitis in Korean children.
Methods: Data for fifth and sixth grade children from six randomly selected elementary schools located in Jeju and Seogwipo City, Korea, were investigated. Serum periostin levels were determined by enzyme-linked immunosorbent assay. Sex, school grade, body mass index, and presence of allergic nasal symptoms were obtained via a self-reported survey and skin prick testing was performed.
Results: There were no significant differences between groups, when stratification was applied according to sex, grade, presence of atopy, and presence of allergic nasal symptoms. Sex and body mass index were significantly associated with serum periostin levels in multivariate linear regression analysis. However, allergic rhinitis was not associated with serum periostin levels.
Conclusion: Allergic rhinitis or allergic sensitization in Korean children did not influence serum periostin levels. Further studies are required to investigate the significance of serum periostin levels in pediatric allergic rhinitis.

1. Introduction

Allergic rhinitis is a T helper type 2 cell (Th2)-mediated inflammatory disease characterized by mucosal eosinophilia, airway hyperresponsiveness, and mucus overproduction [1]. Symptoms of allergic rhinitis, such as watery rhinorrhea, sneezing, and nasal obstruction, impair quality of life and interfere with activities of daily living. With the progression of allergic rhinitis, the airways undergo structural and phenotypic changes, resulting in airway remodeling and include damage to epithelial cells, goblet cell metaplasia, subepithelial fibrosis, and smooth muscle hyperplasia and hypertrophy [2,3].

Periostin is an extracellular matrix protein originally isolated from an osteoblast cell line. Its production is induced by interleukin (IL)-4 and IL-13 in airway epithelial cells [4–7]. Periostin is also a regulator of fibrosis and collagen deposition. It has been recognized for its important role in myocardial repair and remodeling following myocardial infarction and periostin overproduction in the nasal mucosa has been reported to contribute to polyp formation [6,8].

Expression of periostin has been observed in bronchial epithelial tissue and periostin may play an important role in tissue remodeling in bronchial asthma [8]. Periostin may also be found in normal nasal tissues, however, it is expressed more strongly in the basement membranes of patients with allergic rhinitis than in that of control patients [9]. These findings support the concept that periostin is involved in Th2-driven inflammation and tissue remodeling in allergic rhinitis [9].

Therefore, it has been hypothesized that periostin may play a

* Corresponding author. Department of Otorhinolaryngology, Jeju National University Hospital, 102 Jejudaehakno, Jeju, 63243, South Korea.
E-mail address: juwankangmd@gmail.com (J.W. Kang).
[1] Both authors contributed equally to this work.

http://dx.doi.org/10.1016/j.ijporl.2016.12.013
0165-5876/

potential role in allergic disease, particularly in asthma. However, current evidence of the association between periostin and allergic rhinitis is scarce. This study examines the relationship between serum periostin and allergic rhinitis in Korean children.

2. Materials and methods

2.1. Study population

Six elementary schools located in Jeju and Seogwipo City, Jeju Island, were randomly selected and fifth and sixth grade children were identified. A study questionnaire was distributed and completed by students and parents. Skin prick tests (SPTs) and physical examination was performed by trained nurses in November 2014. Of a total of 691 children we excluded children who did not undergo the SPT or did not respond to the questionnaire. Children with a diagnosis of asthma or atopic dermatitis were also excluded. Furthermore, we examined the medication history of children over the 7 days preceding the SPT test and excluded children who were administered medicines, such as antihistamines or other drugs that could affect the result of the SPT. Finally, 140 children were excluded and 551 children were included in the analysis. The details of this study were explained to the students and parents, and written informed consents were obtained from legal guardians. This study was approved by the institutional review board of the Jeju National Hospital University, in accordance with the Declaration of Helsinki. Data collection was in accordance with the principle of respect for the confidentiality of patient records.

2.2. Assessment

Height and weight were measured by trained nurses. Body mass index (BMI) was calculated as weight (kg)/the square of height (m^2). Sex, school grade, and presence of allergic nasal symptoms, were obtained from the self-reported questionnaire. The presence of allergic rhinitis symptoms was determined using the following question in the questionnaire: “Over the past 12 months, has your child ever had a problem with sneezing, or a runny, or a blocked nose when he/she did not have a cold or the flu?”.

The history of asthma and atopic dermatitis was obtained using questionnaire: “Have you had a wheezing or whistling in the chest in the past 12 months?” and “Have you had an itching rash at any time in the past 12 months?”, respectively.

For each subject, a 1.5 ml sample of blood was transferred to a cryotube for the serum periostin concentration measurement. Serum periostin was measured using enzyme-linked immunosorbent assay using human ELISA kit (AdipoGen, CA, USA) and Spectra MAX 190/USA (Molecular devices, CA, US) according to the manufacturer's instructions.

A total of 26 common aeroallergens were evaluated by SPT including: dermatophagoides pteronyssinus, dermatophagoides farinae, cat, citrus red mite, dog, cladosporium, alternaria, timothy grass, mugwort, barley, rapeseed, Japanese hop, Japanese cedar, rye grass, hen's egg (white), tuna, cow's milk, soya flour, mussel, yolk, shrimp, chicken meat, pork, peach, peanut, and wheat flour. All allergens, except citrus red mite and Japanese cedar, were purchased from Allergopharma (Reinbek, Germany). For Japanese cedar, the commercial allergen was purchased (Greer Laboratories Inc., Lenoir, NC, USA). Citrus red mite allergen was prepared as described in a previous study [10]. Histamine hydrochloride at a concentration of 1 mg/mL (Allergopharma, Reinbek, Germany) was used as the positive control, whereas a normal saline solution with 50% glycerin was used as the negative control. SPT was performed on the forearms by trained researchers using a 23-G lancet. Fifteen minutes after SPT, the size of each wheal was calculated as the mean of (A) the longest diameter and (B) the diameter perpendicular to the first axis at the midpoint (i.e., $(A + B)/2$). The skin test was considered positive if an allergen elicited a wheal $\geq$3 mm. Allergic sensitization was established when the subject showed a positive skin test to one or more allergens.

2.3. Statistical analysis

Demographic data were presented as mean ± standard error (SE). The differences in histamine wheal sizes were compared using the Student t-test and ANOVA test. The correlation between serum periostin level and BMI was analyzed by Spearman correlation test. Finally, linear regression analysis was used to show an independent effect after adjusting for confounding variables. SPSS 17.0 (SPSS Inc., Chicago, IL, USA) was used for all analyses. A p-value < 0.05 (two-tailed) was considered significant.

3. Results

Of 551 children included in the study, 267 were boys and 284 were girls. Demographic data of this study population are presented in Table 1. Among 276 children with allergic sensitization, 72 children showed sensitization to two or more allergens and 204 children showed sensitization to only one allergen. Dermatophagoides pteronyssinus (Dp) was a most common allergen which showed a positive skin test to 189 children. And, dermatophagoides farina (Df), Japanese cedar, and citrus red mite were followed (sensitization to 173, 73, and 58 children, respectively). 150 children showed sensitization to both of Dp and Df. 212 children among 276 sensitized children (76.8%) showed sensitization to Dp, Df or both. Mean serum periostin level in boys (51.9 ± 13.0 ng/ml) was significantly higher than in girls (47.5 ± 13.3 ng/ml). However, there were no significant differences between groups, when we stratified according to school grade, presence of atopy, and presence of allergic nasal symptoms (Table 1). When we analyzed the difference of mean serum periostin levels between groups divided by the number of sensitized allergens, there were also no significant differences of mean serum periostin levels between groups. (data not shown) Spearman's correlation test revealed a weak negative association between serum periostin levels and BMI ($P < 0.001$, $R = -0.182$) (Fig. 1).

We investigated the influence of allergic sensitization on serum periostin levels. According to the chi-square test, the rate of allergic sensitization was 56.9% (152/267) in boys and43.7% (124/284) in girls. Rate of allergic sensitization was significantly higher in boys than in girls ($p = 0.002$). Therefore, we stratified according to sex and then compared the mean serum periostin level between sensitized and non-sensitized children. There was no significant difference in serum periostin levels between the sensitized and non-sensitized children (boys or girls) (Fig. 2).

Subjects were divided into 4 groups, according to allergic sensitization and nasal symptoms (Fig. 3). The first group, with no allergic sensitization and no nasal symptoms, was defined as the control group. The second group, the non-allergic rhinitis group, included subjects with no allergic sensitization and with nasal symptoms. The third group, the subclinical allergy group, included subjects with allergic sensitization and no nasal symptoms. The fourth group, the allergic rhinitis group, included subjects with allergic sensitization and nasal symptoms. There were no significant differences in the mean serum periostin level among the 4 groups.

Multivariate linear regression analysis revealed that sex and body mass index were significantly associated with serum periostin levels. Conversely, allergic sensitization and/or allergic nasal