ORIGINAL ARTICLE

Role of Periostin in Uncontrolled Asthma in Children (DADO study)

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Abstract

Background: Asthma is the most common chronic disease in children. Cases of severe asthma (SA) are underdiagnosed. Periostin is a biomarker for SA in adults, but its role in children is poorly understood.
Objectives: The aims of the study were to estimate the percentage of cases of uncontrolled severe asthma (UcSA) in children with poorly controlled asthma and to evaluate the role of periostin as a biomarker.
Materials and Methods: We performed an observational study in children aged 5 to 14 years with poorly controlled asthma. Demographic and clinical data were collected in addition to the results of the lung function test, the fraction of exhaled nitric oxide, the skin prick test, total IgE, specific IgE, blood eosinophil count, serum periostin, treatment, asthma control, and quality of life. Variables were compared between the group with UcSA and the other children.
Results: Fifty children with poorly controlled asthma (72% male) were included. Nineteen children (38%) had UcSA. Most children had limitations in their activities of daily living and had visited the emergency department. In addition, 38% were hospitalized. Quality of life was poor. Only 42% of the children received appropriate treatment. The UcSA group was more likely to have a total IgE >500 kU_A/mL (52.6% vs 19%, *P*=.02) and less likely to have serum periostin >1000 ng/mL (31.2% vs 63%, *P*=.04).
Conclusions: In our setting, 38% of children with poorly controlled asthma have UcSA, which is associated with higher levels of total serum IgE and lower levels of serum periostin.

Key words: Uncontrolled severe asthma. Clinical practice guidelines. Children. Periostin.

Resumen

Introducción: El asma es la enfermedad crónica más frecuente en niños. El asma grave (AG) está infradiagnosticada. La periostina es un biomarcador de asma grave en adultos, pero su papel en niños es pobremente conocido. El objetivo de este estudio ha sido estimar el porcentaje de casos de asma grave no controlada (AGNC) en niños con asma mal controlada y evaluar el papel de la periostina como biomarcador.
Material y métodos: Estudio observacional en niños de 5 a 14 años de edad con asma mal controlada. Se recogieron datos demográficos y clínicos, pruebas de función pulmonar y fracción de óxido nítrico exhalado (FENO), prick test, IgE total, IgE específica, eosinófilos en sangre, periostina en suero, tratamiento, control del asma y calidad de vida. Se compararon las variables entre el grupo con AGNC y el resto de niños.
Resultados: Se incluyeron a 50 niños con asma mal controlada (72% varones). Diecinueve niños (38%) presentaban AGNC. La mayoría de los niños tenían limitaciones en las actividades de la vida diaria, visitas a urgencias y el 38% habían necesitado ingreso hospitalario. La media de calidad de vida fue baja. Solo el 42% de los niños tenían un tratamiento adecuado. El grupo AGNC (19 niños, 38%) tenían más probabilidad de tener una IgE >500 kU/ml (52,6% frente a 19%, p=0,002) y menos probabilidad de tener periostina en suero >1000 ng/ml (31,2% frente a 63%, p = 0,04).
Conclusiones: En nuestra serie, el 38% de niños con asma no controlada tenían AGNC, que está asociado con altos niveles de IgE total y menores niveles de periostina en suero.

Palabras clave: Asma grave no controlada. Guías de práctica clínica. Niños. Periostina.

Introduction

Asthma is a major public health problem that affects nearly 350 million people worldwide. It is also the most common chronic disease in childhood and adolescence. Asthma is more a syndrome than a disease, exhibiting considerable heterogeneity in its presentation and clinical course [1]. Several asthma phenotypes and endotypes have been identified. While 80% of children with asthma have allergies, the differentiation between T_H1 and T_H2 immune mechanisms in this group remains unclear. Some studies show a higher percentage of neutrophils in bronchoalveolar lavage (BAL) fluid or induced sputum in children [2]. The biomarkers whose clinical value is well established in adults with asthma are eosinophils and neutrophils in sputum, eosinophil count in BAL fluid and bronchial biopsy specimens, and periostin in peripheral blood [3]. Induced sputum and BAL are not commonly used in children, and no definitive data on the usefulness of periostin in children have been reported [4-8].

The level of asthma control is the extent to which the manifestations of asthma can be observed in the patient or have been reduced/eliminated by treatment. It is determined by the interaction between the patient's genetic background, underlying disease processes, current treatment, environment, and psychosocial factors. Asthma control is based on management of symptoms and the future risk of adverse outcomes. Both should always be assessed [9]. Asthma severity is assessed retrospectively based on the level of treatment required to control symptoms and exacerbations. It can be assessed once the patient has been on controller treatment for several months and, if appropriate, step down has been attempted to find the patient's minimum effective level of treatment. Asthma severity is not a static feature and may change over months or years. According to the Global Initiative for Asthma guidelines [9], mild asthma is asthma that is well controlled with Step 1 or Step 2 treatment, moderate asthma is asthma that is well controlled with Step 3 treatment, and severe asthma (SA) is asthma that requires Step 4 or Step 5 treatment (eg, high-dose inhaled corticosteroids [ICS]/long-acting ß-agonists [LABA]) to prevent it from becoming uncontrolled or asthma that remains uncontrolled despite this treatment. The definition of uncontrolled severe asthma (UcSA), for older children and adolescents, according to the Spanish Guidelines on the Management of Asthma (GEMA) [10] and the American Thoracic Society Task Force on Severe Asthma [11] is shown in Table 1. This term encompasses other forms such as difficult-to-control asthma, treatment-refractory asthma, and difficult-to-treat asthma. Patients with uncontrolled asthma may be difficult to manage owing to inadequate or inappropriate treatment or persistent problems with adherence or comorbidities (eg, chronic rhinosinusitis or obesity). They may also have refractory asthma, in which the response to treatment of comorbidities is incomplete [9-12]. SA is underdiagnosed, and the concept of severity is not clear among physicians [1]. According to Cowen et al [13], 47% of children with SA are diagnosed with moderate asthma based on symptoms. The World Health Organization (WHO) defines SA as "a form of uncontrolled asthma that can increase the risk of frequent severe exacerbations (or death) and/or adverse reactions to medications and/or chronic morbidity, including impaired lung function or reduced lung growth in children" [14].

Table 1. Definition of Uncontrolled Severe Asthma [10,11]

– OC used for 6 months or more in the last year or
– High-dose IC used in combination with another drug
At least 1 of the following
– Air flow limitation: FEV_1 <80% (after bronchodilator)
– Two or more OC bursts in the previous year
– Hospital admission in the previous year
– Previous life-threatening episode
– ACT <20

Abbreviations: ACT, Asthma Control Test; IC, inhaled corticosteroids; OC, oral corticosteroid.

In recent years, studies on the role of periostin in asthma have been published. Periostin is a cell matrix protein that was first identified in mouse periodontal ligament (hence the name) in 1993. It is secreted by bronchial fibroblasts and epithelial cells, acts as an immunomodulator, repairs connective tissue, and is involved in fibrogenesis. Periostin binds to integrins present on the surface of fibroblasts and epithelial cells. Its main function is to maintain tissue structure by binding to fibronectin, tenascin C, and collagen V. Expression of the periostin gene (POST) is regulated by bronchial epithelial cells, IL-13, and IL-4 [15]. Serum periostin levels exhibit very low variability and high reproducibility [16]. According to some authors, this protein is a safe and stable biomarker of chronic inflammation [17] and of the T_H2 mechanism underlying severe asthma in adults [10]. A link has been established between periostin and bronchial obstruction, elevated levels of fractional exhaled nitric oxide (FeNO), and eosinophil count in adults [18-20]. One of the effects of periostin is to attract inflammatory cells—neutrophils or eosinophils—to the airway. In turn, inflammatory cells, macrophages, and neutrophils stimulate expression of periostin and other cell matrix proteins through the induction of TGF-β and cytokine expression [21]. In their study in mice, Masuoka et al [22] noted that periostin was involved in chronic inflammation of the skin in atopic dermatitis and that it elicited a T_H2 and T_H1 response similar to airway inflammation.

Very few studies have been published in relation to periostin levels in children, although levels are known to be higher in children than in adults owing to the cell turnover that occurs during growth [15].

The objectives of this study were to estimate the percentage of cases of UcSA in a population of children with uncontrolled asthma of differing severity and to analyze associated factors, especially serum periostin.

Materials and Methods

We performed an observational, cross-sectional, prospective, single-center study at the Mother and Children's

Table 2. Criteria for Uncontrolled Asthma According to Level of Asthma Symptom Control (GINA 2016 [9]) and Value of FEV_1

Uncontrolled Asthma
3 or more of the following criteria:
Daytime symptoms >2 times/week
Limitation of activities of daily living
Nighttime symptoms or awakenings
Need for rescue medication >2 times/week
FEV_1 <80%

Table 3. Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
– Diagnosis of uncontrolled asthma	– Serious cardiopulmonary disease
– Age: 5-14 years (inclusive)	– Cancer (excluding cancer in remission for >5 years)
– Signed informed consent form	– Serious psychiatric disorders
– Able to read and understand Spanish	

Hospital, Badajoz, Spain. The study population comprised children aged 5 to 14 years with uncontrolled asthma according to level of asthma symptom control based on the GINA guidelines and FEV_1 (Table 2) [9]. The patients were seen in the allergy units of the Mother and Children's Hospital and 17 health centers of the health care district of Badajoz, where about 25,000 children are aged 5 to 14 years. The inclusion criteria are detailed in Table 3. The recruitment period was 9 months (September to June).

All parents or legal representatives and all children over 12 years gave their informed consent. The study was approved by the Clinical Research Ethics Committee of University Hospital of Badajoz and the Spanish Agency of Medicines and Medical Devices (*Agencia Española de Medicamentos y Productos Sanitarios*, AEMPS) classified it as a Post-Authorization Study with Other Designs (*Estudios Post-Autorización con Otros Diseños*, EPA-OD).

The study protocol included a minimum of 2-3 visits for each child over a 6-month period. Expert recommendations for the diagnosis of SA were thus fulfilled [10,11,23]. The diagnosis was made after the second visit and after proper treatment in mild, moderate, and severe asthma, according to the GINA guidelines [9], and UcSA, for older children and adolescents, according to GEMA [10] and the American Thoracic Society Task Force on Severe Asthma [11]. Parents were given a questionnaire on demographic and psychological factors, characteristics of the patient's home, exposure to cigarette smoke, and personal and family medical history. The data recorded on the case report forms were as follows:

– Age, sex, and body mass index
– Clinical characteristics: age at onset of symptoms, seasonality, diurnal and nocturnal symptoms, limitations in activities of daily living and exercise tolerance, school absenteeism, and parental absenteeism from work
– Comorbidities
– Number of exacerbations, emergency visits, and annual hospital admissions
– Treatment
– Diagnostic tests: FeNO, spirometry and postbronchodilator test, skin prick testing with aeroallergens and food allergens, total IgE, specific IgE and eosinophils in blood, and serum periostin.

FeNO was measured using a NIOX Vero device with a cut-off of 20 ppb (sensitivity of 61%, specificity of 59%) [24,25]. The postbronchodilator test was considered positive with an increase in FEV_1 >9%-12% or >200 cc [26]. The result of the skin prick test with aeroallergens and food allergens was considered positive when wheals were larger than 3 mm and specific IgE was >0.35 kU_A/L [27]. The eosinophil cut-off was set at >400/mm^3. Levels of serum periostin were measured using the Human Periostin DuoSet ELISA (Cat# DY3548, R&D Systems).

Asthma control was measured using the Asthma Control Test (ACT) in children over the age of 12 years and the Childhood Asthma Control Test (cACT) for children under 12 years. The selected cut-off was <19 (sensitivity of 70%, specificity of 88%) [28]. Quality of life was measured using the self-administered version of the Paediatric Asthma Quality of Life Questionnaire (PAQLQ) [29].

Diagnosis was based on the medical history and the results of additional tests. Treatment was prescribed according to clinical practice guidelines, and an action plan was delivered in writing. Finally, 2 groups were formed: one that met the criteria for UcSA (Table 1) (UcSA group) and another made up of the remaining children with uncontrolled asthma and no criteria for UcSA (non-UcSA group)

Statistical Analysis

The statistical package SAS version 9.3 was used. Descriptive analyses of the collected variables were performed. Categorical variables were summarized using frequencies and percentages; continuous variables were summarized using measures of central tendency and dispersion. Contingency tables were used to evaluate the relationship between categorical variables, and the chi-square test or Fisher exact test was used to determine a possible statistical association. The *t* test, ANOVA, or the nonparametric Wilcoxon, Mann-Whitney, and Kruskal-Wallis tests were used for comparison of numerical variables. The relationship between 2 numerical variables was measured using the Pearson or Spearman correlation. *P* values <.05 were considered statistically significant. A logistic regression model was constructed, and the *P* values of the adjusted values and their respective odds ratios and 95% confidence intervals were presented in the model. After performing a post hoc analysis and 2-by-2 comparison of the categories of a given variable, the resulting *P* values were adjusted using the false discovery rate method.

Results

The criteria for uncontrolled asthma were met by 58 children, of whom 50 were included in the study. Of these 50 children, 19 (38%) met the criteria for UcSA, 22 (44%) the criteria for uncontrolled moderate asthma, 8 (16%) the criteria for uncontrolled mild asthma, and 1 patient (2%) the criteria for controlled mild asthma.

Clinical and sociodemographic characteristics are shown in Table 4. The median (IQR) age was 8 (6-13) years. Psychological disturbances were recorded in half of the families, mainly anxiety and depression in the mother. The median (IQR) body mass index was 18 (16-21) kg/m^2. Symptoms had first appeared in the first year of life in 64% of children, and 85% had a family history of atopy. Over 90% had nocturnal and daytime symptoms and limitations in exercise tolerance. Most of the children had comorbidities (96% rhinitis, 62% atopic dermatitis, and 32% food allergy). Comparison of the UcSA and non-UcSA groups revealed significant differences in exposure to cigarette smoke (higher percentage of exposure in children in the non-UcSA group), hospital admission rates (63.2% for the UcSA group and 22% for the non-UcSA group), limitations in the activities of daily living (100% of children with UcSA and 54.8% of those in the non-UcSA group), and recorded rates of school absenteeism (higher for the group with UcSA).

Allergy test results and the comparison between biomarkers are shown in Table 5. Note that total IgE values were elevated, averaging 535 IU/mL, with a higher rate of IgE >500 kU$_A$/L in the UcSA group (52.6% vs. 19%, *P*=.02). Periostin values were generally very high, averaging 972 (median 1000 [554-1275]) ng/mL. Dilution of some of the serums to 1/10 and 1/100 was necessary for the determination of periostin values by ELISA. The difference in values compared with other studies [4,6,7] could be due to the ELISA technique used. A trend toward an increase in mean levels of periostin was observed with increasing patient age (838 ng/mL for children aged 5-7 years, 961 ng/mL for children aged 8-12, and 1242 ng/mL in those aged >12 years); levels of periostin were also higher in boys than in girls (1081 [705] ng/mL vs 690 [528] ng/mL, *P*=.09). No correlation was found between serum periostin and total IgE levels, eosinophil levels, FEV$_1$, or FeNO.

Based on clinical practice guidelines, only 42% of the children received appropriate treatment, with no significant differences between the 2 groups: 72% were treated with high-dose inhaled corticosteroids, 80% required more than 2 oral corticosteroid treatment cycles in the previous year, and 13 children were receiving or had received specific allergen immunotherapy. Only 15% of children were treated with LABAs in combination with inhaled corticosteroids.

Logistic regression showed UcSA to be associated with nonexposure to cigarette smoke (OR, 5.02; 95%CI, 1.02-24.7),

Table 4. Clinical and Sociodemographic Characteristics

Variables	Total (N=50)	UcSA group (n=19)	Non-UcSA group (n=31)	*P* Value
Sociodemographic characteristics				
Age	9.3±3.5	9.3±3.6	9.3±3.4	.9947
Male sex	36 (72%)	12 (63.2%)	24 (77.4%)	.2756
Female	14 (28%)	7 (36.8)	7 (22.6%)	.2756
Exposure to cigarette smoke	18 (36%)	3 (15.8%)	15 (48.4%)	.0198[a]
Clinical data				
Mean (SD) BMI, kg/m^2	19.4 (4.2)	19.6 (4.2)	19.4 (4.3)	.8563
Onset of symptoms				.1243
First year of life	32 (64%)	15/19 (78.9%)	17 (54.8%)	
Preschool	13 (26%)	4/19 (21.1%)	9 (29%)	
School	5 (10%)		5 (16.1%)	
Exacerbations				.0544
1-12/y	16 (32%)	3/19 (15.8%)	13 (41.9%)	
>12/y	34 (68%)	16/19 (84.2%)	18 (58.1%)	
Hospital admissions	19 (38%)	12 (63.2%)	7 (22.6%)	.0041[a]
Limitations in the activities of daily living	36 (72%)	19 (100%)	17 (54%)	<.001[a]
Limitations in exercise tolerance	46 (92%)	19 (100%)	27 (87.1%)	.2839
School absenteeism	38 (76%)	18 (94.7%)	20 (64.5%)	.0182[a]
Parental absenteeism	25/49 (51%)	13 (68.4%)	12 (40%)	.0525
Rhinitis	48 (96%)	18 (94.7%)	30 (96.8%)	1.00
Overweight	9 (18%)	4 (21%)	5 (16.1%)	.7152
Food allergies	16 (32%)	6 (31.6%)	10 (32.3%)	.9601
Atopic dermatitis	31 (62%)	13 (68.4%)	18 (58.1%)	.4640

Abbreviations: BMI, body mass index; UcSA, uncontrolled severe asthma.
[a]Statistically significant differences.

Table 5. Biomarkers and Measuring Tools

Variables	Total (N=50)	UcSA group (n=19)	Non-UcSA group (n=31)	*P* Value
Biomarkers				
Mean (SD) total IgE, IU/mL	536 (682)	608.9 (612.3)	490.7 (727.5)	.2946
IgE >500 IU/mL	16 (32%)	10 (52.6%)	6 (19%)	.02[a]
FeNO >20 ppb	29/42 (69%)	12 (85.7%)	17 (60.7%)	.1587
Eosinophils >400/mm^3	31 (62%)	10 (52.6%)	21 (67.7%)	.2853
Periostin >1,000 ng/mL	22/43 (51,2%)	5/16 (31.2%)	17/27 (63%)	.04[a]
Periostin, ng/mL	972 (678)	727 (499)	1,117 (735)	.05
Sensitization to aeroallergens	42 (84%)	16 (84.2%)	26 (83.9%)	1.00
aeroallergens				
Pollen	35 (70%)	13 (68.4%)	22 (71.0%)	
Mites	25 (50%)	11 (57.9%)	14 (45.2%)	
Fungi	20/49 (40.8%)	6 (31.6%)	14 (46.7%)	
FEV_1 (prebronchodilator), %				.0233a
>80%	40 (80%)	12 (63.2%)	28 (90.3%)	
80-70%	7 (14%)	4 (21.1%)	3 (9.7%)	
<70%	3 (6%)	3 (15.8%)	0	
Measuring tools				
cACT/ACT (score)				.1173
>19	15/49 (30.6%)	3 (15.8%)	12/30 (40%)	
14-19	18/49 (36.7%)	7 (36.8%)	11/30 (36.7%)	
<14	16 (32.7%)	9 (47.4%)	7/30 (23.3%)	
Mean (SD) PAQLQ	4.3 (1.3)	3.9 (1.5)	4.6 (1.2)	.0729

Abbreviations: cACT/ACT, Childhood Asthma Control Test/Asthma Control Test; FeNO, fractional exhaled nitric oxide; PAQLQ, Paediatric Asthma Quality of Life Questionnaire; UcSA: uncontrolled severe asthma.
[a]Statistically significant differences.

hospital admissions for asthma (OR, 8.48; 95%CI, 1.86-38.63), and FEV_1 <80% (OR, 7.16; 95%CI, 1.11-46.14).

Discussion

We performed a real-world study of uncontrolled asthma in children in a health care district in the southwest of Spain. Patients were referred by pediatricians following hospital and primary care consultations; consequently, the sample is representative of children with asthma in the area. Thirty-eight percent of the children with uncontrolled asthma met the clinical criteria for UcSA. At present, it is estimated that people with severe forms of asthma account for less than 15% of the total asthma population [30]. According to the ISAAC study, there is a general trend in Europe toward an increased prevalence of SA [31]. The results of the Spanish multicenter study on difficult-to-control asthma in children showed that 8.8% had SA and 24.2% had difficult-to-control asthma [32]. Although we studied only children with poorly controlled asthma, the percentage of UcSA seems high, possibly owing to selection bias and because the children studied may have had a very poor clinical course. This high percentage could also be due to poor management of the disease. As in other epidemiological studies, the frequency was higher in boys [30]. The percentage of children exposed to cigarette smoke was lower in the UcSA group: their parents may have been more aware of the disease and taken appropriate action.

In most patients, the onset of bronchial symptoms occurred in the first year of life, and this phenotype was associated with poor asthma control and a worse prognosis [33]. Most patients exhibited significant limitations in activities of daily living and exercise tolerance, which negatively affected the children and their families on an emotional and social level. We recorded a high percentage of visits to the emergency department and hospital admissions for asthma exacerbations, which indicates a risk of impaired lung function in adult life. These data are alarming from both a health care and an economic standpoint.

Body mass index was lower than expected; children with severe forms of asthma tend to have a low body weight and height. Lung function measurements revealed normal FEV_1 values in 80% of children; this finding was consistent with the findings of the TENOR study [30]. Lung function in children is not directly related to the severity of asthma, since many children with moderate or severe asthma have normal lung function. However, the use of lung function tests is essential for disease management. According to the TRAP study [34], only a third of Spanish pediatricians use spirometry for the diagnosis of asthma, and about half of these pediatricians use it to monitor the disease. There is an urgent need to increase the use of lung function testing, which seems to be crucial for improving management of childhood asthma [35]. In children

with an FEV_1 <80% in the UcSA group, irreversible obstruction or remodelling may well have occurred already.

Levels of total serum IgE, which have been linked to greater asthma severity, have been found to be higher in the UcSA group [36], and most children were sensitized to aeroallergens. According to various studies [37,38], unlike adults [39], children tend to be atopic with high levels of total IgE and FeNO and with peripheral eosinophilia and aeroallergen sensitization.

There is evidence that the ACT is a useful tool in the management of asthma and that it is a better predictor of poor asthma control than FeNO measurements. Our results are very similar to those found in the SA group of the recent European U-BIOPRED study [38], where 70% had an ACT score <19. More than half of the children in the UcSA group had an ACT score <14 owing to poorly controlled asthma and a high risk of serious exacerbations [28]. The mean PAQLQ score was 4.3, which was slightly lower than the SA group of the European study (mean 4.7 for school-aged group) [38] and the TENOR study (5.4 in children) [30], suggesting poor quality of life among the patients in our study. Subjective measures of asthma control and quality of life are useful for identifying children with problematic asthma [40]. Both approaches have clinical value and provide a subjective perception of the disease.

Only 42% of patients had been prescribed appropriate treatment in line with the clinical practice guidelines [9,10]. Inappropriate treatment of asthma in children is known to be associated with a risk of exacerbations and worse prognosis. It has also been shown that proper follow-up of severe asthma ensures control of the disease in over 80% of cases and that the implementation of an asthma management program improves quality of life while being cost-effective [9].

Serum and sputum periostin are linked with eosinophilic asthma and airway remodelling in some studies in adults. Periostin is considered a biomarker of asthma, and serum levels exhibit very low variability and high reproducibility [16]. Other studies have found no differences between eosinophilic and noneosinophilic airway inflammation in terms of serum levels of periostin [41]. Some published studies have also concluded that adult patients with high levels of periostin show a better response to treatment with inhaled corticosteroids [42], omalizumab [44], or lebrikizumab (anti–IL-13) [44], suggesting that periostin is linked to increased inflammatory or immunological activity.

There are few published studies on periostin in children. Levels of periostin have been shown to be higher in children than in adults [4]. Lopez-Guinsa et al [5] detected more pronounced expression of periostin in the nasal and bronchial mucosa of children with asthma. Song et al [6] found significantly higher periostin values in children with asthma than in healthy children or atopic children without asthma. Moreover, Konradsen et al [7] analyzed biomarkers of T_H2-associated inflammation in 96 children with persistent asthma, finding that levels of eosinophils and FeNO have a high predictive value for identifying SA. However, the authors found no relationship between periostin and SA. Recently, Inoue et al [8] suggested that measuring levels of serum periostin combined with the measurement of FeNO, eosinophilia, and lung function could improve the diagnosis of asthma in children. We found serum periostin levels to be much higher than in published studies. We must take into account that in these studies, all patients had mild or moderate controlled asthma with appropriate treatment, whereas the children in our study had uncontrolled disease and did not receive appropriate treatment. We found lower mean serum periostin values and a lower proportion of patients with levels >1000 ng/mL in the group with UcSA. Unlike studies on adults, we found no correlation between the presence of periostin in serum and total IgE, eosinophil counts, FEV_1, or FeNO. Possible confounding factors such as atopic dermatitis, rhinitis, and age were similar in both groups. In our series, high levels of serum total IgE, eosinophilia, and FeNO >20 ppb were observed in the group with UcSA, which is consistent with data from other studies; however, there was no relationship between these biomarkers and periostin.

The limitations of this study included not having a healthy control group to compare variables, wide variability in levels of asthma control and severity over time, and sample size, which may have influenced some statistical findings. Nevertheless, ours is the first study on periostin in children with poorly controlled asthma, and our findings suggest that differences in levels of periostin may be related to the severity of asthma in children. We are continuing with this line of research by measuring serum periostin in healthy children without allergies and allergic children without asthma as control groups. We are also studying levels of serum periostin after a prospective 1-year follow-up.

Periostin appears to be related to the inflammatory process in asthma, although the mechanisms underlying this potential association are not fully understood. The inflammatory mechanism is not a unique and isolated characteristic of each type of asthma patient, especially in children. This disease is caused by a complex interaction of many molecular and cellular factors, as well as genetic predisposition and environmental factors.

In our sample of children with uncontrolled asthma, serum periostin levels did not discriminate between severe and nonserious asthma. Further studies are needed with controlled and uncontrolled asthma to establish clinical relevance. New, interesting research lines can improve the future management of asthma in children.

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Conflicts of Interest

The authors declare that they have no conflicts of interest in relation to this article.

Previous Presentation

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