The role of periostin as an inflammatory marker in bronchial asthma in children

RAR — научная статья

https://doi.org/10.53529/2500-1175-2024-3-54-64

Date of receipt: 11.03.2024
Date of acceptance: 15.04.2024
Date of publication: 30.09.2024

Natalia A. Belykh, Inna V. Pisnyur, Aleksandr A. Nikiforov, Larisa V. Nikiforova

Ryazan State Medical University, 390026, Ryazan, Vysokovoltnaya str., 9, Russia

Natalia Anatolyevna Belykh — Dr. Sci., Associate Professor, Head of the Department of Faculty and Polyclinic Pediatrics with the Course of Pediatrics of Ryazan State Medical University. ORCID ID: 0000-0002-5533-0205, e-mail: nbelyh68@mail.ru.

Inna Vladimirovna Pisnyur — Assistant of the Department of Faculty and Polyclinic Pediatrics with the Course of Pediatrics of Ryazan State Medical University, ORCID ID: 0000-0002-9267-439X, e-mail: innaabramova@yandex.ru.

Alexander Alekseevich Nikiforov — Cand. Sci., Associate Professor, Head of the Central Research Laboratory, Ryazan State Medical University, ORCID ID: 0000-0001-9742-4528, e-mail: a.nikiforov@rzgmu.ru.

Larisa Vladimirovna Nikiforova — Senior Researcher at the Central Research Laboratory, Ryazan State Medical University, ORCID ID: 0000-0001-6296-9034, e-mail: a.nikiforov@rzgmu.ru.

Abstract

Introduction. The extracellular matrix protein periostin, expressed in a number of body tissues, is considered as a marker of type 2 T cell inflammation and of asthma control.

Objective. To study the relationship the serum periostin concentration in blood serum depending on the severity of asthma and indicators of respiratory function in children.

Materials and methods. The cross-sectional (simultaneous) study included 80 children aged 6 to 17 years (average age 12±3.2), who were divided into 2 groups: 1st — children with asthma (n = 40); 2nd — comparison group (n = 40). The concentration of periostin in the blood serum was determined by the ELISA method. The spirographic study was performed on a computer spirometer Spirolab 1, MIR (Italy).

Results. The Me of periostin in group 1 was within the normal range (730.2 ng/ml), but statistically significantly exceeded the indicator of group 2 (539.7 ng/ml, $p < 0.05$) and did not depend on the age, duration and severity of asthma, anthropometric parameters of the examined. The level of periostin in the blood serum significantly correlated with the frequency of exacerbations of the disease during the year ($r = 0.74$, $p = 0.000$), with the status of asthma control ($r = 0.32$, $p = 0.04$). A moderate correlation was found between the level of periostin and FEV_1 ($r = -0.34$; $p = 0.03$).

Conclusions. In children with asthma, the median periostin in the blood serum increased in proportion to the severity of asthma, disease control and the frequency of exacerbation of the disease.

Keywords: periostin, bronchial asthma, children, spirometry

Competing interests:
The authors declare that they have no competing interests.

For citation: Belykh N.A., Pisnyur I.V., Nikiforov A.A., Nikiforova L.V. The role of periostin as an inflammatory marker in bronchial asthma in children. *Allergology and Immunology in Pediatrics*. 2024; 3: 54–64. https://doi.org/10.53529/2500-1175-2024-3-54-64

Роль периостина как воспалительного маркера при бронхиальной астме у детей

https://doi.org/10.53529/2500-1175-2024-3-54-64

УДК 616.248-053.2-008.9:577.122
Дата поступления: 11.03.2024
Дата принятия: 15.04.2024
Дата публикации: 30.09.2024

For correspondence:
Inna Vladimirovna Pisnyur, Assistant of the Department of Faculty and Polyclinic Pediatrics with the Course of Pediatrics of Ryazan State Medical University.

Address: 390026, Ryazan, Vysokovoltnaya str., 9, Russia.

E-mail: innaabramova@yandex.ru.

Для корреспонденции:
Пизнюр Инна Владимировна, ассистент кафедры факультетской и поликлинической педиатрии с курсом педиатрии ФДПО, ФГБОУ ВО «Рязанский государственный медицинский университет имени академика И. П. Павлова».

Адрес: 390026, г. Рязань, ул. Высоковольтная, д. 9, Россия.

E-mail: innaabramova@yandex.ru.

Белых Н. А., Пизнюр И. В., Никифоров А. А., Никифорова Л. В.

Федеральное государственное бюджетное образовательное учреждение высшего образования «Рязанский государственный медицинский университет имени академика И. П. Павлова» Министерства здравоохранения Российской Федерации, 390026, г. Рязань, ул. Высоковольтная, д. 9, Россия

Белых Наталья Анатольевна — д. м. н., доцент, заведующая кафедрой факультетской и поликлинической педиатрии с курсом педиатрии ФДПО, ФГБОУ ВО «Рязанский государственный медицинский университет имени академика И. П. Павлова», ORCID ID: 0000-0002-5533-0205, e-mail: nbelyh68@mail.ru.

Пизнюр Инна Владимировна — ассистент кафедры факультетской и поликлинической педиатрии с курсом педиатрии ФДПО, ФГБОУ ВО «Рязанский государственный медицинский университет имени академика И. П. Павлова», ORCID ID: 0000-0002-9267-439X, e-mail: innaabramova@yandex.ru.

Никифоров Александр Алексеевич — к. м. н., доцент, заведующий Центральной научно-исследовательской лабораторией ФГБОУ ВО «Рязанский государственный медицинский университет имени академика И. П. Павлова», ORCID ID: 0000-0001-9742-4528, e-mail: a.nikiforov@rzgmu.ru.

Никифорова Лариса Владимировна — старший научный сотрудник Центральной научно-исследовательской лаборатории, ФГБОУ ВО «Рязанский государственный медицинский университет имени академика И. П. Павлова», ORCID ID: 0000-0001-6296-9034, e-mail: a.nikiforov@rzgmu.ru.

Аннотация

Актуальность. Белок внеклеточного матрикса периостин, экспрессируемый в ряде тканей организма, рассматривается в качестве маркера воспаления Т-клеток 2-го типа и контроля БА.

Цель. Изучить взаимосвязь концентрации периостина в сыворотке крови в зависимости от степени тяжести бронхиальной астмы и показателей функции внешнего дыхания у детей.

Материалы и методы. Проведено поперечное (одномоментное) исследование, куда были включены 80 детей в возрасте от 6 до 17 лет (средний возраст 12±3,2 года), которые были разделены на 2 группы: 1-я — дети с бронхиальной астмой (n = 40); 2-я — группа сравнения (n = 40). Концентрацию периостина в сыворотке крови определяли методом ИФА. Спирографическое исследование проводилось на компьютерном спирометре Spirolab 1, MIR (Италия).

Результаты. Медиана (Me) периостина в 1-й группе была в пределах нормы (730,2 нг/мл), но статистически значимо превышала показатель 2-й группы (539,7 нг/мл, $p < 0,05$) и не зависела от возраста, длительности и степени тяжести БА, антропометрических показателей обследованных. Уровень периостина в сыворотке крови значимо коррелировал с частотой обострений заболевания в течение года ($r = 0,74$, $p = 0,000$), со статусом контроля астмы ($r = 0,32$, $p = 0,04$). Выявлена умеренная корреляция между уровнем периостина и $ОФВ_1$ ($r = -0,34$; $p = 0,03$).

Заключение. У детей с БА медиана периостина в сыворотке крови возрастала пропорционально степени тяжести БА, контроля заболевания и частоты обострения заболевания.

Ключевые слова: периостин, бронхиальная астма, дети, спирометрия

Конфликт интересов:
Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Для цитирования: Белых Н.А., Пизнюр И.В., Никифоров А.А., Никифорова Л.В. Роль периостина как воспалительного маркера при бронхиальной астме у детей. *Аллергология и иммунология в педиатрии*. 2024; 3: 54–64. https://doi.org/10.53529/2500-1175-2024-3-54-64

INTRODUCTION

BA continues to be the most common chronic respiratory disease in the world [1]. Currently, there is a need to search for new biomarkers that will help to distinguish and classify different phenotypes of asthma, predict the clinical course of the disease and response to drug treatment [2].

The discovery of biomarkers associated with underlying airway inflammation is an active area of research in adults and children. In recent years, studies have been published on the role of periostin in the pathogenesis of BA and it is considered as a marker of T2 inflammation (which is based on a type 2 immune response) of T2 inflammation (which is based on a type 2 immune response) [3-5].

Periostin was first discovered by Takeshita S. in 1993 from a mouse osteoblast cell line and was initially known as osteoblast-specific factor-2. It was subsequently renamed periostin (1999) due to its preferential expression in the periosteum and periodontal ligament in adult mice [6]. In 2006, the association of periostin with allergic diseases was first reported [7]. In 2009, Woodruff P. G. et al. showed that periostin expression is associated with type 2 inflammation in BA. The authors indicated that periostin was observed in the thickened basal membrane of bronchioles as well as in the serum of BA patients with eosinophilic airway inflammation [8].

To date, it is known that the periostin protein is encoded by the osteoblast-specific factor-2 gene,

which is the official name for periostin. In humans, this gene is also known as POSTN, PN, OSF-2 and PDLPOSTN (Gene ID: 10631). The human periostin gene is located on the long arm of chromosome 13 (13q13.3) with 24 exons [9]. Periostin is a protein with a molecular mass of 90 kDa. It belongs to the fasciclin family together with the protein induced by transforming growth factor β (TGF-β), which shows 48% homology with periostin [10]. Periostin can induce differentiation of fibroblasts into myofibroblasts and enhance fibrosis by binding to other extracellular matrix proteins such as collagen type I, fibronectin and tenascin C, by induction of collagen fibrillogenesis and cross-binding. Periostin can influence epithelial remodeling by promoting epithelial-mesenchymal transition, in which respiratory epithelial cells gradually transform into mesenchymal cells in the process of fibrosis development. Basal secretion of periostin by epithelial cells can alter the underlying matrix by modifying the deposition and cross-linking of collagen fibrils. Periostin can also induce activation of the TGF-β signaling pathway and increase collagen deposition, thereby promoting airway remodeling and potentially altering its biomechanical properties [11, 12].

Periostin levels are elevated in many pathologic conditions in blood, urine, sputum, exhaled air, and tears. This suggests that periostin is easily moved or secreted from inflamed areas into various body fluids, although the exact mechanism of movement or secretion still needs to be clarified [13]. Serum periostin levels are affected by many factors, including body mass index, age, active bone growth, etc. [2, 14].

In a study of age-related changes in serum periostin in allergic patients and healthy children Fujitani H. et al. (2019) found that serum periostin concentrations were highest in infants, decreasing by 7 years of age and then increasing again by 15 years of age due to age-related changes caused by bone metabolic activity.

Basal serum periostin levels in childhood and adolescence exceed 100 ng/mL; after cessation of bone growth, serum periostin concentrations decrease to ~50 ng/mL. The authors noted that healthy children showed higher serum periostin levels than children with allergic disease up to 5 years of age, with a subsequent decline. This finding supports the view that the contribution of allergic conditions to serum periostin levels cannot be assessed in children under 5 years of age, but in older children it can be investigated as a biomarker of allergic inflammation [15, 16].

STUDY OBJECTIVE. To study the concentration of periostin in serum depending on the severity of bronchial asthma and indicators of external respiratory function in children.

MATERIALS AND METHODS. A one-stage, single-center randomized study included 80 children aged 6 to 17 years (mean age — 12±3.2 years), permanently residing in Ryazan city. The children were divided into 2 groups: the 1st group included 40 children with BA. The average age of children was 12.0±2.8 years; 15 girls (37.5%), 25 boys (62.5%). 17 children (42,5%) had mild degree of BA, 23 children (57,5%) had moderate degree of BA severity.

The comparison group (group 2) consisted of 40 children: mean age — 11.9±3.3 years; 14 girls (35.0%), 26 boys (65.0%) ($p > 0.05$).

The study design was approved by the local ethical committee of the Federal State Budgetary Educational Institution of Higher Professional Education (FSBEI HE RYazHMU) of the Ministry of Health of Russia (Protocol of 09.03.2021). Parents of all children who participated in the study were familiarized with the study regulations and signed informed consent.

The bases for the study were GBI RO "City Children's Polyclinic No. 3" (chief physician — A. Burdukova). (chief physician — A. O. Burdukova), Central

Research Laboratory of FSBI HE RyazSMU of the Ministry of Health of Russia (head of the laboratory — Candidate of Medical Sciences, Associate Professor A. A. Nikiforov).

Inclusion criteria for the study: established diagnosis of bronchial asthma for at least 1 year, verified according to GINA 2022 [17] and Federal Clinical Guidelines [1]; age of patients from 6 to 17 years; obtaining informed consent of parents and patients for the study.

Exclusion criteria: presence of malignant neoplasms, acute illness or exacerbation of other chronic diseases, endocrine or genetic pathology, surgical intervention within the last 4 weeks in the subjects.

Serum concentration of periostin was determined by ELISA method using ELISA Kit for Periostin, (Cloud-Clone Corp., USA) in the Central Research Laboratory of FSBEI HE RyazGMU of the Ministry of Health of Russia with further calculation of median and interquartile range (Me; 25-75%). Norms of periostin in human serum/plasma samples in 500-fold dilution: 132.4~859.6 ng/mL л [18].

Anthropometric measurements were performed during the medical examination. Body weight was measured in kilograms to the nearest 0.1 kg using portable electronic (digital) scales and corrected for clothing. Children's height was measured in centimeters using a medical height meter in the standing position to the nearest 0.1 cm. Body mass index (BMI) was calculated using the formula: m/h^2, where m — body weight (kg), h — height (m). Children's physical development was assessed using the WHO AnthroPlus program. (2009). Weight-for-Age Z-score (WAZ) and BMI-for-AgeZ-score (BAZ) were calculated. In accordance with WHO recommendations, the obtained Z-scores were interpreted according to the following criteria: malnutrition — at <-2SDS, undernutrition from -2 to -1SDS, normal — from -1 to +1SDS, overweight — at SDS from +1 to +2, obesity — at SDS > +2 [19]. According to anthropometry data, all children were divided into 2 subgroups. In group 1 of children with BA, 28 children (70.0%) had normal body weight (BM) and 12 children (30.0%) had excessive BM. In group 2, there were 33 children (82.5%) with normal BMI and 7 children with excessive BMI (17.5%). No obese children were found in the examined groups.

Questionnaires were administered to assess BA control: the c-ACT (Children Asthma Control Test) adapted for children aged 4-11 years (16 children) and the ACT (Asthma Control Test) for children aged 12 years and older (24 children). The degree of disease control was assessed according to the results of the tests: for ACT 25 points and more — complete control of BA, 20-24 points — insufficient control and less than 20 points — uncontrolled BA. For the c-AST test, 20 points or more corresponds to controlled asthma, while 19 points or less means that asthma is not controlled effectively [1]. The results of the questionnaire showed that 31 children (77.5%) had controlled asthma, 7 children (17.5%) had partially controlled asthma, and 2 patients (5.0%) had uncontrolled asthma.

There were no exacerbations of BA in 15 children (37.5%), 1 exacerbation of BA in 10 children (25.0%), 2 exacerbations in 6 children (15.0%), 3 or more exacerbations in 9 children (22.5%).

Spirographic examination was performed on a computerized spirometer Spirolab 1, MIR (Italy). The following parameters were assessed: vital lung capacity (VLC), forced expiratory vital capacity (FEV), forced expiratory volume in the first second (FEV_1), maximum expiratory volume velocity at 25% FEV (MOS_{25}), maximum expiratory volume velocity at 50% FGF (MOS_{50}), maximum expiratory volume velocity at 75% FGF (MOS_{75}), OPV_1/FGF ratio (Tiffno index), OPV_1/FGF ratio (Gensler index). The results were evaluated in accordance with the current spirometry guidelines [20].

Statistical processing of the data was performed using the standard software package MS Excel 2016 and Statistica 6.0. The Shapiro-Wilk criteria were used to analyze the normality of sign distribution. Continuous variables were presented as median (Me) with interquartile range (25-75 percentiles). Categorical variables were defined as percentages (%). Intergroup

Table 1. **Median concentration periostin in blood serum in children with asthma, depending on the duration of the disease and severity (ng/ml) (author's table)**
Таблица 1. **Медиана концентрации периостина в сыворотке крови у детей с БА в зависимости от длительности заболевания и степени тяжести (нг/мл) (таблица автора)**

Duration of BA disease	Mild BA Me [25%; 75%] n = 17	Moderate BA Me [25%; 75%] n = 23	p
1–3 years(n = 13)	267,0 [244,5; 292,5]	587,5 [357,2; 1122,2]	> 0,05
4–6 years (n = 15)	455,5 [277,5; 687,8]	617,0 [250,5; 1167,8]	
7–13 years (n = 12)	375,7 [307,75; 882,25]	505,0 [375,5; 622,7]	

differences were assessed using the nonparametric Mann-Whitney (U-test) and Pearson (χ^2) criteria with adjustments for small samples. The Spearman rank correlation method (r) was used to determine the strength and direction of the correlation between two traits. Differences were considered statistically significant at $p < 0.05$.

RESULTS AND DISCUSSION

The median periostin concentration in the group of children with BA was statistically significantly higher than the control group, 730.0 ng/mL [390.8; 1109.7] versus 536.7 ng/mL [452.0; 666.2] in Group 2, respectively ($p = 0.044$).

In the 1st group of children the value did not depend on the duration of the disease, but it was twice as high at the average degree of BA severity, but statistically significant differences were not found (Table 1).

No gender differences were found among children with BA: in girls, the Me of periostin content was 954.0 [414.25; 1115.0] ng/mL vs. 760.0 [418.25; 1356.62] ng/mL ($p = 0.72$) in the girls of the comparison group, and in boys, 406.0 [261.0; 751.0] ng/mL vs. 614.0 [486.87; 923.12] ng/mL ($p = 0.017$), respectively.

There was no significant correlation between periostin levels and patient age in both the BA group and the comparison group.

Periostin levels were significantly higher in children with 3 or more exacerbations of BA per year: Me = 1283.0 [1140.0; 1490.0] ng/mL ($p = 0.0001$).

In the group of children without exacerbations during the year, periostin levels were 318.0 [262.5; 469.25], with 1 exacerbation of BA — 469.3 [253.5; 723.0] ng/mL, with 2 exacerbations of BA — 546.2 [333.25; 686.5] ng/mL, respectively ($p > 0.05$). There was a direct correlation of moderate intensity between serum periostin levels and the frequency of BA exacerbations during the year ($r = 0.74$; $p < 0.000$) (fig. 1).

Periostin levels were within normal limits in children with BA with complete disease control (n = 31), Me = 455.5 [265.5; 789.5] ng/mL, and with partial disease control (n = 7), Me = 740.5 [378.5; 1115.0] ng/mL, respectively ($p > 0.05$).

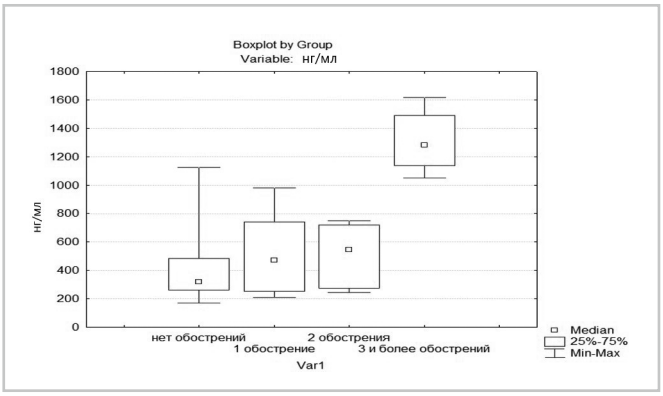

Fig. 1. **Median periostin in blood serum in children with asthma, depending on the frequency of exacerbations of the disease (ng/ml) (illustrations by the author)**
Рис. 1. **Медиана периостина в сыворотке крови у детей с БА в зависимости от частоты обострений заболевания (нг/мл) (иллюстрация автора)**

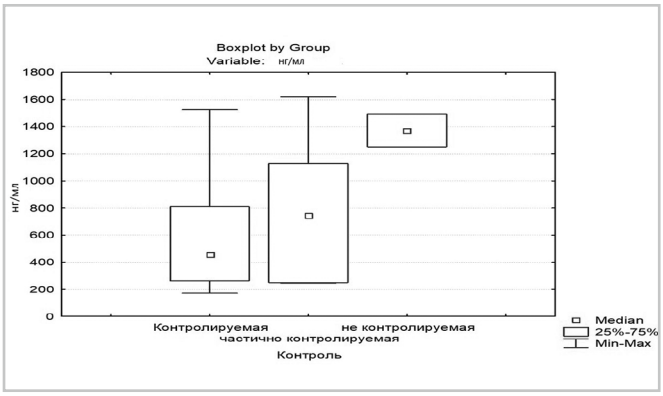

Fig. 2. **Median periostin in blood serum in children with asthma, depending on the degree of BA control (ng/ml) (illustrations by the author)**
Рис. 2. **Медиана периостина в сыворотке крови у детей с БА в зависимости от степени контроля БА (нг/мл) (иллюстрация автора)**

Table 2. **Spearman correlation coefficients between serum periostin levels and other clinical variables in children with asthma (author's table)**
Таблица 2. **Коэффициенты корреляции Спирмена между уровнем периостина в сыворотке крови и другими клиническими переменными у детей с БА (таблица автора)**

	Serum periostin (ng/mL)	
	r	p
Age	0,09	0,55
Duration of the disease	−0,03	0,82
Disease severity	−0,15	0,33
Degree of disease control	0,32	0,04
BMI	0,17	0,28
FEV_1, %	−0,34	0,03
AFR_{50}	−0,21	0,17
Frequency of disease exacerbations during the year	0,74	0,000

In the absence of disease control in patients with BA (n = 2), serum periostin levels exceeded normal values and corresponded to Me = 1369.5 [1309.25; 1429.75] ng/mL (p = 0.041) (Fig. 2).

Me periostin concentration was higher in children with uncontrolled BA 1369.5 [1309.25; 1429.75] ng/mL (p = 0.04). In the group of children with partially controlled course of the disease Me = 740.0 [378.5; 1115.0], with controlled Me = 455.5 [265.5; 789.5] (p = 0.39) (Fig. 2).

Serum periostin levels were found to be significantly correlated with the frequency of disease exacerbations during the year (r = 0.74, p = 0.000), with asthma control status (r = 0.32, p = 0.04), and with FEV_1 score (r = -0.34, p = 0.03), while no correlations were found with age, disease duration, and disease severity (Table 2).

Results of single-factor linear regression analysis showed an increase in periostin of 213.38 ng/mL per 1 exacerbation of BA (coefficient of determination 0.547, Fisher's criterion $F_{1,38} = 46.047$ ($p < 0,00002$).

The analysis also revealed a positive correlation of moderate intensity between BMI and BA severity (Table 3).

According to the data of spirographic study in children with BA during the examination period, the Me of lung vital capacity was 87.0 [81.0; 95.0] %, which corresponds to the norm. The values of forced lung vital capacity (FLVC) were also within the normal range, the median of FLVC in children with BA was 85.5 [82,8; 90,3] %.

Due to the fact that the severity of ventilatory disorders is usually assessed by changes in FEV1, we found a decrease in FEV_1 in our patients, which confirmed the diagnosis of BA. The FEV_1 median was 89.5 [79.8; 95.3] %. In 75.0 % (n = 30) of children, the values of FEV_1 corresponded to age criteria (> 80 % of the norm). Tiffno index and Genslar index values were normal (100.6 [92.5; 107.3] %, 102.4 [95.1; 109.9] %, respectively).

Spirography also showed a decrease in the maximum volumetric flow velocity in children with BA. Changes were noted at the point of 25, 50, 75 % (MOS_{25} — 79.0 [69.5; 87.8] %, MOS_{50} — 83.0 [71.8; 97.3] %, MOS_{75} — 85.5 [73.3; 103.3] %). Spirographic parameters in children with BA depending on severity are presented in Table 4.

When evaluating BA control by c-ACT and ACT tests, the median FEV_1 in patients with complete control of BA was 90.0 [85.0;95.5]%, with partial control 79.0 [78.5;90.5]%, and with no control 73.5 [72.75;74.25]% (p = 0,05).

Table 3. **Spearman's correlation coefficients of BMI with serum periostin levels in children with mild to moderate AD and control group (author's table)**
Таблица 3. **Коэффициенты корреляции Спирмена ИМТ с уровнем периостина в сыворотке крови у детей с легкой и средней степенью тяжести БА и контрольной группы (таблица автора)**

	Serum periostin (ng/mL)	
	r	p
BMI of children with mild BA	−0,38	0,12
BMI of children with moderate BA	0,65	0,0006
BMI of children in the control group	0,09	0,57

Table 4. **Spirometry indicators in children with asthma, depending on the severity, % (author's table)**
Таблица 4. **Показатели спирометрии у детей с БА в зависимости от степени тяжести, % (таблица автора)**

Spirographic values	Mild BA Me [25 %; 75 %] n = 17	Moderate BA Me [25 %; 75 %] n = 23	p
LVC	89,0 [81,0; 101,5]	87,0 [82,5; 91,0]	p > 0,05
FLVC	87,0 [84,0; 89,0]	84,0 [79,0; 91,5]	
FEV1	90,0 [84,8; 100,0]	87,5 [78,8; 94,0]	
MEF25	80,0 [68,0; 98,3]	83,0 [76,8; 93,3]	
Genslar Index	97,7 [94,6; 109,6]	103,7 [97,6; 109,9]	
Tiffno index	99,1 [92,3; 111,4]	100,6 [94,9; 105,2]	

The results obtained from the study are in accordance with the literature on the presence of a relationship between serum periostin levels and the activity of allergic inflammation in asthma. Inoue T. et al. (2016) in a cross-sectional study also found higher serum periostin levels in children with asthma compared to children without atopy and indicated a possible role of periostin assessment in the diagnosis of asthma in children. The authors stated that serum periostin levels in children are significantly higher than in healthy adults, which may be due to increased bone metabolism during childhood [21]. Song J. S. et al. (2015) showed that in children with BA, high serum periostin levels were associated with airway hyperresponsiveness [22]. Masalsky S. S. et al. (2018) found that serum periostin levels were significantly higher in children with BA compared to healthy children and directly correlated with the severity of BA [23]. In our study, serum periostin levels were higher in the group of children with BA, especially in moderate BA.

There are contradictory results about the relationship between serum periostin levels and asthma control status in children. El Basha N. R. et al. (2018) found significantly higher serum periostin levels in children during asthma exacerbation compared to children with stable BA and healthy children in control groups [24]. In contrast, Mena A. et al. (2017) found an inverse relationship — lower serum periostin levels occurred in children with uncontrolled asthma [25]. Licari A. et al. (2019) found no association between asthma control and serum periostin levels in 121 children with allergic asthma [26]. In our study, the serum periostin rate was higher in children with uncontrolled BA.

Asthma severity may be the best tool in the search for a biomarker reflecting the degree of inflammation in a chronic disease such as BA. There are controversial results of studies that have investigated the relationship between asthma severity and serum periostin levels. Licari A. et al. (2019) and Konradsen J. R. et al. (2015) found no association between asthma severity and serum periostin levels [5]. In our study, we also found no correlation between periostin levels and the severity of BA, the indicators were within the range of normal values, but the indicator was higher in moderate BA ($p < 0.05$).

According to Kimura H. et al. (2018) and Shirai T. et al. (2019), we found a negative correlation between serum periostin levels and body mass index in children with bronchial asthma, as well as in the control group [27-298]. We found a correlation between body mass index and periostin levels in children with BA of moderate severity, but no correlation in children in the control group ($p > 0,05$).

According to the literature, special attention has been paid to the study of the relationship

between periostin concentration and indicators of external respiratory function in patients with BA. Kanemitu Y. et al. (2013) in a study reported that high serum periostin levels correlated with decreased forced expiratory volume in one second with age in patients with asthma. Inoue T. et al. (2016) in a cross-sectional study found no correlation between periostin level and lung function [21]. Our study revealed a moderate correlation between periostin level and FEV_1 value, but no correlation between periostin and MOC_{50}. Obstructive changes in the spirogram are detected by the level of decrease in the FEV_1, VLC and their ratio (FEV_1/VLC — Tiffno index). In the absence of ventilatory disorders, the values of VLC, FEV_1, and FEV_1/VLC are within the normal range. According to the current clinical recommendations, the obstructive type of ventilatory disorders occurs in case of normal VLC index, normal or decreased FEV_1, decreased FEV_1/VLC [20]. Thus, in our study, no ventilation disorders were found in children with BA. Assessment of periostin levels in serum may help us to better study the possibilities of BA control in children.

CONCLUSIONS:

1. Periostin concentration in serum increased in proportion to the severity of BA.
2. Periostin levels varied according to the degree of BA control and frequency of disease exacerbations during the year.
3. A moderate correlation between serum periostin level and FEV_1 was revealed.
4. It is advisable to determine serum periostin levels in children with BA to assess the activity of allergic inflammation in atopic BA.

REFERENCES

1. Bronchial asthma: federal clinical guidelines for diagnosis and treatment. 2021. 118 p. (In Russ.)
2. Habib N., Pasha M.A., Dale D., Tang D.D. Current Understanding of Asthma Pathogenesis and Biomarkers. Cells. 2022; 11 (17): 2764. https://doi.org/10.3390/cells11172764.
3. Kunc P., Fabry J., Lucanska M., Pecova R. Biomarkers of Bronchial Asthma. Physiol Res. 2020; 69 (Suppl 1): S29–S34. https://doi.org/10.33549/physiolres.934398.
4. Oppenheimer J., Hoyte F.C.L, Phipatanakul W., et al. Allergic and eosinophilic asthma in the era of biomarkers and biologics: similarities, differences and misconceptions. Ann Allergy Asthma Immunol. 2022; 129 (2): 169–180. https://doi.org/10.1016/j.anai.2022.02.021.
5. Yavuz S.T., Bagci S., Bolat A., Akin O., Ganschow R. Association of serum periostin levels with clinical features in children with asthma. Pediatr Allergy Immunol. 2021; 32 (5): 937–944. https://doi.org/10.1111/pai.13444.
6. Yang L., Guo T., Chen Y., Bian K. The Multiple Roles of Periostin in Non-Neoplastic Disease. Cells. 2023; 12 (1): 50. https://doi.org/10.3390/cells12010050.
7. Izuhara K., Nunomura S., Nanri Y., et al. Periostin: An emerging biomarker for allergic diseases. Allergy. 2019; 74 (11): 2116–2128. https://doi.org/10.1111/all.13814.
8. Novosad J., Krčmová I., Bartoš V., et al. Serum periostin levels in asthma patients in relation to omalizumab therapy and presence of chronic rhinosinusitis with nasal polyps. Postepy Dermatol Alergol. 2020 Apr; 37 (2): 240–249. https://doi.org/10.5114/ada.2020.94842.
9. Yu L., Wang J., Liu K. Role of periostin in ECRS. Eur Arch Otorhinolaryngol. 2021; 278 (8): 2665–2672. https://doi.org/10.1007/s00405-020-06369-x.
10. Turczyn A., Pańczyk-Tomaszewska M. The role of periostin in kidney diseases. Cent Eur J Immunol. 2021; 46 (4): 494–501. https://doi.org/10.5114/ceji.2021.110317.
11. Krasilnikova S.V., Tush E.V., Frolov P.A., et al. Periostin as a Biomarker of Allergic Inflammation in Atopic Bronchial Asthma and Allergic Rhinitis (a Pilot Study). Sovrem Tekhnologii Med. 2021; 12 (5): 37–45. https://doi.org/10.17691/stm2020.12.5.04.
12. Shakhanov A.V., Nikiforov A.A., Uryazyev O.M. Polymorphism of nitric oxide synthase genes (NOS1 84G/A and NOS3 786C/T) in patients with bronchial asthma and hypertension. I. P. Pavlov Russian Medical Biological Herald. 2017; 25 (3): 378–390. https://doi.org/10.23888/PAVLOVJ20173378-390. (In Russ.)
13. Dorafshan S., Razmi M., Safaei S., et al. Periostin: biology and function in cancer. Cancer Cell Int. 2022; 22 (1): 315. https://doi.org/10.1186/s12935-022-02714-8.
14. Sonnenberg-Riethmacher E., Miehe M., Riethmacher D. Periostin in Allergy and Inflammation. Front Immunol. 2021; 27: 12: 722170. https://doi.org/10.3389/fimmu.2021.722170.

15. Asano T., Ohbayashi H., Ariga M., et al. Serum periostin reflects dynamic hyperinflation in patients with asthma. ERJ Open Res. 2020; 6 (2): 00347–2019. https://doi.org/10.1183/23120541.00347-2019.
16. Kumar K., Singh M., Mathew J.L., et al. Serum Periostin Level in Children with Asthma. Indian J Pediatr. 2023; 90 (5): 438–442. https://doi.org/10.1007/s12098-022-04282-1.
17. Global Strategy for Asthma Management and Prevention. Updated 2022. https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf.
18. Scichilone N., Crimi C., Benfante A., et al. Higher serum levels of periostin and the risk of exacerbations in moderate asthmatics. Asthma Res Pract. 2016; 2: 1. https://doi.org/10.1186/s40733-015-0019-x.
19. World Health Organization, Asthma Key Facts. URL: https://www.who.int/news-room/fact-sheets/detail/asthma.
20. Kameneva M.Y., Chernyak A.V., Aisanov Z.R. et al. Spirometry: a methodological guide for conducting research and interpreting the results. Pulmonology. 2023; 33 (3): 307–340. https://doi.org/10.18093/08690189-2023-33-3-307-340. (In Russ.)
21. Inoue T., Akashi K., Watanabe M., et al. Periostin as a biomarker for the diagnosis of pediatric asthma. Pediatr Allergy Immunol. 2016; 27 (5): 521–526. https://doi.org/10.1111/pai.12575.
22. Song J.S., You J.S., Jeong S.I., et al. Serum periostin levels correlate with airway hyper-responsiveness to methacholine and mannitol in children with asthma. Allergy. 2015; 70 (6): 674–681. https://doi.org/10.1111/all.12599.
23. Masalskiy S.S., Kalmykova A.S., Ukhanova O.P. Complex evaluation of serum periostin — new marker of allergic inflammation at uncontrolled bronchial asthma at children. Russian Journal of Allergy. 2018; 15 (1S): 55–57. https://doi: https://doi.org/10.36691/RJA49. (In Russ.)
24. El Basha N.R., Osman H.M., Abdelaal A.A., et al. Increased expression of serum periostin and YKL40 in children with severe asthma and asthma exacerbation. J Investig Med. 2018; 66: 1102–1108. https://doi.org/10.1136/jim-2017-000680.
25. Habernau Mena A., Del Pozo A.V., Rodriguez Vidigal F.F., et al. Role of periostin in uncontrolled asthma in children (DADO study). J Investig Allergol Clin Immunol. 2017; 27: 291–298. https://doi.org/10.18176/jiaci.0144.
26. Licari A., Brambilla I., Sacchi L., Marseglia G., Ciprandi G. Periostin, type 2 biomarker, is not associated with asthma control grade in asthmatic allergic children. Respir Med. 2019; 151: 118–120. https://doi.org/10.1016/j.rmed.2019.04.010.
27. Kimura H., Konno S., Makita H., et al. Serum periostin is associated with body mass index and allergic rhinitis in healthy and asthmatic subjects. Allergol Int. 2018; 67: 357–363. https://doi.org/10.1016/j.alit.2017.11.006.
28. Shirai T., Hirai K., Gon Y., et al. Combined assessment of serum periostin and YKL-40 may identify asthma-COPD overlap. J Allergy Clin Immunol: Pract. 2019; 7 (1): 134–145.e1. https://doi.org/10.1016/j.jaip.2018.06.015.
29. Byalovsky Yu.Yu., Rakitina I.S. The effect of the initial reinforcement value on the physiological parameters of the conditioned respiratory reflex. Eruditio Juvenium. 2021; (3): 377–386. (In Russ.). https://doi.org/10.23888/HMJ202193377-386.

ЛИТЕРАТУРА

1. Бронхиальная астма: федеральные клинические рекомендации по диагностике и лечению. 2021. 118 с.
2. Habib N., Pasha M.A., Dale D., Tang D.D. Current Understanding of Asthma Pathogenesis and Biomarkers. Cells. 2022; 11 (17): 2764. https://doi.org/10.3390/cells11172764.
3. Kunc P., Fabry J., Lucanska M., Pecova R. Biomarkers of Bronchial Asthma. Physiol Res. 2020; 69 (Suppl 1): S29–S34. https://doi.org/10.33549/physiolres.934398.
4. Oppenheimer J., Hoyte F.C.L, Phipatanakul W., et al. Allergic and eosinophilic asthma in the era of biomarkers and biologics: similarities, differences and misconceptions. Ann Allergy Asthma Immunol. 2022; 129 (2): 169–180. https://doi.org/10.1016/j.anai.2022.02.021.
5. Yavuz S.T., Bagci S., Bolat A., Akin O., Ganschow R. Association of serum periostin levels with clinical features in children with asthma. Pediatr Allergy Immunol. 2021; 32 (5): 937–944. https://doi.org/10.1111/pai.13444.
6. Yang L., Guo T., Chen Y., Bian K. The Multiple Roles of Periostin in Non-Neoplastic Disease. Cells. 2023; 12 (1): 50. https://doi.org/10.3390/cells12010050.
7. Izuhara K., Nunomura S., Nanri Y., et al. Periostin: An emerging biomarker for allergic diseases. Allergy. 2019; 74 (11): 2116–2128. https://doi.org/10.1111/all.13814.
8. Novosad J., Krčmová I., Bartoš V., et al. Serum periostin levels in asthma patients in relation to omalizumab therapy and presence of chronic rhinosinusitis with nasal polyps. Postepy Dermatol Allergol. 2020 Apr; 37 (2): 240–249. https://doi.org/10.5114/ada.2020.94842.

9. Yu L., Wang J., Liu K. Role of periostin in ECRS. Eur Arch Otorhinolaryngol. 2021; 278 (8): 2665–2672. https://doi.org/10.1007/s00405-020-06369-x.
10. Turczyn A., Pańczyk-Tomaszewska M. The role of periostin in kidney diseases. Cent Eur J Immunol. 2021; 46 (4): 494–501. https://doi.org/10.5114/ceji.2021.110317.
11. Krasilnikova S.V., Tush E.V., Frolov P.A., et al. Periostin as a Biomarker of Allergic Inflammation in Atopic Bronchial Asthma and Allergic Rhinitis (a Pilot Study). Sovrem Tekhnologii Med. 2021; 12 (5): 37–45. https://doi.org/10.17691/stm2020.12.5.04.
12. Шаханов А.В., Никифоров А.А., Урясьев О.М. Полиморфизм генов синтаз оксида азота (NOS1 84G/A И NOS3 786C/T) у больных бронхиальной астмой и гипертонической болезнью. Российский медико-биологический вестник им. академика И. П. Павлова. 2017; 25 (3): 378–390. https://doi.org/10.23888/PAVLOVJ20173378-390.
13. Dorafshan S., Razmi M., Safaei S., et al. Periostin: biology and function in cancer. Cancer Cell Int. 2022; 22 (1): 315. https://doi.org/10.1186/s12935-022-02714-8.
14. Sonnenberg-Riethmacher E., Miehe M., Riethmacher D. Periostin in Allergy and Inflammation. Front Immunol. 2021; 27: 12: 722170. https://doi.org/10.3389/fimmu.2021.722170.
15. Asano T., Ohbayashi H., Ariga M., et al. Serum periostin reflects dynamic hyperinflation in patients with asthma. ERJ Open Res. 2020; 6 (2): 00347–2019. https://doi.org/10.1183/23120541.00347-2019.
16. Kumar K., Singh M., Mathew J.L., et al. Serum Periostin Level in Children with Asthma. Indian J Pediatr. 2023; 90 (5): 438–442. https://doi.org/10.1007/s12098-022-04282-1.
17. Global Strategy for Asthma Management and Prevention. Updated 2022. https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf.
18. Scichilone N., Crimi C., Benfante A., et al. Higher serum levels of periostin and the risk of exacerbations in moderate asthmatics. Asthma Res Pract. 2016; 2: 1. https://doi.org/10.1186/s40733-015-0019-x.
19. World Health Organization, Asthma Key Facts. URL: https://www.who.int/news-room/fact-sheets/detail/asthma.
20. Каменева М.Ю., Черняк А.В., Айсанов З.Р. и др. Спирометрия: методическое руководство по проведению исследования и интерпретации результатов. Пульмонология. 2023; 33 (3): 307–340. https://doi.org/10.18093/08690189-2023-33-3-307-340.
21. Inoue T., Akashi K., Watanabe M., et al. Periostin as a biomarker for the diagnosis of pediatric asthma. Pediatr Allergy Immunol. 2016; 27 (5): 521–526. https://doi.org/10.1111/pai.12575.
22. Song J.S., You J.S., Jeong S.I., et al. Serum periostin levels correlate with airway hyper-responsiveness to methacholine and mannitol in children with asthma. Allergy. 2015; 70 (6): 674–681. https://doi.org/10.1111/all.12599.
23. Масальский С.С., Калмыкова А.С., Уханова О.П. Комплексная оценка сывороточного периостина — нового маркера аллергического воспаления при неконтролируемой БА у детей. Российский Аллергологический Журнал. 2018; 15 (1S): 55–57. https://doi: https://doi.org/ 10.36691/RJA49.
24. El Basha N.R., Osman H.M., Abdelaal A.A., et al. Increased expression of serum periostin and YKL40 in children with severe asthma and asthma exacerbation. J Investig Med. 2018; 66: 1102–1108. https://doi.org/10.1136/jim-2017-000680.
25. Habernau Mena A., Del Pozo A.V., Rodriguez Vidigal F.F., et al. Role of periostin in uncontrolled asthma in children (DADO study). J Investig Allergol Clin Immunol. 2017; 27: 291–298. https://doi.org/10.18176/jiaci.0144.
26. Licari A., Brambilla I., Sacchi L., Marseglia G., Ciprandi G. Periostin, type 2 biomarker, is not associated with asthma control grade in asthmatic allergic children. Respir Med. 2019; 151: 118–120. https://doi.org/10.1016/j.rmed.2019.04.010.
27. Kimura H., Konno S., Makita H., et al. Serum periostin is associated with body mass index and allergic rhinitis in healthy and asthmatic subjects. Allergol Int. 2018; 67: 357–363. https://doi.org/10.1016/j.alit.2017.11.006.
28. Shirai T., Hirai K., Gon Y., et al. Combined assessment of serum periostin and YKL-40 may identify asthma-COPD overlap. J Allergy Clin Immunol: Pract. 2019; 7 (1): 134–145.e1. https://doi.org/10.1016/j.jaip.2018.06.015.
29. Бяловский Ю.Ю., Ракитина И.С. Влияние исходной величины подкрепления на физиологические показатели условного дыхательного рефлекса. Наука молодых. 2021; (3): 377–386. https://doi.org/10.23888/HMJ202193377-386.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted taking into account the requirements of the Helsinki Declaration of the World Association "Ethical Principles of Conducting Scientific Medical Research with human Participation" as amended in 2000 and the "Rules of Clinical Practice in the Russian Federation" approved by Order of the Ministry of the Russian Federation dated 06/19/2003, No. 266. This study was approved by the local Ethics Committee of

the Federal State Budgetary Educational Institution of the Ryazan State Medical University of the Ministry of Health of the Russian Federation (Protocol dated 03/09/2021).

ЭТИЧЕСКОЕ ОДОБРЕНИЕ И СОГЛАСИЕ НА УЧАСТИЕ

Исследование было проведено с учетом требований Хельсинкской декларации Всемирной ассоциации «Этические принципы проведения научных медицинских исследований с участием человека» с поправками 2000 г. и «Правил клинической практики в Российской Федерации», утвержденных Приказом Министерства РФ от 19.06.2003 № 266. Данное исследование было одобрено локальным этическим комитетом ФГБОУ ВО РязГМУ Минздрава России (Протокол от 09.03.2021 г.).

FINANCING SOURCE

This study was not supported by any external sources of funding.

ИСТОЧНИК ФИНАНСИРОВАНИЯ

Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

THE AUTHORS' CONTRIBUTION TO THE WORK

Natalia A. Belykh — conceptualization, formal analysis, visualization, writing — review & editing.
Inna V. Pisnyur — formal analysis, investigation, visualization, writing — original draft.
Aleksandr A. Nikiforov, Larisa V. Nikiforova — investigation.

ВКЛАД АВТОРОВ В РАБОТУ

Белых Н. А. — разработка концепции, формальный анализ, подготовка текста — оценка и редактирование.
Пизнюр И. В. — проведение исследования, формальный анализ, работа с данными, подготовка текста.
Никифоров А. А., Никифорова Л. В. — проведение исследования, работа с данными.

Во 2 номере неверно указаны электронные идентификаторы статей.

Исправленный вариант:

1. Локальные проявления перекрестной пищевой аллергии у детей с клиническими симптомами респираторной аллергии на пыльцу березы: пути решения

Т. С. Лепешкова

https://doi.org/10.53529/2500-1175-2024-2-68-81

2. Пациент с коморбидной патологией: возможна ли АСИТ?

Е. А. Орлова, Ю. А. Кандрашкина, Е. Ю. Трушина, Е. М. Костина

https://doi.org/10.53529/2500-1175-2024-2-82-88

3. Опыт аллерген-специфической иммунотерапии у пациента с оральными и системными проявлениями аллергии к пыльце березы

Е. Ю. Трушина, Е. М. Костина, Е. А. Орлова, А. А. Туровская, Т. А. Нефедова

https://doi.org/10.53529/2500-1175-2024-2-89-96