DOI: https://doi.org/10.17816/PED12435-43

METHOD FOR ASSESSING THE SUBLINGUAL IMMUNOTHERAPY WITH HOUSE DUST MITE ALLERGENS EFFECTIVENESS IN CHILDREN WITH BRONCHIAL ASTHMA AND ALLERGIC RHINITIS

© Dmitrii S. Korostovtsev [1], Olga V. Trusova [2], Andrey V. Kamaev [2]

[1] St. Petersburg State Pediatric Medical University, Saint Petersburg, Russia;

[2] Academician I.P. Pavlov First St. Petersburg State Medical University, Saint Petersburg, Russia

For citation: Korostovtsev DS, Trusova OV, Kamaev AV. Method for assessing the sublingual immunotherapy with house dust mite allergens effectiveness in children with bronchial asthma and allergic rhinitis. *Pediatrician (St. Petersburg)*. 2021;12(4):35-43. https://doi.org/10.17816/PED12435-43

Received: 07.06.2021 Revised: 14.07.2021 Accepted: 27.08.2021

Background. For practical health care, tools for assessing the effect of allergen-specific immunotherapy have not been developed.

Aim. Approbation of the system for evaluating the effectiveness of sublingual immunotherapy with house dust mite allergens in patients with bronchial asthma with allergic rhinitis.

Materials and methods. 28 cases of sublingual immunotherapy treatment in patients aged 5 to 13 years, (8,6 [6,7; 11,6]) with control in pairs-copies matched by age, sex, and asthma severity were analyzed. Thus, the study included 56 patients. Patients in the control group did not receive sublingual immunotherapy. For 1 year before the start of treatment, and for the first year of treatment, the complex of clinical signs of bronchial asthma and allergic rhinitis, the need for basic and emergency therapy was assessed. The scores were calculated for symptoms, for drugs, and a total Score of symptoms and drugs.

Results. During 1 year of therapy, patients showed dynamics of the total Score from 23,32 ± 1,21 points to 16,21 ± 1,77 in the main group, and from 23,99 ± 1,2 points to 20.92 ± 2.09 in control group (p = 0.028). The greatest difference was found within medication domain.

Conclusion. The developed system for assessing the symptoms and the need for medications makes it possible to show the difference between groups of patients, in favor of the sublingual immunotherapy group. For 1 year of sublingual immunotherapy therapy, a difference in the total Score dynamics and the domain of drugs was revealed between the groups. The proposed assessment system is recommended for further investigation.

Keywords: allergen-specific immunotherapy; bronchial asthma; children; assessment of effectiveness.

СИСТЕМА ОЦЕНКИ ЭФФЕКТИВНОСТИ СУБЛИНГВАЛЬНОЙ ИММУНОТЕРАПИИ АЛЛЕРГЕНАМИ КЛЕЩЕЙ ДОМАШНЕЙ ПЫЛИ У ДЕТЕЙ С БРОНХИАЛЬНОЙ АСТМОЙ И АЛЛЕРГИЧЕСКИМ РИНИТОМ

© Д.С. Коростовцев [1], О.В. Трусова [2], А.В. Камаев [2]

[1] Санкт-Петербургский государственный педиатрический медицинский университет, Санкт-Петербург, Россия;

[2] Первый Санкт-Петербургский государственный медицинский университет им. акад. И.П. Павлова, Санкт-Петербург, Россия

Для цитирования: Коростовцев Д.С., Трусова О.В., Камаев А.В. Система оценки эффективности сублингвальной иммунотерапии аллергенами клещей домашней пыли у детей с бронхиальной астмой и аллергическим ринитом // Педиатр. – 2021. – Т. 12. – № 4. – С. 35–43. https://doi.org/10.17816/PED12435-43

Поступила: 07.06.2021 Одобрена: 14.07.2021 Принята к печати: 27.08.2021

Актуальность. Для практического здравоохранения не разработаны инструменты оценки эффективности аллерген-специфической иммунотерапии.

Цель. Апробация системы оценки эффективности сублингвальной иммунотерапии с аллергенами клещей домашней пыли у пациентов с бронхиальной астмой в сочетании с аллергическим ринитом.

Материалы и методы. Проанализировано 28 случаев сублингвальной иммунотерапии пациентов в возрасте от 5 до 13 лет (медиана 8,6 [6,7; 11,6] лет) с контролем в парах-копиях, подобранных по возрасту, полу, тяжести течения бронхиальной астмы. Таким образом, в исследование включено 56 пациентов. Пациенты группы пар-копий не получали сублингвальной иммунотерапии. За 1 год до начала лечения и за первый год лечения оценивали комплекс клинических проявлений бронхиальной астмы и аллергического ринита, потребность в базисной и экстренной терапии. Подсчитывали суммарный балл симптомов, суммарный балл препаратов и общий индекс симптомов и препаратов.

Результаты. За 1 год терапии у пациентов отмечена динамика суммарного балла симптомов и медикаментов: с 23,32 ± 1,21 до 16,21 ± 1,77 балла в основной группе и с 23,99 ± 1,2 до 20,92 ± 2,09 балла в контрольной группе (различия групп значимы при $p = 0,028$). Наибольшее различие выявлено между группами по домену препаратов.

Заключение. Разработанная система оценки симптомов заболевания и потребности в медикаментах позволяет показать разницу между группами пациентов в пользу группы, получающей сублингвальную иммунотерапию. За 1 год сублингвальной иммунотерапии между группами выявлена разница в динамике общего индекса и домена медикаментов. Предложенная система оценки рекомендована для дальнейшего изучения.

Ключевые слова: аллерген-специфическая иммунотерапия; бронхиальная астма; дети; оценка эффективности.

BACKGROUND

Respiratory allergic diseases, including bronchial asthma (BA) and allergic rhinitis (AR), are characterized by a variable course. Over the years, the disease progresses with an increase in the frequency and severity of exacerbations. The need for pharmaceuticals to control the disease also increases [5, 7, 9]. As it is impossible to eliminate the contact with allergens, patients undergo several months of pharmacotherapy. However, even in this case, a certain proportion of patients retain severe symptoms and exacerbations [5]. Sublingual immunotherapy (SLIT) is indicated both in cases of pharmacotherapy inefficiency and in milder manifestation of the disease. An important aim of SLIT is modifying the natural course of the disease, such as reduction of exacerbation frequency, even in patients who reduce the amount of pharmacotherapy [5]. SLIT is required for 3–5 years to achieve a long-lasting impact [13].

The method for the evaluation of treatement efficacy has not yet been discovered.

Laboratory markers, including immunoglobulins [total IgE, allergen-specific IgE, and IgG (subclass G_4)] in blood serum, serum inactivating activity for IgE, activation of basophils and cytokines (mainly interleukin 10), the count and functions of regulatory T- and B-lymphocytes, are studied to evaluate the effect of SLIT. Furthermore, the dynamics of tissue sensitivity (*in vivo*) to an allergen is assessed through skin tests with allergen and challenge tests. So far, none of the potential biomarkers have been approved for routine clinical practice [14].

The evaluation of BA dynamics based on the control criterion is ineffective because only patients who have achieved a controlled BA course are allowed to receive SLIT. SLIT can only be initiated in the absence of disorders (the forced expiratory volume in the second 1 (FEV1) is at least 80% of the norm in children [5]); therefore, the dynamic assessment of the external respiratory function parameters may not be informative. Over the years, the FEV1 increases according to the growth of the body and lung size in children receiving SLIT and in children not receiving it. SLIT has not been found to have a pronounced impact on asthma control, lung function, and the degree of nonspecific bronchial hypersensitivity in studies [8].

In clinical studies on the use of SLIT in AR, validated indices are calculated, considering the severity of the disease symptoms induced by the allergen for which the treatment is performed and the required amount of pharmacotherapy [10, 12]. Federal clinical guidelines for AR therapy [1] recommend an international scale for evaluating nasal symptoms, considering the need for drugs [12]. The severity of AR symptoms (nasal congestion, sneezing, itching, and rhinorrhea) is evaluated daily (zero to three points), and the score for symptoms is calculated. Medication score is added to the symptom score [score 1 for the usage of first-line treatment medications, such as histamine blockers, score 2 for the use of topical glucocorticosteroids (GCS), and score 3 for the need for systemic GCS]. Moreover, we calculated the integral indicator for the period. The index value correlates with the disease severity, quality of life, and frequency of seeking medical help. Indices of symptoms and medications enabled us to objectively evaluate the disease course in a patient and to obtain quantitative indicators suitable for statistical processing. The situation is taken into account when the patient does not experience pronounced exacerbations only due to the intake of pharmacological preparations. However, long-term collection of information and the need for subsequent data processing reduce the probability of introducing such indices into the practice of outpatient doctors.

Regarding BA, there is no consensus on which indicators should be assessed. For the formation of rating scales, it is proposed to use the daytime and nighttime symptoms, the number of days without symptoms, various types and combinations of medications, integral assessments of the disease course on a visual analog scale, time to the first exacerbation, spirometry indicators, exhaled air nitric oxide, sputum eosinophils, bronchial hypersensitivity to methacholine, etc.

The search for valid parameters for evaluating the treatment outcome is an urgent task in the field of SLIT for treating BA [5]. The heterogeneity of scoring systems complicates the comparison between results of different studies. Therefore, the role of SLIT in BA remains insufficiently substantiated on a global scale [8].

The European Academy of Allergology and Clinical Immunology recommendations, published in 2019, on immunotherapy for tick-borne asthma [4] provide a "List of positive changes in immunotherapy with house dust mites (HDM)." Significant signs included exacerbations, asthma control, the possibility of reducing steroid therapy during treatment, whereas insignificant signs included indicators of external respiration functions and bronchial hypersensitivity (to methacholine or histamine).

The advantage of this list is the ability to evaluate the BA course over a long reporting period (for example, 1 year). In the given assessment system, the quantitative weight of each characteristic is not determined, and there is no indication on reaching a conclusion about the presence or absence of immunotherapy effect.

In pediatric patients of preschool and primary school age with AR who received immunotherapy with various allergens, there was a decrease in the frequency of acute respiratory infections. In children treated with SLIT, the probability of using antibiotic therapy for acute respiratory infections was also decreased [6, 11]. Therefore, there is a need to develop a system for evaluating the efficiency of SLIT that is suitable for use by medical practitioners. The system should include symptoms and aspects of allergic disease course that are significant for determining SLIT effects and cover significant periods of time during treatment.

This study aimed to develop and examine a system for evaluating the efficiency of SLIT with HDM allergens in children with BA along with AR.

MATERIALS AND METHODS

We conducted an open-label prospective controlled study.

Inclusion criteria were as follows:

1. Boys and girls aged 5–15 years.

2. BA induced by sensitization to HDM, detected at least six months before the examination, along with AR. The diagnoses of BA and AR were established and the severity was determined, according to clinical guidelines [1, 2].

3. Sensitization to HDM, proven using allergological examination methods and identified as significant in disease genesis.

Exclusion criteria were as follows:

1. Severe and uncontrolled course of BA.

2. Pollen allergy with the manifestation of seasonal exacerbations.

Children of the main group received SLIT using standardized sublingual drops with extracts of *Dermatophagoides pteronyssinus* and *Dermatophagoides farina,* according to the manufacturer's recommended method. The maintenance dose was determined individually, with a maximum of 240 RI/day, daily (IR–reactivity indices, the drug standardization unit).

For each patient of the main group, we selected a copy-pair based on gender coincidence, age (±6 months), and severity of BA. The copy-pair group included patients with sensitization to HDM who did not plan treatment using the SLIT method.

The follow-up schedule included visits with a frequency of one in three months, a year before SLIT initiation, and a year of treatment. At each study visit (once every three months), complaints and anamnesis were collected, as well as the examination and clinical assessment of disease control and sufficiency of therapy were performed.

Following this, we obtained information about BA and AR therapies. At the end of each follow-up year, we performed a staged assessment of the course of BA and AR in the patient, and an epicrisis was drawn up (Table 1) [3]. The epicrisis consisted of a set of BA and AR symptoms and a list of drugs used for a year.

We assigned a value in points to each sign. The total score of BA and AR symptoms, the total score for the use of drugs for basic and emergency therapy, and the general index of symptoms and drugs for each follow-up year were calculated. The minimum total index of symptoms and drugs was zero points (corresponding to complete remission of BA and AR within a year and pharmacotherapy independence).

Moreover, we processed the results using the Statistica for Windows 10.0 package (StatSoft Inc., USA). Data with a normal distribution were presented as mean (M) and its standard deviation (±σ); the rest was presented in the form of a median (Me), indicating the first and third quartiles [Q_{25}; Q_{75}]. We performed the nonparametric Mann–Whitney test (U-test), considering the probability of deviations from the normal distribution, to evaluate the differences in the quantitative indicators of the sample. When comparing the proportions of patients in different groups, the chi-square test was used. Differences were considered statistically significant at $p < 0.05$.

Table 1 / Таблица 1

A staged epicrisis of a course of sublingual immunotherapy with a score assessment of the severity of symptoms and the need for pharmacopreparations
Этапный эпикриз курса сублингвальной иммунотерапии с балльной оценкой выраженности симптомов и потребности в фармакопрепаратах

Sign / Признак	Before / До	1 year / 1 год	2 years / 2 года
Symptoms / Блок симптомов			
Sneezing, nasal itch, nasal congestion when cleaning the room or going to bed. Present = 2 points, none = 0 points / Реакция на уборку, укладывание в постель и т. д. (контакт с пылью) в виде чихания, зуда в носу, заложенности носа (симптомы АР). Есть = 2 балла, нет = 0 баллов			
Cough, wheezing, dyspnea when cleaning the room or going to bed. Present = 2 points, none = 0 points / Прямая реакция на пыль (уборка, укладывание в постель и т. д.) в виде кашля, свистящего дыхания, одышки (симптомы БА). Есть = 2 балла, нет = 0 баллов			
Asthma exacerbations, months per year. 1 month = 2 points / Обострения БА, месяцев в год. 1 месяц = 2 балла			
Rhinitis exacerbations, months per year. 1 month = 1 point / Обострения АР, месяцев в год. 1 месяц = 1 балл			
Absenteeism due to allergic disease exacerbation. 1 week = 1 point / Пропуски детского учреждения / нетрудоспособность, вызванные обострениями АР или БА. 1 неделя = 1 балл			
Inpatient hospitalization due to allergic disease exacerbation. 1 week = 2 points / Госпитализации, с обострениями, осложнениями АР или БА. 1 неделя = 2 балла			
Upper or lower respiratory tract infections (sinusitis, otitis, adenoiditis, pneumonia, bronchitis). 1 week = 1 point / Инфекции верхних или нижних дыхательных путей (синуситы, отиты, аденоидит, пневмонии, бронхиты). 1 неделя = 1 балл			
Wheezing in a child with allergic rhinitis. 1 week = 2 points / Обструктивный бронхит у пациента с АР. 1 неделя = 2 балла			
Mild persistent symptoms: incomplete asthma control, nasal congestion, etc., sometimes not requiring therapy. 1 month = 0.5 points / Фоновые симптомы: неполный контроль БА, заложенность носа и т. д., иногда не требующие терапии. 1 месяц = 0,5 балла			
Unscheduled visit to Ear and Nose department. Each = 4 points / Экстренные посещения оториноларинголога (с манипуляциями). Каждое = 4 балла			
In total, points for Symptoms / Итого: баллы за симптомы			
Medications / Блок препаратов			
ICS low dose. 1 month = 0.5 points / иГКС, низкая доза. 1 месяц = 0,5 балла			
ICS medium dose. 1 month = 1 point / иГКС, средняя доза. 1 месяц = 1 балл			
ICS low dose + LABA. 1 month = 1 point / иГКС, низкая доза + ДДБА. 1 месяц = 1 балл			
ICS medium dose + LABA. 1 month = 1.5 points / иГКС, средняя доза + ДДБА. 1 месяц = 1,5 балла			
Montelukast. 1 month = 1 point / Монтелукаст. 1 месяц = 1 балл			
Intranasal CS. 1 month = 1 point / Интраназальные ГКС. 1 месяц = 1 балл			
Antihistamines. 1 month = 0.5 points / Антигистаминные препараты. 1 месяц = 0,5 балла			
Decongestants. 1 month = 2 points / Деконгестанты. 1 месяц = 2 балла			
Antibiotic for respiratory infection. 1 course = 4 points / Антибиотики при инфекциях дыхательных путей. 1 курс = 4 балла			
Systemic CS (for allergic rhinitis or bronchial asthma treatment). 1 day = 1 point / Системные ГКС (по показанию АР, либо БА). 1 день = 1 балл			
In total, points for Medications / Итого: баллы за препараты			
Total Score for symptoms and medications / Сумма: баллы за симптомы + баллы за препараты			

Note. CS – corticosteroids; ICS – inhaled corticosteroids; LABA – long acting beta-agonists.
Примечание. АР — аллергический ринит; БА — бронхиальная астма; ГКС — глюкокортикостероиды; иГКС — ингаляционные глюкокортикостероиды; ДДБА — длительно действующие β_2-агонисты.

RESULTS

The study was conducted between 2015 and 2019. Following the inclusion and exclusion criteria, the main group and the copy-pair group included 30 patients each. During the follow-up period, we excluded two patients of the main group from the study (one patient due to noncompliance with treatment and the other one due to family relocation). If a patient was excluded from the study, his/her copy-pair was also excluded from the analysis. Therefore, 56 patients were accepted for statistical analysis, including 28 patients of the main group who underwent a preliminary year of the follow-up and SLIT for one year, and 28 copy-pairs.

Twenty-eight patients of the main group included 18 boys (64.3%) and ten girls (35.7%), aged from five years seven months to 13 years two months at the time of inclusion, with median (*Me*) and extreme quartiles [Q_{25}; Q_{75}] of 8.6 and [6.7; 11.6] years, respectively.

All children were diagnosed with BA, including moderate (19 pediatric patients, 67.9%) and mild severity (nine pediatric patients, 32.1%).

In all children, BA occurred along with persistent AR, including moderate severity/severe course (17 pediatric patients, 60.7%) and mild severity (11 pediatric patients, 39.3%).

Table 2 presents the demographic characteristics of the patients included in this study.

According to clinical guidelines, we administered basic therapy to pediatric patients with BA [2]. Table 3 shows the information on the types of basic BA therapy during the first year of follow-up (before SLIT initiation in children of the main group).

Thus, during year one of follow-up (before the start of treatment), the groups of patients did not significantly differ in the scope of BA therapy.

Over the next year (one year of treatment in the SLIT group; follow-up in the copy-pair group), the personal change in the total symptom score and total drug score, as well as the total index as a percentage of the initial one, was determined for each patient. Tables 4 and 5 present the data on the initial level of symptoms and the need for medicines, as well as changes in indicators over time.

DISCUSSION

The results of patients receiving SLIT with HDM allergens and control group patients receiving only standard pharmacotherapy one year after treatment significantly differ in favor of the SLIT method.

The total symptom score in year one of treatment decreased to some extent in both groups. In the SLIT group, this decrease was more pronounced, but the differences between the groups did not reach statistical significance. Simultaneously, in the main group, symptom improvement was achieved despite a significant decrease in drug therapy. In the copy-pair

Table 2 / Таблица 2

Demography of enrolled patients in the main group and pair-copy control group
Демографические характеристики пациентов основной группы и группы пар-копий, включенных в исследование

Group / Группа	Main group / Основная группа	Pairs-copies / Пары-копии	*p*
Number of patients / Количество пациентов, чел.	28	28	НП / NA
Age, years, *Me* [Q_{25}; Q_{75}] / Возраст, годы, *Me* [Q_{25}; Q_{75}]	8.4 [6.3; 11.9]	8.6 [6.9; 11.3]	0.69
Boys, *n* (%) / Доля мальчиков, *n* (%)	18 (64.3)	18 (64.3)	НП / NA
Years from asthma diagnosis, *Me* [Q_{25}; Q_{75}] / Давность постановки диагноза бронхиальной астмы, годы, *Me* [Q_{25}; Q_{75}]	1.9 [1.2; 2.3]	2.4 [1.5; 5.1]	0.062
Concomitant allergic rhinitis, *n* (%) / Сопутствующий аллергический ринит, *n* (%)	28 (100)	28 (100)	НП / NA

Note. NA – not applicable.
Примечание. НП — не применимо.

Table 3 / Таблица 3

Maintenance therapy of asthma in patients of the main group and pair-copy control group in the first year of observation
Базисная терапия бронхиальной астмы у пациентов основной группы и группы пар-копий за первый год наблюдения

Maintenance asthma therapy / Виды базисной терапии	Main group / Основная группа		Pairs-copies group / Группа пар-копий	
	n	%	*n*	%
Mild asthma, *n* = 9 / Бронхиальная астма легкой степени тяжести, *n* = 9				
None / Не было	5	55.6	4	44.4
Montelukast / Монтелукаст натрия	2	22.2	2	22.2
ICS, low doses / иГКС, низкие дозы	2	22.2	3	33.3
ICS, medium doses / иГКС, средние дозы	0	0	0	0
ICS, low doses + LABA / иГКС, низкие дозы + ДДБА	0	0	0	0
In total / Всего	9	100	9	100
Moderate asthma, *n* = 19 / Бронхиальная астма средней степени тяжести, *n* = 19				
None / Не было	1	5.3	0	0
Montelukast / Монтелукаст натрия	2	10.5	1	5.3
ICS, low doses / иГКС, низкие дозы	2	10.5	3	15.8
ICS, medium doses / иГКС, средние дозы	2	10.5	6	31.6
ICS, low doses + LABA / иГКС, низкие дозы + ДДБА	12	63.2	9	47.4
In total / Всего	19	100	19	100
Average medication score for the first year of observation, score, $M \pm \sigma$ / Средний балл за препараты для лечения бронхиальной астмы и аллергического ринита за первый год наблюдения, баллы, $M \pm \sigma$	23.32 ± 1.21	–	23.99 ± 1.2	–

Note. ICS – inhaled corticosteroids, LABA – long acting beta-agonists.
Примечание. иГКС — ингаляционные глюкокортикостероиды; ДДБА — длительно действующие β_2-агонисты.

Table 4 / Таблица 4

Baseline symptom levels and treatment needs in patients of the main group and pair-copy control group in the first year of observation
Исходные уровни симптомов и потребности в терапии у пациентов основной группы и группы пар-копий за первый год наблюдения

Group / Группа	Main group, *n* = 28 / Основная группа, *n* = 28	Pairs-copies group, *n* = 28 / Группа пар-копий, *n* = 28	*p*
Symptom, score, $M \pm \sigma$ / Суммарный балл симптомов, $M \pm \sigma$	10.88 ± 1.3	11.26 ± 1.64	0.38
Medication, score, $M \pm \sigma$ / Суммарный балл препаратов, $M \pm \sigma$	12.33 ± 0.91	12.69 ± 0.72	0.6
Total symptom and medication, score, $M \pm \sigma$ / Общий индекс симптомов и препаратов, баллы, $M \pm \sigma$	23.32 ± 1.21	23.99 ± 1.2	0.68

Table 5 / Таблица 5

Dynamics of symptom scores, medication scores and general score of symptoms and medications in patients of the main group and pair-copy control group for 1 year of treatment
Динамика балльной оценки симптомов, лекарственной нагрузки и общего индекса симптомов и препаратов у пациентов основной группы и группы пар-копий за первый год лечения

Group / Группа	Main group, $n = 28$ / Основная группа, $n = 28$	Pairs-copies group, $n = 28$ / Группа пар-копий, $n = 28$	p
Initial Symptom score, $M \pm \sigma$ / Исходный балл симптомов, $M \pm \sigma$	10.88 ± 1.3	11.26 ± 1.64	0.38
1 year of treatment, Symptom score, $M \pm \sigma$ / 1 год терапии, баллы симптомов, $M \pm \sigma$	6.29 ± 1.06	8.83 ± 1.39	0.063
Initial Medication score, $M \pm \sigma$ / Исходный балл препаратов, $M \pm \sigma$	12.33 ± 0.91	12.69 ± 0.72	0.6
1 year of treatment, Medication score, $M \pm \sigma$ / 1 год терапии, баллы препаратов, $M \pm \sigma$	9.92 ± 1.07	12.84 ± 1.16	0.041
Initial Total symptom and medication score, $M \pm \sigma$ / Исходный общий индекс, баллы, $M \pm \sigma$	23.32 ± 1.21	23.99 ± 1.2	0.68
1 year of treatment, Total symptom and medication score, $M \pm \sigma$ / 1 год терапии, баллы общего индекса, $M \pm \sigma$	16.21 ± 1.77	20.92 ± 2.09	0.028

group, the patients almost did not reduce the pharmacotherapy amount during the follow-up year. Hence, the primary difference between the groups in terms of drug load favors the SLIT group (the difference is statistically significant). The difference between the groups was statistically significant and in favor of the SLIT group, as noted by the change in the total index of symptoms and medications. Therefore, the trait scoring system enables the documentation of differences between groups within the first year of treatment.

The developed system of the comprehensive assessment of changes in the BA and AR course over time in children has the following advantages:

1) It does not require the multi-day collection of information. The signs assessed in the system are included in the structure of the usually collected anamnesis in a patient with a chronic disease; these are the terms of exacerbations, pharmacotherapy, considering the timing and dosages;

2) The epicrisis form comprises a minimum field for filling, which saves the doctor's time;

3) The assessment covers a long period of time (1 year), which enables us to assess the changes over time in diseases with a variable nature of the course, long-term remissions, and/or protracted exacerbations;

4) The system provides a comprehensive assessment of the allergic disease course, by considering the main symptoms, exacerbations, complications, and all types of basic therapy.

The assessment system includes acute respiratory and bacterial infections (otitis media, sinusitis, etc.) These signs are not considered in validated questionnaires [10, 12], but are fundamentally important when working with pediatric patients with BA and AR.

CONCLUSIONS

1. The developed system for assessing the symptoms of the disease and the need for medications reveals the difference between groups of patients in favor of the group receiving SLIT.

2. The indicator that changes most noticeably in the first year of SLIT is the level of drug therapy. Therefore, the general index of symptoms and medications decreases significantly in the SLIT group.

3. The proposed assessment system enables us to comprehensively evaluate the aspects of allergic disease course (BA and AR) in a pediatric patient and includes the most significant clinical signs and all types of pharmacotherapy.

4. The proposed assessment system is recommended for further study (at longer periods, such as 2–3 years from the start of SLIT therapy with HDM allergens) in children.

ADDITIONAL INFORMATION

Author contributions. All authors confirm the compliance of their authorship with the international ICMJE criteria (all authors significantly contributed to the development of the concept, research, and preparation of the article, as well as read and approved the final version before its publication).

Conflict of interest. The authors declare no conflict of interest.

Funding. The study had no external funding.

REFERENCES

1. Allergicheskiy rinit 2020. Federal'nye klinicheskie rekomendatsii. Accessed 10.03.2021. Available at: https://raaci.ru/education/clinic_recomendations/471.html. (In Russ.)
2. Bronchial'naya astma u detey 2017. Klinicheskie rekomendatsii. Available at: https://www.pediatr-russia.ru/information/klin-rek/deystvuyushchie-klinicheskie-rekomendatsii/Бронхиальная%20астма%20дети%20СПР%20рубрикатор.v2_2017_обновление.pdf (In Russ.)
3. Trusova OV, Kamaev AV, Makarova IV. Patient drop-outs from sublingual allergen specific immunotherapy with house dust mites. Solving a problem. *Russian Journal of Allergy*. 2020;17(2):53–60. (In Russ.) DOI: 10.36691/RJA1364
4. Agache I, Lau S, Akdis CA, et al. EAACI Guidelines on Allergen Immunotherapy: House dust mite-driven allergic asthma. *Allergy*. 2019;74(5):855–873. DOI: 10.1111/all.13749
5. Alvaro-Lozano M, Akdis CA, Akdis M, et al. EAACI Allergen Immunotherapy User's Guide. *Pediatr Allergy Immunol*. 2020;31(25):1–101. DOI: 10.1111/pai.13189
6. Barberi S, Ciprandi G, Verduci E. Effect of high-dose sublingual immunotherapy on respiratory infections in children allergic to house dust mite. Asia Pac. *Allergy*. 2015;5(3):163–169. DOI: 10.5415/apallergy.2015.5.3.163
7. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy*. 2008;63(Suppl 86):8–160. DOI: 10.1111/j.1398–9995.2007.01620.x
8. Dhami S, Kakourou A, Asamoah F, et al. Allergen immunotherapy for allergic asthma: A systematic review and meta-analysis. *Allergy*. 2017;72(12):1825–1848. DOI: 10.1111/all.13208
9. Global Initiative for Asthma. Global strategy for asthma management and prevention, 2018. Available at: http://www.ginasthma.org
10. Häfner D, Reich K, Matricardi PM, et al. Prospective validation of 'Allergy-Control-SCORETM': a novel symptom–medication score for clinical trials. *Allergy*. 2011;66(5):629–636. DOI: 10.1111/j.1398-9995.2010.02531.x
11. Occasi F, De Castro G, Zicari AM, et al. Sublingual immunotherapy in children and its potential beneficial collateral effect on respiratory tract infections. *Curr Med Res Opin*. 2019;31(5):939–941. DOI: 10.1185/03007995.2015.1027182
12. Pfaar O, Demoly P, Gerth van Wijk R, et al. Recommendations for the standardization of clinical outcomes used in allergen immunotherapy trials for allergic rhinoconjunctivitis: an EAACI Position Paper. *Allergy*. 2014;69(7):854–867. DOI: 10.1111/all.12383
13. Roberts G, Pfaar O, Akdis CA, et al. EAACI Guidelines on Allergen Immunotherapy: Allergic rhinoconjunctivitis. *Allergy*. 2018;73(4):765–798. DOI: 10.1111/all.13317
14. Shamji MH, Kappen JH, Akdis M, et al. Biomarkers for monitoring clinical efficacy of allergen immunotherapy for allergic rhinoconjunctivitis and allergic asthma: an EAACI position paper. *Allergy*. 2017;72(8):1156–1173. DOI: 10.1111/all.13138

СПИСОК ЛИТЕРАТУРЫ

1. Аллергический ринит 2020. Федеральные клинические рекомендации. Режим доступа: https://raaci.ru/education/clinic_recomendations/471.html. Дата обращения: 24.10.2021.
2. Бронхиальная астма у детей 2017. Клинические рекомендации. Режим доступа: https://www.pediatr-russia.ru/information/klin-rek/deystvuyushchie-klinicheskie-rekomendatsii/Бронхиальная%20астма%20дети%20СПР%20рубрикатор.v2_2017_обновление.pdf. Дата обращения: 24.10.2021.
3. Трусова О.В., Камаев А.В., Макарова И.В. Проблемы выбывания пациентов с лечения сублингвальной аллерген-специфической терапией с аллергеном клещей домашней пыли, и пути их преодоления // Российский аллергологический журнал. 2020. Т. 17, № 2. С. 53–60. DOI: 10.36691/RJA1364
4. Agache I., Lau S., Akdis C.A., et al. EAACI Guidelines on Allergen Immunotherapy: House dust mite-driven allergic asthma // Allergy. 2019. Vol. 74, No. 5. P. 855–873. DOI: 10.1111/all.13749
5. Alvaro-Lozano M., Akdis C.A., Akdis M., et al. EAACI Allergen Immunotherapy User's Guide // Pediatr Allergy Immunol. 2020. Vol. 31, No. S25. P. 1–101. DOI: 10.1111/pai.13189
6. Barberi S., Ciprandi G., Verduci E. Effect of high-dose sublingual immunotherapy on respiratory infections in children allergic to house dust mite. Asia Pac // Allergy. 2015. Vol. 5, No. 3. P. 163–169. DOI: 10.5415/apallergy.2015.5.3.163
7. Bousquet J., Khaltaev N., Cruz A.A., et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008. Vol. 63, Suppl 86. P. 8–160. DOI: 10.1111/j.1398–9995.2007.01620.x
8. Dhami S., Kakourou A., Asamoah F., et al. Allergen immunotherapy for allergic asthma: A systematic review and meta-analysis // Allergy. 2017. Vol. 72, No. 12. P. 1825–1848. DOI: 10.1111/all.13208
9. Global Initiative for Asthma. Global strategy for asthma management and prevention, 2018. Available at: http://www.ginasthma.org
10. Häfner D., Reich K., Matricardi P.M., et al. Prospective validation of 'Allergy-Control-SCORETM':

a novel symptom–medication score for clinical trials // Allergy. 2011. Vol. 66, No. 5. P. 629–636. DOI: 10.1111/j.1398-9995.2010.02531.x
11. Occasi F., De Castro G., Zicari A.M., et al. Sublingual immunotherapy in children and its potential beneficial collateral effect on respiratory tract infections // Curr Med Res Opin. 2019. Vol. 31, No. 5. P. 939–941. DOI: 10.1185/03007995.2015.1027182
12. Pfaar O., Demoly P., Gerth van Wijk R., et al. Recommendations for the standardization of clinical outcomes used in allergen immunotherapy trials for allergic rhinoconjunctivitis: an EAACI Position Paper // Allergy. 2014. Vol. 69, No. 7. P. 854–867. DOI: 10.1111/all.12383
13. Roberts G., Pfaar O., Akdis C.A., et al. EAACI Guidelines on Allergen Immunotherapy: Allergic rhinoconjunctivitis // Allergy. 2018. Vol. 73, No. 4. P. 765–798. DOI: 10.1111/all.13317
14. Shamji M.H., Kappen J.H., Akdis M., et al. Biomarkers for monitoring clinical efficacy of allergen immunotherapy for allergic rhinoconjunctivitis and allergic asthma: an EAACI position paper // Allergy. 2017. Vol. 72, No. 8. P. 1156–1173. DOI: 10.1111/all.13138

◆ Information about the authors

Dmitrii S. Korostovtsev – MD, Dr. Sci. (Med.), Professor, Department of Pediatrics them. Professor I.M. Vorontsov AF and DPO. St. Petersburg State Pediatric Medical University, Ministry of Health of the Russian Federation, Saint Petersburg, Russia. E-mail: dsk552@mail.ru

Olga Valerievna Trusova – MD, Cand. Sci. (Med.), Associate Professor, Department of Therapy with the Course on Allergy and Immunology. Academician I.P. Pavlov First St. Petersburg State Medical University, Saint Petersburg, Russia. E-mail: o-tru@mail.ru.

Andrey V. Kamaev – MD, Cand. Sci. (Med.), Associate Professor, Department of General Practice. Academician I.P. Pavlov First St. Petersburg State Medical University, Saint Petersburg, Russia. E-mail: andykkam@mail.ru.

◆ Информация об авторах

Дмитрий Сергеевич Коростовцев — д-р мед. наук, профессор кафедры педиатрии им. профессора И.М. Воронцова ФП и ДПО. ФГБОУ ВО «Санкт-Петербургский государственный педиатрический медицинский университет» Минздрава России, Санкт-Петербург, Россия. E-mail: dsk552@mail.ru.

Ольга Валерьевна Трусова — канд. мед. наук, доцент кафедры терапии госпитальной с курсом аллергологии и иммунологии им. акад. М.В. Черноруцкого с клиникой. ФГБОУ ВО «Первый Санкт-Петербургский государственный медицинский университет им. акад. И.П. Павлова» Минздрава России, Санкт-Петербург, Россия. E-mail: o-tru@mail.ru.

Андрей Вячеславович Камаев — канд. мед. наук, доцент кафедры общей врачебной практики. ФГБОУ ВО «Первый Санкт-Петербургский государственный медицинский университет им. акад. И.П. Павлова» Минздрава России, Санкт-Петербург, Россия. E-mail: andykkam@mail.ru.