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SENSITIZATION PROFILE IN CHILDREN WITH ALLERGIC RESPIRATORY DISEASES

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Abstract. Currently, little is known about the sensitization profile of children with asthma, allergic rhinitis (AR) and comorbid asthma in Ukraine. *Aim.* To study the sensitization profile in children with allergic respiratory diseases. *Material and methods.* Ninety-three children aged 5–17 years with allergic respiratory diseases were examined, including: 51 children with AR (1st group), 31 children with AR combined with asthma (2nd group) and 11 children with isolated asthma (3rd group). All children underwent multicomponent molecular diagnostics in the form of a multiplex test ALEX. *Results.* In monosensitized (17.2 %) and polysensitized (82.8 %) children with isolated asthma, with isolated AR and AR combined with asthma, sensitization to Fel d 1 was most common. Monosensitization to the ragweed molecule (Amb a 1) is characteristic only for children with AR, AR combined with asthma; to the cat molecule Fel d 1 — for children with all allergic respiratory diseases. In monosensitized children with isolated AR, sensitization occurs only to the mold molecules Alt a 1, the fenugreek Lol p 1, timothy-grass (Phl p 1, Phl p 2, Phl p 5.0101, Phl p 6), in children with AR combined with asthma—to mites household dust (Der f 1, Der p 1), in children with isolated asthma — to the dog's epidermal allergen (Can f 1). In polysensitized children with respiratory allergy, the most common molecules to which sensitization is detected are Fel d 1, Bet v 1, Lol p 1, Phl p 1, Amb a 1 and Alt a 1. *Conclusions.* Children with allergic respiratory diseases exhibit different sensitization profiles. Sensitization to only one group of allergens was significantly more common in children with isolated asthma than in children with isolated AR and AR combined with asthma. Sensitization to Fel d 1 looks like a marker of respiratory allergy.

Key words: children, multicomponent molecular diagnostics, asthma, Allergic rhinitis, sensitization.

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Introduction. The prevalence of asthma, allergic rhinitis (AR) in children worldwide is 12–12.7 % [8] and the number of patients continues to increase in Ukraine and other countries [7]. AR is known to be a risk factor for the development of asthma [1, 6]. According to the literature, 76–80 % of patients with asthma suffer from AR and 15–40 % of patients with AR are diagnosed with asthma [1]. The combined pathology of the respiratory tract causes a more severe course and affects the level of disease control. Early diagnosis and appointment of adequate treatment can improve the quality of children's life, as well as avoid complications and disabilities. Finding out the causes, analyzing the factors of exacerbation and progression of allergic disease are important for the selection and prescribing of asthma and AR therapy [2]. The profile of sensitization in children with asthma, with AR has its differences depending on the climatic conditions of the environment of different countries [9] and is insufficiently studied in Ukraine.

The use of molecular diagnostics is ability to detect sensitization to the components of allergens, to distinguish primary from cross-sensitization and to rationally select patients for allergen-specific immunotherapy [9].

Aim. To study the sensitization profile in children with allergic respiratory diseases.

Materials and methods of research. Ninety-three children aged 5–17 years with a diagnosis of respiratory allergy were examined. Among the children included in the study: 51 children with AR (1st group), 31 children with AR combined with asthma (2nd group) and 11 children with isolated asthma (3rd group). All children were interviewed, underwent multicomponent molecular diagnostics and given a general clinical examination.

This study received approval by the local ethical committee.

All groups of children were identical in age and gender. The diagnoses of asthma and AR were established in accordance with the approved criteria (Order No. 868 of the Ministry of Health of Ukraine, 9.10.2013 and international recommendations GINA, 2020) and international criteria ARIA (2016) [3, 4, 5]. To perform multicomponent molecular diagnostics, all children underwent a multiplex ALEX test, which included 157 allergen extracts and

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125 recombinant or highly purified molecules. Other reference methods for determining sensitization to allergens were not used. Statistical processing of the obtained results was performed using the program "STATISTICA 10.0".

Results and discussion. Demographic characteristics of children in groups are shown in table 1.

The most common allergic respiratory disease among the surveyed children was isolated AR (54.8 %), less frequently – AR combined with asthma (or 33.3 %). Isolated asthma was present in only 11.8 % of children. According to the results of multicomponent molecular diagnostics in most children (82.8 %) suffering from AR, AR combined with asthma and isolated asthma showed sensitization to more than one group of allergens (17.2 %) (table 2). Sensitization to only one group of allergens was significantly more frequent in children with isolated asthma ($p < 0.05$) than in children with isolated asthma and AR combined with asthma (table 2).

Sensitivity data for only one component of the allergens are shown in table 3. There was only the cat mole-

cule Fel d 1 to which sensitization in children of all groups were detected. The Amb a 1 molecule was most often found in monosensitized children suffering from AR associated with asthma, rarely – children with isolated AR, and it was no cases in children with isolated asthma. There were molecules to which only monosensitized children from one group with the same frequency (25 % for each) were sensitive. In monosensitized children with isolated AR sensitization were only to the molecule of mold Alt a 1, fenugreek Lol p 1 and to molecules of timothy-grass Phl p 1, Phl p 2, Phl p 5.0101, Phl p 6; in children with isolated asthma – only to the epidermal allergen of the dog Can f 1 and to the molecule wasp venom Ves v 5, in children with AR combined with asthma – only to the molecules of house dust mites Der f 1, Der p 1 (table 3).

Table 4 presents the profile of sensitization in polysensitized children depending on allergic respiratory diseases. Sensitization to the cat epidermal allergen Fel d 1, to the allergen molecule Bet v 1, fenugreek Lol p 1, timothy-grass

Table 1. Demographic characteristics of children (n) in groups 1, 2, 3, absolute number (%)

Indicator	The number of children (n) in groups			P _{1,2}	P _{2,3}	P _{1,3}
	1group (n = 51)	2group (n = 31)	3group (n = 11)			
The average age of children	9.43 (±0.55)	9.23 (±3.63)	8.55 (±0.91)	1.000	0.555	0.555
Children 5-11 years	38 (74.51)	25 (80.65)	9 (81.82)	0.482	0.801	0.340
Children 12-17 years	13 (25.49)	6 (19.35)	2 (18.18)	0.482	0.801	0.340
Girls	15 (29.41)	14 (45.16)	7 (63.64)	0.103	0.075	0.0005
Boys	36 (70.59)	17 (54.84)	4 (36.36)	0.103	0.075	0.0005

Table 2. Frequency of sensitization in children (n) in groups 1, 2, 3, absolute number (%)

Indicator	The number of children (n) in groups			P _{1,2}	P _{2,3}	P _{1,3}
	1 group (n = 51)	2 group (n = 31)	3 group (n = 11)			
Polysensitization	43 (84.31)	27 (87.10)	7 (63.64)	0.782	0.006	0.0132
Monosensitization	8 (15.69)	4 (12.90)	4 (36.36)	0.782	0.006	0.0132

Table 3. Sensitization profile in monosensitized children depending on allergic respiratory disease (n) in groups 1, 2, 3, absolute number (%)

Molecules of allergens	1 group (n = 8)	2 group (n = 4)	3 group (n = 4)	P _{1,2}	P _{2,3}	P _{1,3}
Mold:						
Alt a 1	2 (25)	0	0	0.148	n.d.	0.148
Pollen:						
Lol p 1	2 (25)	0	0	0.148	n.d.	0.148
Phl p 1	2 (25)	0	0	0.148	n.d.	0.148
Phl p 2	2 (25)	0	0	0.148	n.d.	0.148
Phl p 5.0101	2 (25)	0	0	0.148	n.d.	0.148
Phl p 6	2 (25)	0	0	0.148	n.d.	0.148
Amb a 1	1 (12.5)	2 (50)	0	0.120	0.019	0.334
House dust mites:						
Der f 1	0	1 (25)	0	0.148	0.148	n.d.
Der p 1	0	1 (25)	0	0.148	0.148	n.d.
Animal allergens:						
Fel d 1	1 (12.5)	1 (25)	1 (25)	0.553	1.000	0.553
Can f 1	0	0	1 (25)	n.d.	0.148	0.148
Profilin:						
Phl p 12	0	0	1 (25)	n.d.	0.148	0.148
Wasp venom:						
Ves v 5	0	0	1 (25)	n.d.	0.148	0.148

Note: n. d.: not determined.

Phl p 1, ragweed Amb a 1 and mold Alt a 1 were most common in polysensitized children with allergic respiratory diseases of all groups. Sensitization to PR-10 molecules (alder allergen Aln g 1, birch Bet v 1, hazelnut Cor a 1.0103

and Cor a 1.0401) were twice more often diagnosed in polysensitized children with isolated AR and with AR combined with asthma, compared with patients suffering from only isolated asthma (table 4). There were found sensitization in

Table 4. Sensitization profile in polysensitized children depending on allergic respiratory disease (n) in groups 1, 2, 3, absolute number (%)

Molecules of allergens	1 group (n = 43)	2 group (n = 27)	3 group (n = 7)	P _{1,2}	P _{2,3}	P _{1,3}
PR-10: Aln g 1	13 (30.23)	8 (32)	1 (14.29)	0.818	0.041	0.070
Api g 1	8 (18.6)	0	1 (14.29)	0.002	0.010	0.564
Bet v 1	19 (44.19)	13 (52)	1 (14.29)	0.522	0.0001	0.001
Mal d 1	11 (25.58)	0	1 (14.29)	0.0002	0.010	0.179
Gly m 4	0	0	1 (14.29)	n.d.	0.010	0.010
Ara h 8	10 (23.26)	0	2 (28.57)	0.0005	0.0001	0.625
Cor a 1.0103	14 (32.56)	10 (40)	1 (14.29)	0.506	0.006	0.042
Cor a 1.0401	12 (27.91)	8 (32)	1 (14.29)	0.643	0.042	0.114
Mold: Alt a 1	20 (46,51)	12 (48)	3 (42.86)	0.830	0.830	0.668
Pollen:						
Amb a 1	23 (53.49)	10 (40)	2 (28.57)	0.199	0.259	0.015
Amb a 4	0	0	1 (14.29)	n.d.	0.010	0.010
Art v 1	11 (25.58)	0	1 (14.29)	0.0002	0.010	0.179
Lol p 1	17 (39.53)	11 (44)	4 (57.14)	0.828	0.134	0.086
Phl p 1	18 (41.86)	11 (44)	4 (57.14)	1.000	0.134	0.134
Phl p 2	5 (11.63)	0	0	0.021	n.d.	0.021
Phl p 5.0101	11 (25.58)	8 (32)	3 (42.86)	0.635	0.266	0.112
Phl p 6	8 (18.6)	0	1 (14.29)	0.002	0.010	0.564
Wasp venoms:						
Api m 1	0	0	1 (14.29)	n.d.	0.010	0.010
Api m 10	0	0	1 (14.29)	n.d.	0.010	0.010
Api m 2	0	0	1 (14.29)	n.d.	0.010	0.010
Food storage proteins:						
Ara h 1	0	0	1 (14.29)	n.d.	0.010	0.010
Ara h 2	0	0	1 (14.29)	n.d.	0.010	0.010
Ara h 3	0	0	1 (14.29)	n.d.	0.010	0.010
Ara h 6	0	0	1 (14.29)	n.d.	0.010	0.010
Foodallergens:						
Cor a 14	0	0	1 (14.29)	n.d.	0.010	0.010
Cyp c 1	0	0	1 (14.29)	n.d.	0.010	0.010
Dau c 1	0	0	1 (14.29)	n.d.	0.010	0.010
Gad m 1	0	0	1 (14.29)	n.d.	0.010	0.010
Skin fungus: Mala s 9	0	0	1 (14.29)	n.d.	0.010	0.010
Animal allergens:						
Can f 1	13 (30.23)	0	4 (57.14)	0.00005	0.0000	0.008
Can f 2	0	0	1 (14.29)	n.d.	0.010	0.010
Fel d 1	27 (62.79)	10 (40)	6 (85.71)	0.017	0.00001	0.013
Fel d 4	0	0	2 (28.57)	n.d.	0.0001	0.0001
Lipocalin: Mus m 1	0	0	2 (28.57)	n.d.	0.0001	0.0001
Profilins:						
Bet v 2	10 (23,26)	0	0	0.0005	n.d.	0.0005
Hev b 8	9 (20,93)	0	0	0.001	n.d.	0.001
Phl p 12	9 (20,93)	0	0	0.001	n.d.	0.001
Pho d 2	11 (25.58)	0	0	0.0002	n.d.	0.0002
House dust mites:						
Der f 1	0	4 (16)	1 (14.29)	0.010	1.000	0.010
Der f 2	11 (25.58)	0	3 (42.86)	0.0002	0.0000	0.112
Der p 1	8 (18.6)	4 (16)	2 (28.57)	0.779	0.198	0.313
Der p 2	11 (25.58)	0	3 (42.86)	0.0002	0.0000	0.112
Der p 23	8 (18.6)	0	1 (14.29)	0.002	0.010	0.564
Der p 5	0	0	1 (14.29)	n.d.	0.010	0.010

Note: n. d.: not determined.

polysensitized children with isolated AR only to timothy-grass Phl p 2, to date palm Pho d 2 and to profilin (Bet v 2, Hev b 8, Phl p 12,) in polysensitized children with isolated asthma only to ambrosia Amb a 4, to bee venoms Api m 1, Api m 2, Api m 10, to peanuts Ara h 1, Ara h 2, Ara h 3, Ara h 6, to dogs Can f 2, to hazelnuts Cor a 14, to carp Cyp c 1, to carrots Dau c 1, to house dust mites Der p 5, to cat Fel d 4, to tryptomyosin Gad m 1, to soybean Gly m 4 (table 4).

Discussion. The molecule Der p 1, according to the literature, is considered one of the most clinically important and widespread aeroallergens in the world [11]. In Italy, more than 50 % of school-age children are sensitive to Der f 1 and Der p 1 [12]. In this study, sensitization to Der p 1 is present in polysensitized children of all groups, but the prevalence of this molecule was not first. The molecule Fel d 1 is ranked second by scientists after house dust mites indoors [10], but in Ukraine it has taken the lead. After the cat molecule, the most common sensitization to pollen molecules (Lol p 1, Phl p 1, Phl p 5.0101, Amb a 1) and mold (Alt a 1) were found in polysensitized children of all groups. Absent (table 4) was a significant difference in prevalence between groups of children with different allergic diseases of the respiratory tract. Fel d 1 was the only molecule to which children of all groups with monosensitization are sensitive (table 3). Polysensitized children with isolated asthma (85.7 %) are more sensitive to this molecule than children with isolated AR (62.8 %) ($p = 0.028$) and AR combined with asthma (40 %) ($p = 0.00001$) (table 4). Children with isolated AR and with AR combined with asthma were significantly more likely to be sensitive to the PR-10 proteins mole-

cules of Bet v 1, Cor a 1.0103 than polysensitized children with isolated asthma (Table 4). Children in Sweden have increased sensitization to cat and dog molecules with age [12]. German scientists report the most common molecules Phl p 1 and Bet v 1 among children under 10 years, and then the sensitization to Fel d 1, Phl p 5, Der p 2, Der p 1, Pla a 2, Phl p 2, Alt a 1, Phl p 11 and Act d 2 [12]. Researchers from Japan studying sensitization in children of different ages note that some children developed sensitization first to the components of house dust mites, and later to pollen allergens. The other children developed sensitization to these allergens alone or to pollen and mites together, but none of the children had sensitization to pollen before developing it from domestic dust mites [12]. According to the results of this study, high sensitization to profiles in polysensitized children with isolated AR were determined: to date palm pal Pho d 2 (25.6 %), to birch Bet v 2 (23.3 %), to latex Hev b 8 (20.9 %), to timothy-grass Phl p 12 (20.9 %), as well as the most frequent sensitization to lipocalins of cat Fel d 4 (28.6 %) and house mice Mus m 1 (28.6 %) in polysensitized children with isolated asthma.

Conclusions. Children with allergic respiratory diseases exhibit different sensitization profiles. Sensitization to only one group of allergens was significantly more common in children with isolated asthma than in children with isolated AR and AR combined with asthma. Polysensitization is observed four times more frequently than monosensitization in children with allergic respiratory diseases. Sensitization to Fel d 1 looks like a marker of respiratory allergy.

ПРОФІЛЬ СЕНСИБІЛІЗАЦІЇ У ДІТЕЙ З АЛЕРГІЧНИМИ РЕСПІРАТОРНИМИ ЗАХВОРЮВАННЯМИ

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Резюме. Поширеність бронхіальної астми (БА), алергічного риніту (АР) у дітей в усьому світі складає 12–12,7 %. Профіль сенсibilізації у дітей різних країн з БА та АР залежить від кліматичних умов і недостатньо вивчений в Україні. Молекулярна діагностика дозволяє виявити сенсibilізацію до компонентів алергенів, відрізнити первинну сенсibilізацію від перехресної та раціонально призначити алерген-специфічну імунотерапію. *Мета дослідження* полягає у вивченні профілю сенсibilізації у дітей з респіраторними алергічними захворюваннями. *Матеріали і методи досліджень.* Обстежено 93 дитини віком 5–17 років з респіраторними алергічними захворюваннями. У 51 дитини був діагностований АР (1 група), у 31 дитини поєднання АР з БА (2 група) та у 11 дітей мала місце ізольована БА (3 група). Усім дітям проведена багатокомпонентна молекулярна діагностика з використанням мультиплексного тесту ALEX. *Результати та їх обговорення.* У полісенсibilізованих (82,8 %) та моносенсibilізованих (17,2 %) дітей з ізольованою БА, з ізольованим АР та АР, поєднаним з БА, сенсibilізація до Fel d 1 зустрічалась найчастіше. Моносенсibilізація до молекули амброзії (Amb a 1) характерна тільки для дітей з АР та АР, поєднаним з БА; до молекули kota Fel d 1 — для дітей з усіма респіраторними алергічними захворюваннями. У моносенсibilізованих дітей з ізольованим АР зустрічається сенсibilізація тільки до молекул плісняви Alt a 1, пажитниці Lol p 1, тимофіївки (Phl p 1, Phl p 2, Phl p 5.0101, Phl p 6), у дітей з АР, поєднаним з БА — до кліщів домашнього пилу (Der f 1, Der p 1), у дітей з ізольованою БА — до епідермального алергену собаки (Can f 1). У полісенсibilізованих дітей з респіраторною алергією найрозповсюдженими молекулами, до яких виявлена сенсibilізація є Fel d 1, Bet v 1, Lol p 1, Phl p 1, Amb a 1 та Alt a 1. *Висновки.* Діти з респіраторними алергічними захво-

рюваннями демонструють різний сенсibilізаційний профіль. Сенсibilізація тільки до однієї групи алергенів спостерігалась достовірно частіше у дітей з ізольованою БА, ніж у дітей, які страждають на ізольований АР та АР, поєднаний з БА. Сенсibilізація до Fel d1 виглядає як маркер респіраторної алергії.

Ключові слова: діти, багатокомпонентна молекулярна діагностика, бронхіальна астма, алергічний риніт, сенсibilізація.

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ПРОФИЛЬ СЕНСИБИЛИЗАЦИИ У ДЕТЕЙ С АЛЛЕРГИЧЕСКИМИ РЕСПИРАТОРНЫМИ ЗАБОЛЕВАНИЯМИ

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Резюме. Распространенность бронхиальной астмы (БА), аллергического ринита (АР) у детей во всем мире составляет 12–12,7 %. Профиль сенсibilізації у дітей різних країн з БА і АР залежить від кліматических умов і недостатньо вивчений в Україні. Молекулярна діагностика дозволяє виявити сенсibilізацію к компонентам алергенів, відличити первичну сенсibilізацію від перехресної і раціонально назначити алерген-специфічну імунотерапію. *Цель исследования* заключається в вивченні профіля сенсibilізації у дітей с респіраторними алергіческими захворюваннями. *Материалы и методы исследований.* Обстежено 93 ребенка в візасті 5–17 лет с респіраторними алергіческими захворюваннями. У 51 ребенка был діагностирован АР (1 група), у 31 ребенка — АР в сочетании с БА (2 група) и у 11 детей имела место ізольована БА (3 група). Всем детям проведена багатокомпонентна молекулярна діагностика с использованием мультиплексного теста ALEX. *Результаты и их обсуждение.* У полісенсibilізованих (82,8 %) и моносенсibilізованих (17,2 %) дітей с ізольованою БА, с ізольованим АР и АР в сочетании с БА сенсibilізація к Fel d1 зустрічалась чаще. Моносенсibilізація к молекуле амброзії (Amb a1) характерна тільки для дітей с АР, АР в сочетании с БА, к молекуле кота Fel d1 — для дітей со всіма респіраторними алергіческими захворюваннями. У моносенсibilізованих дітей с ізольованим АР зустрічається сенсibilізація тільки к молекулам плесени Alt a1, райграса Lol p1, тимофеевки (Phl p1, Phl p2, Phl p5.0101, Phl p6), у дітей с АР в сочетании с БА — к кліщам домашньої пылі (Der f1, Der p1), у дітей с ізольованою БА — к епідермальному алергену собаки (Can f1). У полісенсibilізованих дітей с респіраторної алергією самыми распространеними молекулами, к которым виявлена сенсibilізація, являются Fel d1, Bet v1, Lol p1, Phl p1, Amb a1 и Alt a1. *Выводы.* Діти с респіраторними алергіческими захворюваннями демонструють різний сенсibilізаційний профіль. Сенсibilізація тільки к одній групі алергенів набудалась достовірно чаще у дітей с ізольованою БА, чем у дітей, страдаючих ізольованим АР и АР в сочетании с БА. Сенсibilізація к Fel d1 виглядає як маркер респіраторної алергії.

Ключевые слова: діти, багатокомпонентна молекулярна діагностика, бронхіальна астма, алергіческий риніт, сенсibilізація.

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