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CENTER FOR INTERNATIONAL SCIENTIFIC PUBLICATIONS
JOURNAL OF APPLIED MEDICAL SCIENCES
ISSN(Online): 2984-6730
SJIF Impact Factor |(2023): 5.817|
Volume-6, Issue-4, Published |20-11-2023|

CLINICAL AND IMMUNOLOGICAL FEATURES IN PATIENTS WITH COMORBID ALLERGIC RHINITIS

https://doi.org/10.5281/zenodo.10156407

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This article shows the effectiveness of antigen-specific immunotherapy in 79 sick children with suspected allergic rhinitis. In order to study the course of allergic rhinitis, the effectiveness of the diagnostic and treatment the method was assessed using an individual questionnaire offered by Allergic Rhinitis and its Impact on Asthma (ARIA).

Key words
allergic rhinitis, children, treatment, antigen-specific immunotherapy

Results: Positive results were observed in 14 children (87.5%) with intermittent allergic rhinitis from the 1st group and 13 children (86.6%) with persisting allergic rhinitis from the 2nd group after ASIT sublingual courses ($p < 0.05$). Complete clinical remission in 100% of the children in the 1st group with intermittent allergic rhinitis was confirmed by positive dynamics observed after the 2nd and 3rd courses of ASIT; a very strong correlation $r = 0.946$ was determined, $p < 0.01$. Among the patients of the 2nd group with persisting allergic rhinitis we did not observe complete clinic remission, though 11 (73.3%) of them had a positive tendency (partial clinic remission) after ASIT.

Among the problems of modern allergology the problem of allergic rhinitis (AR) in children occupies a special place [1,5,9,11]. Allergic rhinitis is one of allergic diseases with a great prevalence rate in childhood [2,3,12,19]. This pathology is considered to be a global problem, as it is of a high rank in the system of allergic pathologies (60-70%); its high prevalence (10-15%) in pediatric population also confirms the significance of the problem [4,6,10,16,20].

Continuous growth of the number of sick children in most countries of the world is conditioned by wrong interpretation of the disease manifestations, late application for medical help, late diagnosis and therapy.

Being the most effective therapy for allergic diseases, allergen-specific immune therapy (ASIT) is an introduction of a small dose of the allergen responsible for the development of the disease to a certain patient [5,7,8,14,18,20]. In that condition sensitivity of the body to that antigen decreases. The history of ASIT application is over 100 years old and within that period a great evidence base of the therapeutic

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method application was collected [3,13,15,17,19]. Due to decrease of disease manifestations, diminished need in therapy and in addition to that prevention of further development of allergy and its symptoms ASIT provides long-lasting clinical effect. The therapy affects essential immunologic mechanisms responsible for the development of clinical symptoms.

The objective: to study progression of allergic rhinitis in children and to assess the efficacy of ASIT.

Research methods and materials. The study was performed at the Children's Allergology Unit of multifunctional clinic of Tashkent Medical Academy where we examined 79 patients with diagnosed allergic rhinitis.

The age of patients diagnosed with allergic rhinitis varied from 6 to 12 years old with average one 9.1 ± 0.31 years old.

Prior to coming to the clinic all the patients completed a questionnaire aiming definition or confirmation of allergic rhinitis. The questionnaire was worked out and adopted within international ARIA program. The questionnaire consists of two main and 10 minor questions. Minor chapters included "yes" or "no" answers (Table 1).

The diagnosis was determined according to ARIA international classification. In the process of the study forty patients were diagnosed with intermittent AR (IAR) and thirty-nine with persisting AR (PAR). When interviewed about the history we found out that besides AR manifestations all the patients had clinical symptoms of BA (attacks of short-breathing, coughing, and dispnoe).

By means of scratching test we determined sensitivity to various groups of allergens. Efficacy of immune therapy was assessed on the basis of 4 grade scale:

"4" – very good result (complete elimination of clinic manifestations after the course of therapy);

"3" – good result (significant improvement of nasal breathing, restoration of olfactory function, rhinorrhea and sneezing had strong correlation with allergy);

"2" – satisfactory result (significant decrease of manifestation of basic symptoms compared to the state before the therapy, less need in pharmaceutical therapy);

"1" – non-satisfactory result (no effect of therapy).

Table 1

ADOPTED ARIA, ALLERGIC RHINITIS QUESTIONAIRE

Question	Answer	
1.Do you have the following symptoms at least for one hour most days (or are they seasonal)?		
• excretion from nose	Y	No
• sneezing, frequent attacking	Y	No

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• nasal congestion	Y	No
• nasal itching	Y	No
2. Do you have the following symptoms?		
• only unilateral nasal symptoms	Y	No
• nasal congestion without other symptoms	Y	No
• green or yellow thick excretion from nose	Y	No
• thick excretion from nose to throat or/and from nose	Y	No
• recurrent nasal bleeding	Y	No
• deterioration of olfactory function	Y	No

The obtained results were processed using SPSS. Within the study degree of every characteristic was compared between the groups.

Reliability degree (P) of statistic analysis for all tests was calculated, and accepted critical value was equal to 0.05.

Results and discussion. According to the results of the 1 main question of the poll performed among 79 patients we received the following answers: 40 patients (100%) had liquid nasal excretion, 20 children (17.8%) had little mucous excretion. All examined children had sneezing and nasal congestion (100%). Nasal breathing parameter varied from light to complete inability to breath. Nasal itching was registered in all the patients, 32(28.5%) with constant itching, and 45 (40%) with periodical one.

Answering the 2nd question all the patients denied unilateral nasal symptoms, while we could observe nasal congestion without other symptoms, and that confirms the presence of allergic process. Thick excretion from nose to throat was registered in 16 (20.3%) patients, and 7 patients (8.8%) had mucous-putrid excretion, which indicates presence of other ENT pathology. Forty-five (40%) patients had recurrent nasal bleeding, caused by liquid rhinorrhea and forced blowing out the nose. Seventy patients (88.3%) had olfactory dysfunction as an additional symptom of AR.

Thus, with the help of the questionnaire we could determine allergic rhinitis in all the children. Besides that, we observed pathologies of ENT, which required further detailed clear diagnosis.

Later, we analyzed the age of the first AR symptoms. Initial AR manifestations were registered at 5.9 years old. Average age of application for medical help and AR clinic diagnosis was 9.1 years old. It should be noted that, 3 years passed in average from the moment of AR symptoms appearance till the diagnosis. Using non-parametric analysis we determined that, 74 (95.5%) had late diagnosis, while 5

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(4.5%) patients applied for medical help in time. Thus, the aforesaid study confirmed the global data on late application.

Classification of the patients with AR according to the severity of the process showed the following: among the patients with IAR there were 32.5% (13) severe, 42.5% (17) moderate and 25% (10) mild forms.

We did not observe mild persisting AR, while 22 (43.6%) patients had moderate, and 17 (43.6%) had severe one, $p<0.05$. It should be noted that, children with mild AR stay out of doctors' control; parents do not interpret symptoms in their children correctly, and apply to doctor only when AR becomes severe.

In the 1st group of patients with intermittent AR exacerbation of the disease was observed from June till the middle of July. From the group of pollen allergens in most cases (40 (74.1%) patients) we determined sensitivity to cereal plants. Certain number of patients were sensitized to some weeds from the pollen group of allergens. Among them 35 (54.9%) patients had allergy to sagebrush, 7 (13%) to tree pollen, and 5 (11.1%) to poplar. Epidermal sensitivity was registered in 3 (7.5%) patients. There were no children sensitized to household products among the examined ones.

In the 2nd group with AR we registered high sensitivity to pollen and household allergens. In fifty-six (96.6%) patients epidermal sensitivity was dominant over weed allergy. Forty-nine (84.5%) patients had a specific sensitivity to cereal and field herbs pollen. The least number of patients (6 (10.3%) children) had sensitivity to tree pollen.

Almost of half of the patients (25 (43.1%) children) with PAR had sensitivity to household allergens. Air allergen spectrum contained the following: Dermatophagoideus farinae in 13 (22.4%) patients, Dermatophagoideus pteronissinus in 16 (27.5%), and library dust in 6 (10.4%). Besides that, we determined epidermal allergens such as dog hair in 3 (5.1%), cat hair in 8 (13.8%), and pillow feather in 10 (17.2%) patients, who always had a contact with these allergens.

In our study ASIT was performed on the basis of the skin scarification test results. SCIT was applied for 19 (47,5%) out of 40 patients with IAR 1st group and 21 (52.5%) patients from the 2nd group.

After the 1 course of subcutaneous immune therapy 6 (31.6%) children from the 1st group with IAR and 5 (23.8%) children from the 2nd group with PAR had good results, and only because of the exacerbation of the AR symptoms due to season and contact with allergen in 10.5% of the cases results were satisfactory.

Subcutaneous ASITsignificantly increased the efficacy of the therapy in both groups taking into account the annual doses. Next three years after ASIT most of the patients of the 1st group with IAR had positive results of the therapy (89.5%),

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though 10.5% had satisfactory ones due to exacerbation of seasonal AR and contact with allergens. Good results of the therapy were observed in 31.6% of the cases, and it was explained by episodic intensification of AR symptoms due to a significant amount of contact and obligatory usage of allergens. Very good results were registered in 57.9 % of the patients after the end of the whole therapy course; that category of patients did not have AR symptoms even in case of obligatory allergen usage and frequent contact. Among the children with PAR from the 2nd group 66.7% had positive results in three years after the therapy course. In that group of the patients good and satisfactory results were observed in 33.3% and 42.9% of the cases, respectively. After the 3rd course of ASIT the efficacy of subcutaneous therapy was confirmed statistically in children with PAR from the 2nd group ($p < 0.05$) (Table 2).

Table 2

ASSESSMENT OF SUBCUTANEOUS ALLERGEN-SPECIFIC IMMUNE THERAPY EFFICACY IN CHILDREN WITH INTERMITENT ALLERGIC RHINITIS

ASIT efficacy score	*Groups*											
	ASIT 1-course				***ASIT 2-course***				***ASIT 3-course***			
	1-group n=19		*2-group n=21*		*1-group n=19*		*2-group n=21*		*1-group n=19*		*2-group n=21*	
	abs	*%*	*abs*	*%*	*abs*	*%*	*abs*	*%*	*abs*	*%*	*bs*	
1 – non-satisfactory	3	15.8	4	19.0	-	-	1	4.8	-	-		
2 - satisfactory	10	52.6	12	57.1	8	42.1	9	42.9	2	10.5		3.3
3 - good	6	31.6	5	23.8	9	47.4	11	52.4	6	31.6		2.9
4 - excellent	-	-	-	-	2	10.5	-	-	11	57.9		3.8
Total good and excellent scores	6	31.6	5	23.8	11	57.9	11	52.4	17	89.5	4	6.7
P Reliability of differences between	<0.05				<0.05				<0.05			

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the efficacy of certain number of courses in the 1st group						
P Reliability of differences between the efficacy of certain number of courses in the 2nd group		<0.05		<0.05		<0.05

For the assessment of the therapy efficacy in all groups 1-2-3 years after subcutaneous ASIT skin scarification tests were repeated, taking into account sensitizing spectrum. In 1-2-3 years after the therapy course in the group with IAR there were 18 (94.7%) children with positive tendency; there was a strong direct correlation r = 0.512 between therapy efficacy and results of scarification test, which was statistically significant (p<0.05).

In the 2nd group of children with PAR only after the 2nd and 3rd courses of ASIT twelve (57.1%) children had registered positive dynamics, which showed a direct strong correlation r = 0.537, confirmed by skin tests, p <0. 05 (Table 3).

Table 3

DYNAMIC ASSESSMENT OF SUBCUTANEOUS ASIT IN CHLDREN WITH VARIOUS NOSOLOGIES OF ALLERGIC RHINITIS

	GROUPS											
	ASIT 1-course				***ASIT 2-course***				***ASIT 3-course***			
	1-group n=19		*2-group n=21*		*1group n=19*		*2-group n=21*		*1-group n=19*		*2-group n=21*	
ASIT dynamics	*abs*	*%*	*abs*	*%*	*abs*	*%*	*abs*	*%*	*abs*	*%*	*abs*	*%*
Negative	1	5.3	-	-	1	4.8	1	4.8	-	-	1	4.8
Weak	10	52.6	15	71.4	6	28.6	1	4.8	-	-	1	4.8
Positive	8	42.1	6	28.6	14	66.7	11	52.4	18	94.7	12	57.1
P Reliability of dynamic differences in	<0.05				<0.05				<0.05			

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the 1st group						
P Reliability of dynamic differences in the 2nd group		<0.05		<0.05		<0.05

Sublingual ASIT was applied in 31 children with AR. All those patients were divided to two groups: 1-group 16 (51.6%) children with IAR, 2-group 15 (48.4%) patients with PAR received three therapy courses and at the end of each course we performed skin tests for the assessment of ASIT efficacy.

After sublingual ASIT courses 14 children (87.5%) from the 1st group with IAR and 13 (86.6%) patients from the 2nd group with PAR had positive results (p <0.05).

Seasonal intensification of AR symptoms was observed only in 4 (25%) with IAR and after the 3rd course of sublingual ASIT in two (13.3%) patients from the 2nd group with AR. (Table 4)

Table 4

ASSESSMENT OF SUBLINGUAL ASIT EFFICACY IN CHILDREN WITH VARIOUS NOSOLOGIES OF ALLERGIC RHINITIS

ASIT efficacy score	*Groups*											
	ASIT 1-course				***ASIT 2-course***				***ASIT 3-course***			
	1-group n=19		*2-group n=21*		*1-group n=19*		*2-group n=21*		*1-group n=19*		*2-group n=21*	
	abs	*%*	*abs*	*%*	*abs*	*%*	*abs*	*%*	*abs*	*%*	*abs*	*%*
1 – non-satisfactory	-	-	2	13.3	-	-	-	-	-	-	-	-
2 - satisfactory	8	50.0	9	60.0	4	25.0	3	20.0	-	-	2	13.3
3 - good	8	50.0	1	6.7	8	50.0	7	46.7	4	25.0	2	13.3
4 excellent												
Total good and excellent scores												
P Reliability of differences between the efficacy of certain number of courses in the 1st group	<0.05				<0.05				<0.05			
P Reliability of differences			<0.05				<0.05				<0.05	

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between the efficacy of certain number of courses in the 2nd group						

Complete clinical remission was registered in 100% of the patients from the 1st group with IAR and confirmed by positive dynamics after the 2nd and 3rd courses of ASIT; we determined a very strong correlation r= 0.946, p <0.01. in the 2nd group of patients with PAR there were no cases with complete remission, though 11 (73.3%) children had a positive tendency (partial clinic remission) after ASIT (Table 5). In that group of patients we observed progression of the disease and during ASIT period the patients could violate hypoallergic routine and diet; in other words, they could have a contact with allergens [13-15].

Table 5

DYNAMIC ASSESSMENT OF SUBLINGUAL ASIT IN CHILDREN WITH ALLERGIC RHINITIS

ASIT dynamics	*GROUPS*											
	ASIT 1-course				***ASIT 2-course***				***ASIT 3course***			
	1-group n=16		*2-group n=15*		*1-group n=16*		*2-group n=15*		*1-group n=16*		*2-group n=15*	
	abs	*%*	*abs*	*%*	*abs*	*%*	*abs*	*%*	*abs*	*%*	*abs*	*%*
Negative	-	-	-	-	-	-	-	-	-	-	-	-
Weak	8	50.0	14	93.3	3	18.8	8	53.3	-	-	4	26.7
Positive	8	50.0	1	6.7	13	81.3	7	46.7	14	100	11	73.3
Reliability of dynamic differences in the 1st group	<0.05				<0.05				<0.05			

Conclusion

1. The questionnaire offered by ARIA is recommended to apply as a first aid tool. It is recommended to use the questionaire for diagnosis of children suspected to have AR and ENT pathologies prior to going to clinic and to apply to specialists in time.

2. The results we obtained in our study about late application to doctor with AR, its progression together with BA, its underdiagnosis correspond to the global data. Due to that the patients followed in our study were diagnosed with moderate and severe AR. Taking into account that initial symptoms of AR appear in 5-6 years

old age and it proceeds with other comorbidities, children should undergo compulsory allergologic examination.

3. Among the children with IAR the most prevalent sensitivity was that to cereal allergens (60.0%), less often to weeds (72.5%), trees (17.5%), and in a few cases we observed epidermal sensitivity to allergen (7.5%). Among the children with PAR sensitivity to weeds was quite often observed (79.5%), with relatively less sensitivity to cereals (51.3%) and household products (56.4%), household allergen (43.6%), and trees (15.4%).

4. The efficacy of subcutaneous ASIT in the children from the 1st group with IAR (89.5%) was much more higher than in the 2nd group with PAR (66.7%), $p < 0.05$. Efficacy of sublingual ASIT was equal in both groups, with 100% positive dynamic in IAR group. Immediately after the end of the 3rd course there was no registered remission. However, we observed partially positive dynamics, which required further ASIT course.

5. The results of the study are of great importance for the design of prophylactic measures for prevention of AR and BA and provide early diagnosis of AR in children.

6. Step-by-step three-course ASIT in children with IAR and PAR provides clear and continuous efficacy of the treatment

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ISSN(Online): 2984-6730
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Volume-6, Issue-4, Published |20-11-2023|

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