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Original article

Allergen-specific immunotherapy in combination with vitamin D in patients with seasonal allergic rhinitis

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Abstract: *Introduction* — Currently, over 500 million people suffer from allergic rhinitis worldwide. For many decades, allergen-specific immunotherapy (ASIT) was the only effective treatment for seasonal allergic rhinitis. The development of molecular allergy diagnostics via ISAC technology allows identifying true and cross-reactive allergens, thereby increasing the information content in selecting an appropriate ASIT. For many years, studies have been conducted on the immunomodulatory effect of vitamin D. These studies revealed the presence of a link between allergic rhinitis and vitamin D deficiency. In this regard, there is a strong need to assess the status of the population in terms of vitamin D for further examination of the effect of the vitamin D inclusion in the treatment regimen on the efficacy of ASIT.
Objective — To evaluate the efficacy of ASIT in combination with vitamin D in polysensitized patients with seasonal allergic rhinitis in Karaganda Oblast, Kazakhstan.
Material and Methods — Randomized controlled open-label study was conducted during July 2019 – September 2020 at *Divera Allergy Center* in Karaganda. Patients received sublingual ASIT: the experimental group received ASIT in combination with vitamin D, while comparison group received ASIT in accordance with the standard scheme. Clinical efficacy was monitored by assessing the severity of symptoms and the content of allergen-specific immunoglobulin E. ISAC test was employed to determine the allergen-specific immunoglobulin E. The significance of intergroup differences was determined by statistical methods: the nonparametric Mann-Whitney test for comparing independent groups and the Wilcoxon test for comparing dependent groups.
Results — Vitamin D deficiency was revealed in the blood serum of patients in both groups (median value of 16.32 ng/ml and 15.65 ng/ml, respectively). An overall symptom severity score after treatment demonstrated statistically significant changes between the two groups (p=0.777; Mann-Whitney criterion). In the experimental group, the median of overall symptom severity score declined by 46% (from 11 points to 6 points), and in the comparison group by 22% (from 11.5 points to 9 points).
Conclusion — As a result of our study, it was established that the adapted scheme of ASIT in combination with vitamin D in polysensitized patients with seasonal allergic rhinitis in Karaganda Oblast (Kazakhstan) was more effective, compared with the conventional scheme of ASIT. Hence, in patients with seasonal allergic rhinitis in the regions with known vitamin D deficiency, it is necessary to determine the vitamin D content with the purpose of its subsequent inclusion in the complex ASIT-based therapy.

Keywords: Seasonal allergic rhinitis, allergen-specific immunotherapy, vitamin D, molecular allergy diagnostics, ISAC test, allergen-specific immunoglobulin E (IgE).

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Introduction

Currently, over 500 million people suffer from allergic rhinitis worldwide [1]. In the Republic of Kazakhstan, the incidence of allergic rhinitis among urban residents is 15-20%, and among rural residents, it is 10-15% [2]. In addition, the climatic and geographical features of the area contribute to the widespread incidence of seasonal allergic rhinitis with sensitization to the pollen of grasses, herbs and trees [3]. This feature, along with a low availability of vitamin D to the population in our region, is probably one of the causes of an increase in respiratory allergic diseases [4]. Studies of the vitamin D immunomodulating effect revealed a relationship between the development of allergic diseases and vitamin D deficiency in the blood [5].

Allergen-specific immunotherapy (ASIT) was used as the only effective treatment for seasonal allergic rhinitis for many decades. Treatment is carried out solely with allergens responsible for the development of clinical manifestations of allergic pathology in the particular patient. An increase in polyvalent sensitization in patients with seasonal allergic rhinitis complicates the selection of

causative allergens for ASIT and has a significant impact on the treatment outcome [6].

Identification of sensitization spectrum, formulation of the diagnosis and prescription of ASIT becomes much more complicated if polysensitization is detected, based on the results of traditional methods of specific allergy testing, and clinical and anamnestic data are insufficiently informative [7]. The development of molecular allergy diagnostics helps solving the problem of selecting ASIT in patients with polysensitization. Identification of the allergenic profile sensu ISAC technology allows revealing true and cross-reactive allergens, which increases the effectiveness of ASIT. Molecular allergy diagnostics (ISAC test) defines objective criteria for prescribing ASIT and predicts the efficacy of treatment [8].

Studies conducted on patients with respiratory allergic diseases on the effectiveness of ASIT in monosensitization [9], demonstrated good results in relation to polysensitized patients [10]. To date, application of multicomponent ASIT, combined with the use of vitamin D, in relation to polysensitized patients requires a thorough study via with a clear selection of therapy, and such study should employ the method of molecular allergy diagnostics.

Hence, the objective of our study was to evaluate the efficacy of ASIT in combination with vitamin D in polysensitized patients with seasonal allergic rhinitis of Karaganda Oblast (Kazakhstan).

Table 1. Demographic parameters of patients with seasonal allergic rhinitis in Karaganda Oblast

Parameters	*Experimental group*	*Comparison group*	*p-value*
Number of patients	25	26	
Gender:			
Male, absolute number (%)	12 (48%)	12 (46%)	0.802
Female, percent (%)	13 (52%)	14 (54%)	
Age, years (Mean ± SD)	35 (±9.4)	36 (±9.5)	0.651
18-39 years	29.3(±5.6)	30.1(±5.9)	0.956
40-60 years	45.5(±4.4)	46.4(±4.1)	0.929
Allergy history:			
Positive, absolute number (%)	17 (68%)	20 (77%)	0.437
Negative, absolute number (%)	8 (32%)	6 (23%)	
Disease duration, years (Me+Q_{25-75})	6 (5-7)	7 (6-9)	0.051
Number of positive allergens (Me+Q_{25-75})	5 (4-9)	9 (4-13)	0.221
Total score (Me+Q_{25-75})	11 (9-13)	11.5 (10-13)	0.777
Vitamin D (ng/mL) (Me+Q25-75)	16.32 (13.21-24.33)	15.65 (13.6-23.8)	0.987

Absolute number (%) – number of people with a percentage in the group; Mean ± SD – mean value with standard deviation; Me+Q_{25-75} – median, lower and upper quartile.

Table 2. Characteristics in terms of the status of allergen-specific IgE to inhaled allergens in patients with seasonal allergic rhinitis in Karaganda Oblast

Allergen-specific IgE		*Marker*	*Experimental group*		*Comparison group*	
			Number	%	Number	%
Timothy grass	rPhl p 1	Major	17	68	18	69.2
	rPhl p 2	Minor	4	16	2	7.6
	rPhl p 4	Minor	3	12	4	15.3
	rPhl p 5	Major	5	20	4	15.3
	rPhl p 6	Minor	4	16	1	3.8
	rPhl p 11	Minor	1	4	1	3.84
	rPhl p 12	Minor cross-reactive	1	4	7	26.9
Birch	rBet v 1	Major cross-reactive	5	20	7	26.9
	rBet v 2	Minor cross-reactive	4	16	12	46.1
	rBet v 4	Minor cross-reactive	0	0	1	3.8
Wormwood	nArt v 1	Major	19	76	21	80.7
	n Art v 3	Major cross-reactive	7	28	8	30.7
Ragweed	nAmb a 1	Major	15	60	12	46.1
Russian thistle	nSal k 1	Major	4	16	10	38.4
Plantago plantain	rPla l 1	Major	1	4	0	0
Japanese cedar	nCry j 1	Major	10	40	2	7.6
Cypress	nCup a 1	Major	4	16	1	3.8
Goosefoot	rChe a 1	Major	1	4	2	7.6
Alder	rAln g 1	Major cross-reactive	0	0	1	3.8
Hazel pollen	rCor a 1.0101	Major cross-reactive	3	12	2	7.6
Bermuda grass	nCyn d 1	Major	9	36	10	38.4
Plane tree	rPla a 2	Minor	2	8	3	11.5
	rPla a 3	Minor cross-reactive	3	12	5	19.2
Mercury	rMer a 1	Minor cross-reactive	5	20	13	50

Table 3. Baseline and comparative assessments of the 1st and 2nd points in experimental and comparison groups based on the results of allergen-specific IgE

Parameters	*Experimental group*	*Comparison group*	*p-value*
rPhl p 1 (U/mL) (Me+Q_{25-75}) visit 1	9.9 (1.2-17.7)	6.7 (1.9-9.5)	
rPhl p 1 (U/mL) (Me+Q_{25-75}) visit 2	5.3 (0.9-12.6)	5.4 (1.6-7.9)	
Dynamics between visits 1 and 2	-3.9	-1.2	0.232
p-value	<0.001	<0.001	
rPhl p 5 (U/mL) (Me+Q_{25-75}) visit 1	14.7(2.02-15.5)	10.2(6.6-12.5)	
rPhl p 5 (U/mL) (Me+Q_{25-75}) visit 2	7.3(1-8.1)	8(5.1-9.5)	
Dynamics between visits 1 and 2	-7.4	-2.2	0.841
p-value	0.047	0.064	
rBet v 1 (U/mL) (Me+Q_{25-75}) visit 1	5.06(4.92-32.84)	3.68 (1.38-5.06)	
rBet v 1 (U/mL) (Me+Q_{25-75}) visit 2	2.16(2.03-19.31)	2.96 (1.02-4.36)	
Dynamics between visits 1 and 2	-2.9	-0.72	0.068
p-value	0.042	0.011	
nArt v 1 (U/mL) (Me+Q_{25-75}) visit 1	4.47 (2.04-10.26)	9.45 (0.68-16.13)	
nArt v 1 (U/mL) (Me+Q_{25-75}) visit 2	2.03 (1.03-6.34)	6.87 (0.38-12.69)	
Dynamics between visits 1 and 2	-2.66	-2.58	0.516
p-value	<0.001	0.003	
n Art v 3 (U/mL) (Me+Q_{25-75}) visit 1	1.43 (0.48-24.23)	10.12 (2.75-11.13)	
n Art v 3 (U/mL) (Me+Q_{25-75}) visit 2	0.51 (0.26-15.9)	7.23 (2.1-8.31)	
Dynamics between visits 1 and 2	-0.92	-2.16	0.625
p-value	0.017	0.011	
nAmb a 1 (U/mL) (Me+Q_{25-75}) visit 1	5.99 (1.28-9.16)	3.38 (0.71-10.19)	
nAmb a 1 (U/mL) (Me+Q_{25-75}) visit 2	3.01 (0.54-5.38)	2.59 (0.62-7.31)	
Dynamics between visits 1 and 2	-3.09	-0.79	0.076
p-value	<0.001	0.002	

(Me+Q_{25-75}) – median, lower and upper quartile.

Table 4. Baseline and comparative assessments of the 1st and 2nd points in experimental and comparison groups based on vitamin D concentration in blood and total symptom severity score

Parameters	*Experimental group*	*Comparison group*	*p-value*
Vitamin D (ng/mL) (Me+Q_{25-75}) visit 1	16.32 (13.21-24.33)	15.65 (13.6-23.8)	0.977
Vitamin D (ng/mL) (Me+ Q_{25-75}) visit 2	37.6 (32.4-41.06)	13.4 (11.9-18)	<0.001
Dynamics between visits 1 and 2	21.28	-2.25	
p-value	<0.001	<0.001	
Total score (Me+Q_{25-75}) visit 1	11 (9-13)	11.5 (10-13)	0.777
Total score (Me+Q_{25-75}) visit 3	6 (6-10)	9 (7-11)	0.041
Dynamics between visits 1 and 3	-5	-2.5	
p-value	<0.001	<0.001	

(Me+Q_{25-75}) – median, lower and upper quartile.

Material and Methods

Study design

We conducted an open randomized controlled trial on the efficacy of ASIT in combination with vitamin D. It was carried out from July 2019 through September 2020 at *Divera Allergy Center* in Karaganda (Kazakhstan).

Study object

The study included 51 patients aged 18-60 years with a diagnosis of seasonal allergic rhinitis. Verification of the seasonal allergic rhinitis diagnosis was performed on the basis of the anamneses and complaints of patients, an objective examination, and the collection of an allergy anamnesis. Two weeks prior to the study, patients were excluded from taking all medications for allergic rhinitis.

The inclusion criteria were: patients 18 to 60 years old; the presence of seasonal allergic rhinitis for at least two years. Exclusion criteria: refusal to participate in the study; use of vitamin D preparations; receiving ASIT before the study; the presence of severe somatic pathology; pregnant and lactating women; age under 18 and over 60 years old.

All study subjects were randomized into two groups, comparable in terms of the number of participants, gender, age, and severity of the disease course. The experimental group received ASIT in combination with vitamin D according to the scheme determined by the level of deficiency in the patient blood serum (n=25); whereas the comparison group received ASIT in accordance with the conventional scheme (n=26). Patients were subjected to sublingual ASIT (Antipollin, Burli LLP, Kazakhstan). The selection of the composition of the preparation was carried out based on the results of sensitization to the major components of allergens (ISAC test). Patients received a preseason course of ASIT over similar periods of time, in identical doses, with a gradual increase in dosage. The selection of the vitamin D preparation dose was performed sensu international standards of treatment, taking into account an initial concentration of vitamin D in the blood to achieve the expected effective level of 40 ng/mL [4,11]. The follow-up period in conjunction with the screening period lasted 1.5 years. At visit 1 before ASIT and at visit 2 after ASIT (after 2.5 months), blood concentration of vitamin D was measured, and specific immunoglobulin E (IgE) content was identified via the ISAC test.

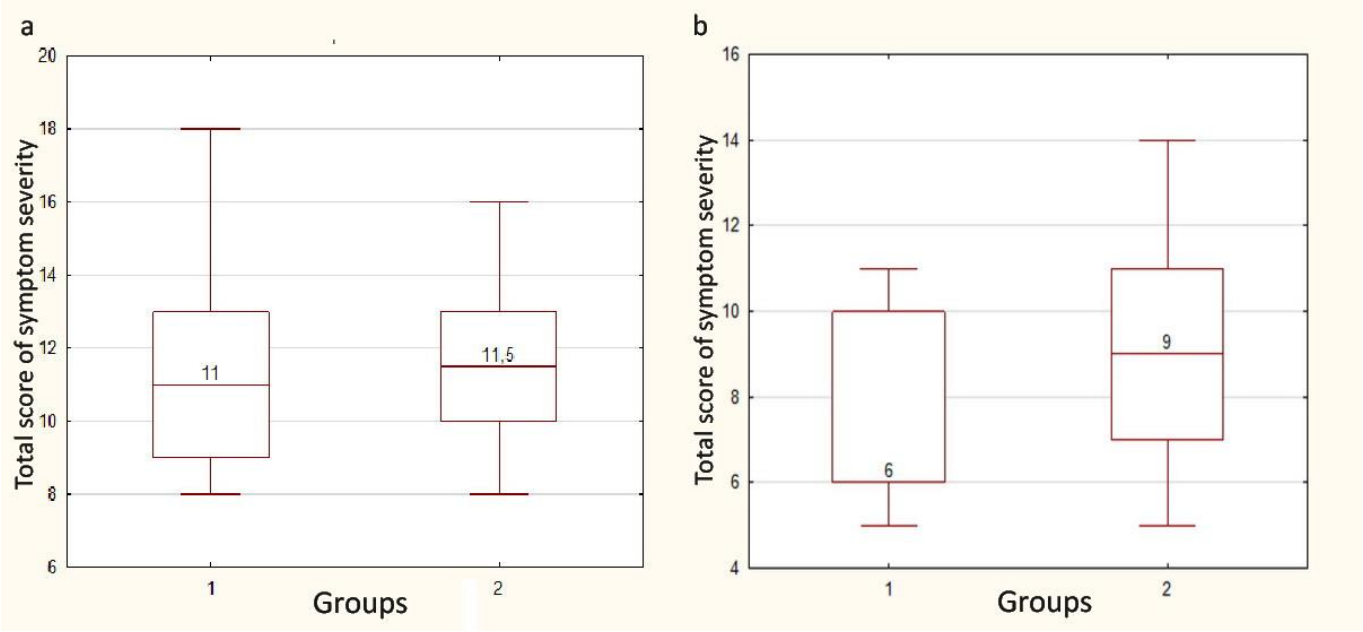

Figure 1. Median total symptom score of disease severity. a – before treatment; b – after treatment in the experimental group (1) and the comparison group (2).

Questionnaire

To monitor the clinical effectiveness of ASIT at visit 1 (before treatment) and visit 3 (8 months after the onset of treatment, during the next seasonal exacerbation), a questionnaire was employed to assess the severity of symptoms of seasonal allergic rhinitis. Self-assessment was based on an adapted questionnaire described by Pfaar et al. [12]. The questionnaire included evaluating nose itch, nasal congestion, watery/mucous nasal discharge, sneezing, itchy eyes, and watery eyes. An assessment of each symptom was expressed on a 3-point scale depending on the severity of the manifestation: 0 – no symptoms; 1 – mild degree (the symptom is minimally pronounced, occurs 1-3 times a week; the state of health is of no concern); 2 – moderate degree (the symptom is pronounced, has a frequency of manifestation 4-5 times a week, moderately affects well-being and sleep); 3 – severe degree (the symptom is very pronounced, has a systematic and persistent character on a daily basis, imposes a pronounced impact on sleep and labor activity). The maximum score constitutes 18 points, which is interpreted as a severe degree of manifestations. A severity score of 1 to 6 suggests mild severity, 7-12 corresponds to a moderate severity, and ≥13 points suggest severe degree of manifestation (Author's Certificate for Invention No. 14535 of January 19, 2021).

Laboratory tests

Blood sampling for the ISAC test and vitamin D content was conducted from 8:00 am to 12:00 pm (noon) at a network of government-licensed laboratories (*Olymp*).

ISAC test

The serum level of allergen-specific IgE was measured using ISAC technology (ThermoFisher Scientific, Sweden), which allowed identifying 112 antigens (allergic components from 51 sources). Reference values of allergen-specific IgE below 0.35 ISU-E were regarded as non-detectable levels. A result between 0.3 and 0.9 ISU-E was considered low level, 1-14.9 ISU-E was interpreted as moderate/high level, and values >15.0 ISU-E suggested very high level.

Vitamin D

The content of vitamin D in blood serum was determined via the chemiluminescence method on Beckman Coulter DxI automatic modular analyzer (USA). The normal range for serum vitamin D levels was at least 30 ng/mL [4,11]. The results in the range of 21-29 ng/mL were regarded as vitamin D insufficiency, and below 20 ng/mL as vitamin D deficiency.

Statistical data processing

All statistical tests were performed using Statistica software version 13.0 for Windows (2019). The results were analyzed using descriptive statistics methods. Quantitative variables were analyzed to assess the nature of the distribution (Shapiro-Wilk test). Categorical data are presented as absolute numbers and as a percentage of the entire group. For quantitative data, central trends were measured: for data with a distribution close to normal, the result is expressed as a mean ± standard deviation; for data with a distribution that differs from normal (asymmetric), the result is expressed as a median and interquartile range. To search for differences in the comparison groups among parameters expressed in quantitative variables, the calculation of the Mann-Whitney test was employed. The Wilcoxon test was used to search for differences in two related (dependent) groups. The critical level of significance of differences in the groups was set at $p<0.05$.

Results

The demographic characteristics of patients included in experimental and comparison groups, based on the results of the last examination, are presented in *Table* 1. The study involved 51 people (24 men, 27 women), 25 of those received ASIT in combination with vitamin D (experimental group), while 26 subjects received the conventional ASIT regimen (comparison group).

A comparative analysis using the Mann-Whitney test demonstrated that, based on examined parameters, the groups of patients, in which different ASIT methods were used during the treatment period, were comparable at baseline (p>0.05): patients of both groups did not differ in terms of demographic indicators (*Table* 1). Female patients predominated both in the experimental group and in the comparison group (52% and 54%, respectively). The average age of patients in the experimental group was 35 years, while in the comparison group, it was 36 years. Patients with a positive allergy anamnesis prevailed in both experimental and comparison groups (68% and 77%, correspondingly). The duration of the disease averaged 6 yrs. in the experimental group and 7 yrs. in the comparison group. The number of positive allergens implied the presence of polysensitization in patients. In the comparison group, the median number of positive allergens was 9, whereas 5 positive allergens were detected in the experimental group. Symptoms of the severity of seasonal allergic rhinitis were expressed by a total score and were comparable among groups (11 points in the experimental group vs. 11.5 points in the comparison group). The median vitamin D content in blood serum before the study had no statistical differences between the experimental and comparison groups (16.32 ng/mL and 15.65 ng/mL, respectively). The median values implied the presence of vitamin D deficiency in patient blood serum in both groups.

Table 2 exhibits the quantitative ratio of identified allergens. It was shown that both groups were comparable before the onset of the study in terms of the quantitative ratio of identified allergens. It should be pointed out that the vast majority of patients in the experimental and comparison groups had sensitization to the major components of the wormwood allergen (76% and 80.7%, respectively).

The level of allergen-specific IgE was chosen as a laboratory biomarker characterizing the efficacy of ASIT. Efficacy dynamics between visits 1 and 2 within study groups demonstrated statistically significant changes in allergen-specific IgE (rPhl p 1 = 0.232; rPhl p 5 = 0.841; rBet v 1 = 0.068; nArt v 1 = 0.516; n Art v 3 = 0.625; nAmb a 1 = 0.076) in both groups; and in the experimental group, we observed a greater decrease vs. the comparison group. Dynamic assessment of the treatment efficacy in the studied groups showed no statistically significant differences (*Table* 3).

Table 4 presents the changes in the concentration of vitamin D in the blood before and after treatment in the study groups. The dynamics of vitamin D levels was positive in the experimental group (ASIT in combination with vitamin D), which was reflected by an increase in blood content of vitamin D between visits 1 and 2 (16.32 ng/mL vs. 37.6 ng/mL, respectively). In the comparison group, where ASIT was performed sensu the traditional scheme, the dynamics of the vitamin D level in blood between visits 1 and 2 was negative, which was demonstrated by its further decline (15.65 ng/mL vs. 13.4 ng/mL, correspondingly). The values of vitamin D levels in the study groups, detected at visit 2, demnstrated statistically significant differences between the experimental and comparison groups (p<0.001).

Additionally, patients were assessed for symptoms of allergy severity using a specific questionnaire (*Table* 4). Evaluation of the dynamics of efficacy between visits 1 and 3 within the study groups showed statistically significant changes in both groups (p<0.001). Besides, the posttreatment total score exhibited statistically significant changes between the two groups (p<0.041). This finding suggested the best efficacy of ASIT in combination with vitamin D in the experimental group.

The clinical score, expressed as the median of the total disease severity symptom score, is presented in *Figure* 1 (a – before ASIT and b – after ASIT during the next flowering season).

The final examination of patients was performed at visit 3, 8 months after the first examination (5.5 months after the completion of medicamentous therapy). The results of the final examination, based on the completion of the severity symptom questionnaire, are presented in *Figure* 1 (b). In the experimental group, the median of the total symptom severity score declined by 46% (from 11 points to 6 points); whereas in the comparison group, it decreased by 22% (from 11.5 points to 9 points), which implied the best clinical efficacy of the adapted ASIT regimen.

Discussion

Our results suggested that the adapted scheme of ASIT in combination with vitamin D in polysensitized patients with seasonal allergic rhinitis of Karaganda Oblast (Kazakhstan) showed better efficacy, compared with the conventional ASIT scheme. The immunomodulatory effects of vitamin D may play a role in enhancing the clinical efficacy of immunotherapy. In this regard, it was proposed to include vitamin D as an independent therapeutic component in the treatment regimens for respiratory allergic diseases in children and adults, as well as in the ASIT regimen as an immunomodulatory component [24].

In the present study, both treatment schemes resulted in an overall clinical improvement. Regarding the assessment of including vitamin D as an immunomodulatory component in the ASIT regimen, our results implied better efficacy relative to the standard treatment regimen. As shown in recent European studies, the inclusion of vitamin D in the ASIT regimen yielded a higher efficacy in relation to the clinical symptoms of allergic rhinitis, and also reduced the frequency of symptomatic therapy [25]. Clinical trials of ASIT with controlled intake of high doses of vitamin D showed progressive clinical improvement after the second and third years of therapy, suggesting an earlier start of immunomodulation [26]. Within the framework of our study, further observation of patients who underwent a course of ASIT in combination with vitamin D is of particular scientific interest, which could allow assessing the prolonged effect of treatment.

Research on the immunomodulatory role of vitamin D in allergic diseases has been ongoing for many years. In recent years, the studies were actively carried out on the role of vitamin D in the development of allergic respiratory pathology [20, 21]. In general, in allergic diseases, the effect of vitamin D on the human immune system is implemented via the stabilization of mast cells, inhibition of dendritic cells, and stimulation of T cells that secrete IL-10 [22, 23]. Many studies have reported the efficacy of vitamin D monotherapy in allergic rhinitis.

The use of molecular allergy diagnostics in our study made it possible to accurately select the allergenic composition of the preparation for ASIT with the exclusion of low-efficiency components and increase in the reliability of the results. There are many studies in the databases of evidence-based medicine that investigated the use of molecular allergy diagnostics for the selection and monitoring of the efficacy of ASIT in polysensitized patients with seasonal allergic rhinitis [8, 13].

Sensu 2017 international recommendations of the European Academy of Allergology and Clinical Immunology (EAACI), the determination of the allergen-specific IgE level was indicated as a biomarker for monitoring the clinical effectiveness of ASIT [8]. In most patients receiving ASIT, an initial increase in the level of allergen-specific IgE in the blood serum was usually observed already in the first few months of treatment. This fact does not entail a change in the clinical situation or exacerbation of the disease and is a natural response to ASIT [16].

In our study, an initial reduction in the level of allergen-specific IgE was detected after 2.5 months from the onset of treatment, i.e., after the full completion of the 1st ASIT course. These data are similar to the results of the 2015 study by Wollmann et al., which demonstrated an initial decline in the level of allergen-specific IgE two weeks after the onset of treatment. A progressive decrease in allergen-specific IgE was detected after 6-12 months from the onset of ASIT [17]. Different results were demonstrated in a 4-year randomized controlled trial by James et al. conducted in 2011. After two years of ASIT, they discovered a slight increase in the level of allergen-specific IgE to the components Phl p 1 and Phl p 5 of Timothy grass. Only four years after the onset of treatment, they observed a decrease in the level of allergen-specific IgE [18]. It should be noted that these results were obtained in ASIT conducted by subcutaneous method.

Study limitations

The strengths of our research are as follows. First, our study was a complete randomized controlled trial. Second, for the first time in the Republic of Kazakhstan, a study was conducted on ASIT-based therapy in combination with vitamin D, as well as on the effect of including vitamin D preparations on the outcome of ASIT. In addition, serum vitamin D deficiency was detected in patients with seasonal allergic rhinitis. Therefore, prior to starting immunotherapy, it is recommended to examine the level of vitamin D in the blood of patients with seasonal allergic rhinitis [24].

Weaknesses of this study include its small sample size due to the limited number of patients and resources. Besides, solely one course of therapy was administered, suggesting a short follow-up period. It is worth noting that in our study, ASIT was performed with allergen extracts rather than with purified recombinant allergens, which may also suggest a weakness of this study. Since the selection and evaluation were carried out taking into account the components of allergens, it is also desirable to select the ASIT preparation considering the composition of major allergenic components. As a result, ASIT was carried out with a preparation that included not only true major components, but also minor and cross-reactive components, regardless of the presence of sensitization to those. Further study of using molecular allergy diagnostics for the selection of ASIT, based on recombinant allergens, and monitoring of its efficacy in combination with vitamin D is required.

Conclusion

Hence, as a result of our study, we established that the adapted scheme of ASIT in combination with vitamin D in polysensitized patients with seasonal allergic rhinitis in Karaganda Oblast (Kazakhstan) was more effective than the standard ASIT scheme. This was expressed by positive dynamics, with a reduction in the symptoms of seasonal allergic rhinitis and a decline in the content of allergen-specific immunoglobulin E in the blood after the first treatment course. Therefore, in patients with seasonal allergic rhinitis, it is necessary to determine the vitamin D concentration in regions with its low availability in order to subsequently include it in the complex ASIT-based therapy.

Conflict of Interest

None declared. This material has not been previously announced for publication in other periodicals and is published for the first time.

Funding

When carrying out this project, there was no funding from third-party organizations and medical institutions.

Ethical approval

The study was performed in accordance with Good Clinical Practice and the principles of the 1964 Declaration of Helsinki and its later amendments, along with comparable ethical standards. The study protocol was approved by the Bioethics Committee of Karaganda Medical University (protocol No. 14 of March 11, 2019). Prior to the study, all participants signed the written informed consent.

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