

## Реферати

**КЛІНІКО-НЕВРОЛОГІЧНІ  
ТА НЕЙРОВІЗУАЛІЗАЦІЙНІ ФАКТОРИ,  
АСОЦІЙОВАНІ З ПОСТІНСУЛЬТНОЮ  
ВТОМОЮ НА ПРОТЯЗІ ДРУГОГО ПІВРІЧЧЯ  
ПІСЛЯ РОЗВИТКУ ГОСТРИХ ПОРУШЕНЬ  
МОЗКОВОГО КРОВООБІГУ**

Дельва І.І.

Постінсультна втома (ПІВ) – розповсюджене ускладнення гострих порушень мозкового кровообігу (ГПМК). Метою роботи було ідентифікувати клінічні та нейровізуалізаційні фактори, асоційовані з різними компонентами ПІВ на протязі другого півріччя після розвитку ГПМК. Обстежено 194 пацієнти через 6, 9 та 12 місяців після ГПМК. Глобальну ПІВ та окремі її компоненти вимірювали за допомогою багатомірної шкали оцінки втоми (MIF-20). Виявлена достовірно вища розповсюдженість глобальної та фізичної ПІВ при інсультах, порівняно з транзиторними ішемічними атаками. В одновимірному логістичному регресійному аналізі знайдено достовірні асоціації між ступенем функціональної неспроможності, згідно модифікованої шкали Ренкіна, та ризиком наявності глобальної і фізичної ПІВ. Наявність інфарктенторіальних інфарктів асоціювалася з підвищеним ризиком глобальної ПІВ, а ступінь лейкоареозу, згідно шкали Фазекас, прямо асоціювалася з підвищеним ризиком психічної та мотиваційної ПІВ. Рівень функціональної неспроможності, інфарктенторіальна локалізація інфарктів та ступінь лейкоареозу можуть розглядатися як прогностичні фактори наявності ПІВ протягом другого півріччя після розвитку ГПМК.

**Ключові слова:** постінсультна втома, гострі порушення мозкового кровообігу, одновимірний логістичний регресійний аналіз.

Стаття надійшла 21.11.17 р.

**КЛИНИКО-НЕВРОЛОГИЧЕСКИЕ  
И НЕЙРОВИЗУАЛИЗАЦИОННЫЕ ФАКТОРЫ,  
АССОЦИИРОВАННЫЕ С ПОСТИНСУЛЬТНОЙ  
УСТАЛОСТЬЮ НА ПРОТЯЖЕНИИ ВТОРОГО  
ПОЛУГОДИЯ ПОСЛЕ РАЗВИТИЯ ОСТРЫХ  
НАРУШЕНИЙ МОЗГОВОГО КРОВООБРАЩЕНИЯ**

Дельва И.И.

Постинсультная усталость (ПИУ) – распространенное осложнение острых нарушений мозгового кровообращения (ОНМК). Целью работы было идентифицировать клинические и нейровизуализационные факторы, ассоциированные с разными компонентами ПИУ на протяжении второго полугодия после развития ОНМК. Обследовано 194 пациента через 6, 9 и 12 месяцев после ОНМК. Глобальную ПИУ и отдельные ее компоненты измеряли с помощью многомерной шкалы оценки усталости (MIF-20). Выявлена достоверно большая распространенность глобальной и физической ПИУ при инсультах, в сравнении с транзиторными ишемическими атаками. В одномерном логистическом регрессионном анализе найдены достоверные ассоциации между степенью функциональной несостоятельности, согласно модифицированной шкале Рэнкина, и риском глобальной и физической ПИУ. Инфарктенторіальні інфаркти прямо асоціювалися з підвищеним ризиком глобальної ПІУ, а ступінь лейкоареозу, по шкалі Фазекас, - з підвищеним ризиком психічної і мотиваційної ПІУ. Рівень функціональної несостоятельности, інфарктенторіальна локалізація інфарктів і ступінь лейкоареозу можуть розглядатися в якості прогностических факторів наявності ПІУ на протязі другого полугодія після розвитку ОНМК.

**Ключевые слова:** постинсультная усталость, острые нарушения мозгового кровообращения, одномерный логистический регрессионный анализ.

Рецензент Литвиненко Н. В.

DOI 10.26724/2079-8334-2018-4-66-56-62

УДК 616-022.854-092.19-085.218.373(477.4)(477.8)

S.O. Zubchenko<sup>1</sup>, O. Sharikadze<sup>2</sup><sup>1</sup>Danylo Halytsky Lviv National Medical University, Lviv<sup>2</sup>Shupyk National Medical Academy of Post-Graduate Education, Kyiv

**ANALYSIS OF SENSITIZATION FEATURES TO WEED POLLEN AND EFFICACY  
OF ALLERGEN IMMUNOTHERAPY IN PATIENTS OF THE CENTRAL  
AND WESTERN REGIONS IN UKRAINE**

E-mail: svitlana\_zu@meta.ua

Incidence of sensitization is changing geographically based on multiple environmental factors. About 1.5 thousand different types of weeds are common in Ukraine. Climatic and geographical conditions such as air temperature, humidity and plant diversity in the region is of great importance in the prevalence of allergic diseases. Allergy to weeds is a global problem due to development of respiratory allergy – seasonal allergic rhino-conjunctivitis (hay fever) with/without bronchial asthma in patients living in Ukraine. Allergen immunotherapy is a disease-modifying treatment for patients with seasonal hay fever with/without bronchial asthma. However, in Ukraine there are little data on the efficacy of sublingual form of allergen immunotherapy. The use of standardized sublingual immunotherapy is efficient in treating patients with seasonal hay fever with/without bronchial asthma.

**Key words:** *Ambrosia, Artemisia*, molecular allergodiagnosis, VAS, SLIT efficacy.

*The present study is a fragment of the research project “Peculiarities of allergic genesis diseases formation in children of all ages and the possibilities of their prevention and treatment” (State Registration No. 0111U002801)*

There are over 1.5 thousand types of weeds on the territory of Ukraine. They not only significantly pollute agricultural land – some of them possess strong allergenic activities [5]. Allergy to weed pollen is considered the late wave of hay fever, which usually begins in the second half of summer (end of July to August) and lasts until the first frosts [9]. However, today these data are relative due to global warming

and environmental pollution, which greatly affects the terms and duration of weed pollination and changes the antigenic structure of pollen [6].

The most widespread clinically significant weed allergens worldwide are *Artemisia*, *Ambrosia*, pigweed, tumbleweed, and fleaworts.

*Ambrósia artemisiifólia* comes from North America; its distribution on the territory of Ukraine began in 1960-1970 from Crimea [1]. Today, the total area of *Ambrosia* occupies 1 328 377.863 hectares. It has been recorded in 23-24 regions of Ukraine, most frequently in the southern and eastern parts of Ukraine. Eventually, *Ambrosia* "captured" the agro-climatic zones of the central part of Ukraine. *Ambrosia* appeared in Western Ukraine over 20 years ago, its area is growing rapidly. Therefore, according to our observation, latent sensitization to *Ambrósia artemisiifólia* pollen is most frequently detected in patients of the western regions of Ukraine [5].

*Artemisia vulgaris* is a native plant for Europe and Asia [4]. Throughout Ukraine, it grows in fields, pastures, meadows, gardens, parks, near water, etc. Besides, it is often artificially cultivated as a medicinal plant.

Despite significant prevalence and allergenic properties of the pollen of these weeds, there are little data on the incidence of sensitization caused by *Ambrosia* and *Artemisia* in Ukraine. Instead, the development of molecular diagnostics nowadays enables to clearly identify the major allergen of weed pollen and, thus, offer the patient a personalized choice of allergic immunotherapy (AIT) with a prediction of its efficacy [8].

**The purpose** of the study was to compare peculiarities of sensitization to weed allergens in patients of central and western regions in Ukraine; to assess SLIT efficacy in people of different ages with allergic rhinitis (AR) and bronchial asthma (BA) following two years of treatment.

**Materials and methods.** Study design. This cohort prospective study was carried out in medical centers of Central and Western Ukraine: at the Department of Pediatrics № 1, Shupyk National Medical Academy of Postgraduate Education, National Children's Hospital "OKHMATDIT" and the Children's Outpatient Clinic "OKHMATDIT" in Kyiv; Department of Clinical Immunology and Allergology of Danylo Halytsky Lviv National Medical University and Lviv Regional Medical Center of Clinical Immunology and Allergology, Ukraine. The study was being conducted for three years from October 2014 to December 2017. The study involved children and adults with bronchial asthma and / or allergic rhinitis or hayfever who were treated or consulted at the clinic. Clinical diagnosis of AR and / or BA, intermittent course, was defined by criteria, ICON (2012), GINA (2014).

Clinical parameters selected for the evaluation of bronchial asthma control were day and night symptoms, activity restriction, need in heaters or rescue medications, exacerbations, and peak expiratory flow (PEF) or forced expiratory volume (FEV1) measurements (according to age) on visiting the clinic / diagnostic center.

In general, 1400 patients aged from 3 to 65 years were examined, among them 820 (58.5%) – from Central (Kyiv, Vinnytsia, Chernihiv) regions and 580 (41.4%) – Western regions (Lviv, Ternopil, Ivano-Frankivsk, Volyn). The exclusion criteria were serious and / or uncontrolled asthma, children / adults who were treated with SIT in the previous stages; children / adults who have contraindications to SIT.

Thus, 105 individuals from the Central region (66 (62.8%) children and 39 (37.2%) adults), 80 people from the Western region (24 (30.0%) children and 56 (70.0%) adults) were selected for further study according to inclusion criteria. These were the age 3 to 65 years old, clinical diagnosis of intermittent AR and / or intermittent BA, controlled, determined by the criteria ICON (2012) and GINA (2014), sensitization to extracts of *Ambrosia* and *Artemisia* allergens (based on the results of skin tests).

The examined individuals followed the procedure (evaluation of allergy symptoms, case history, skin test, total and specific IgE). Clinical monitoring was conducted every 6-12-24 months during visits to outpatient clinics / consultations. Skin tests, cytology of the nasal mucosa smear, allergen-specific IgE-assessments, assessment of allergic symptoms in medical history (nasal symptoms, conjunctival symptoms, episode of bronchial asthma, skin manifestations), and general examinations were performed. ImmunoCAP (Thermo Scientific, Uppsala, Sweden) was used to determine the levels of specific antibodies of IgE class following the manufacturer's recommendations. Three marker allergens of genuine sensitization to *Artemisia* (nArt v 1, rArt v 3) and *Ambrosia* (rAmb a 1) pollen were determined. The levels of sIgE > 0.35 KU/l were considered to be positive.

Accordingly, patients were divided into two groups: I. BA and / or AR of the individuals who had undergone a two-year course of immunotherapy using sublingual allergens containing "Ambrosia", "Artemisia" mixtures, Diater, Spain. The control group consisted of persons with the AR and / or BA, sensitization to *Ambrosia*, *Artemisia*, who received only symptomatic treatment, not SLIT. More detailed information is given in table 1.

The study was conducted in accordance with the seventh revision of the principles of the Declaration of Helsinki on Human Rights (2013). Information consent was received from patients / or parents.

Skin tests. They were performed on the flexor area of the forearm, avoiding the wrist and cubital fossa. The forearm was encoded with a marker pen to test the allergens from a distance of about 3 cm. A drop of the extract settled to the specified position [10]. Then, each drop of skin was pricked vertically using a standard syringe needle. The solution extract was washed with tissue paper. The results of skin prick tests were evaluated in 15 minutes following European requirements. The following standard inhaled allergens were tested (Diater-Laboratories, Spain): Der. pteronyssinus, Der. farina, a mixture of spring trees, a mixture of herbs, Artemisia, Ambrosia, Alternaria alternata, cats, dogs. These extracts were used for all patients at the beginning of the study and during observation. Both positive and negative test controls used a solution of histamine hydrochloride in a concentration of 10 mg / ml and 0.9% salt solution, respectively.

The skin reaction was evaluated in 15 minutes. As a sample in which 3-mm papules were formed, or when the papules exceeded the size of a negative control for more than 3 mm, it was considered positive [2]. The study was conducted in accordance with the seventh revision of the principles of the Declaration of Helsinki on Human Rights (2013). Information consent was received from patients / or parents.

Table 1

Clinical characteristics of patients

Indicator	Group I (Central region)	Group I (Western region)	Control group
Number	105	80	20
Sex, n (%)			
Male	66 (60.8%)	46 (57.5%)	13 (65%)
Female	39 (39.2%)	34 (42.5%)	7 (35%)
Age (M±m), years	12.3±2.95	16.5±2.98	13.5±3.48
Clinical symptoms, n (%)*			
Rhinitis	102 (97.1%)	77 (96.2%)	19 (95%)
Rhinoconjunctivitis	54 (51.4%)	63 (78.7%)	13 (65%)
Allergic asthma	8 (7.6%)	4 (5.0%)	3 (15%)
Wheezing	7 (6.6%)	3 (3.7%)	–
Upper palate itching	11 (10.4%)	11 (13.7%)	3 (15%)
Cough	60 (57.1%)	46 (57.5%)	13 (65%)
Sneezing	86 (81.9%)	66 (82.5%)	16 (80%)
The results of SPT (average diameter of papule, mm)	4.7±2.7 – Artemisia 11.2±3.4 – Ambrosia	8.2±2.8 – Artemisia 6.7±2.6 – Ambrosia	7.2±2.5 – Artemisia 9.7±3.3 – Ambrosia
Patients with polyvalent sensitization (SPT), n (%)	100 (95.2%)	74 (92.5%)	20 (100%)
Monosensitized (%)			–
Ambrosia	3 (50.9%)	2 (43.8%)	
Artemisia	2 (49.1%)	4 (56.2%)	

\*- symptom combination is possible

Specific immunotherapy. Totally, 185 people in the Western and Central regions of Ukraine with BA and / or AR received a two-year course of immunotherapy using sublingual allergens Artemisia and Ambrosia Diater, Spain. Patients in the first group from both regions received SLIT by the following treatment protocol: drug was administered by single spraying on a sublingual area daily [11]. The initial phase lasted 6 months (a total dose for a patient was – 144.9 HEP for Ambrosia, 40.5 HEP – Artemisia), a supporting phase lasted for the next 18 months (a total allergen dose was on average 333.9 HEP for Ambrosia and 95.4HEP – Artemisia). After the first dose of the drug was taken by the patients, they stayed in the clinic under supervision for 40 minutes to detect and record possible adverse effects; then the drug was introduced by patients or their parents themselves, the control of possible adverse effects was carried out via Internet by an allergist.

During the monitoring period, patients had four visits per year, and if necessary, an additional control check-up was possible. Patients in both groups underwent basic protocol therapy [7]. If required, second generation antihistamines, inhalation beta-agonists, inhalation corticosteroids and leukotriene inhibitors were prescribed to control breathing symptoms.

Statistical analysis. The data that met normal distribution criteria, such as age and disease duration, were analyzed using Student's t-test for independent variables. Other non-parametric data were compared with the chi-square test. The summary odds ratio, 95% confidence intervals and standard errors using random-effects models were also computed.

Statistical processing of the obtained results was made using the standard statistical package Statistical for Windows 7.0.

For the statistical significance of the results, we used a value of  $\alpha=0.05$ . The p value of the statistical test is used for accepting or rejecting the hypothesis ( $p \geq \alpha$ : hypothesis is accepted;  $p < \alpha$ : hypothesis is rejected). All results are elaborated, documented and presented in absolute and relative numbers and with statistical results using statistical markers.

**Results of the study and their discussion.** Among 580 patients in the Western region, positive prick-tests were revealed in 557 (96.0%) individuals, in particular, 153 (27.5%) showed monosensitization: 50 (32.7%) – house dust mites, 39 (25.5%) – mixture of spring trees, 37 (24.2%) – grass mixture, 11 (7.1%) – cat, 10 (6.5%) – *Alternaria alternata*, and monosensitization to dogs was not detected. Monosensitization to *Artemisia* was revealed in 4 (2.6%) individuals, to *Ambrosia* – 2 persons (1.3%).

At the same time, the majority – 404 (72.5%) patients were polysensitized and showed different sensitization options. Among polysensitized individuals, positive SPT to *Artemisia* and *Ambrosia* were detected in 67 (16.6%) and 26 (6.4%) individuals, respectively, of which a combined sensitization to two types of weeds was found in 15 (16.1%) patients.

Thus, sensitization to *Artemisia* was detected in 71 (12.7%) patients from the Western region. Concerning *Ambrosia*, positive SPT were in 28 (5.0%) individuals, predominantly among polysensitized ones. Notably, monosensitization to *Ambrosia* was confirmed in two (100.0%) children of immigrants from Crimea, and polysensitization was found only among adult local people.

Among 820 patients in the central region, positive SPT were found in 794 (96.8%) individuals, in particular, 248 (31.2%) showed monosensitization (83 (33.5%) – to house dust mites, 57 (22.9%) – mixture of spring trees, 53 (21.4%) – *Alternaria alternata*, 36 (14.5%) – mixture of grass, and 14 (5.6%) – cat. Monosensitization to *Artemisia* was detected in 2 (0.7%) individuals, to *Ambrosia* – in 3 (1.1%) persons. Respectively, polysensitization in different combinations of allergen extracts was found in 546 people (68.8%). Among polysensitized individuals, 84 (15.4%) patients had positive SPT to *Artemisia* and 124 (22.7%) to *Ambrosia*, including 30 patients (14.4%) with a combined sensitization to two types of weeds. In general, in patients in the Central region, sensitization to *Artemisia* was detected in 86 (10.8%), to *Ambrosia* – in 127 (16.0%) individuals. Moreover, positive SPT to *Ambrosia* were mostly observed among polysensitized local residents without association with certain age groups.

Having compared peculiarities of sensitivity to weed pollen among patients in Western and Central Ukraine, we detected that positive SPT to *Artemisia* were by 1.2 times more frequent among patients in the western parts than in the central regions. Considering sensitization to *Ambrosia*, it was, on the contrary, by 3.2 times higher among patients in the central region compared to the western one. Concerning a combined sensitization with two types of weeds among polysensitized individuals, it was by 1.12 times more common among patients in the western region. It should be mentioned that in the central region, sensitization to *Ambrosia* was more frequent among polysensitized locals without age-specific features, among western patients – monosensitization occurred only among children from Crimea, and polysensitization was present only in the local adult population.

In general, the most common sensitizing allergen was house dust mite in the Central and Western regions of Ukraine; and no individuals with monosensitization to a dog were detected in both regions. It should be noted that the prevalence of positive SPT to *Alternaria alternata* was higher among patients in the central areas, and sensitization to grass – among patients in the Western regions of Ukraine. Concerning sensitization to spring trees, no specific features between regions were revealed.

Since among polysensitized patients in both experimental groups there were individuals with positive skin prick tests to *Artemisia* and *Ambrosia* in combination with herbs, false-positive results of skin prick tests due to the presence of sIgE to cross-reactive markers of profilin (Phl p 12) and polcalcin (Phl p 7) could be expected. As noted above, patients with combined sensitization to two types of weeds (*Ambrosia* + *Artemisia*) were in both experimental groups. The average data from sIgE levels to nArt v 1, rArt v 3, rAmb a 1 and SPT data in regions are presented in Table 2.

Table 2

**Results of SPT and Component Research in Patients in Central and Western regions of Ukraine**

Groups of patients	SPT to <i>Artemisia</i> (Ø of papule mm), M±m	SPT to <i>Ambrosia</i> , (Ø of papule mm), M±m	nArt v 1 kU/L, %	nArt v 1+rArt v 3 kU/L, %	rAmb a 1 kU/L, %	nArt v1+rAmb a1 kU/L, %
Western region	8.2±2.8	6.7±2.6	57 (80.3%)	3 (4.2%)	17 (60.7%)	7 (7.07%)
Central region	4.7±2.7	11.2 ±3.4	60 (69.7%)	3 (3.4%)	98 (77.1%)	17 (7.9%)

As it is seen from table 2, among 71 patients in the western region with positive SPT to *Artemisia*, the presence of major allergen of *Artemisia* nArt v 1 was found in 73 (94.4%) individuals. Among them, it was in combination with another major allergen of *Artemisia* rArt v 3 in three persons and co-sensitization with major allergen of *Ambrosia* – in seven persons. At the same time, among 28 patients with positive SPT to *Ambrosia*, the presence of major allergen to *Ambrosia* rAmb a 1 was found in 24 (85.7%) individuals, in seven of them – in combination with nArt v 1.

Among 86 patients in the Central region with positive SPT to *Artemisia*, the presence of genuine allergy was confirmed in 80 (93.0%) persons, among them two major molecules of *Artemisia* were detected

in three patients, and the presence of co-sensitization to Artemisia and Ambrosia was recorded in 17 cases. Out of 127 patients with positive SPT to Ambrosia, genuine allergy was confirmed in 115 (90.5%) individuals; in particular, 17 persons were co-sensitized to Ambrosia and Artemisia.

Thus, the results of component diagnostics confirmed the results of SPT studies and indicated that genuine sensitization to Artemisia prevailed among patients in Western regions of Ukraine, and to Ambrosia – in central ones. The presence of co-sensitization to Art v 1 and Amb a 1 was almost the same in the Central and Western regions: 7.9% and 7.07%, respectively.

In component studies, attention was paid to several features:

1) the presence of major allergens of Artemisia (nArt v 1) or Ambrosia (rAmb a 1) was confirmed in all monosensitized patients;

2) there was a discrepancy between a high level of sensitization to Ambrosia and Artemisia and the presence of significant clinical manifestations of allergy, especially in children under the age of 6;

3) about 30% of the examined patients and, to a greater extent, children had positive SPT to Ambrosia and Artemisia, provided they had monosensitization associated with major allergen of Ambrosia;

4) in anamnesis of patients with detected major allergen of Artemisia Art v 3, no complaints related to food allergy were observed.

According to the results of molecular studies, immunotherapy was used for 185 patients of the central (105 individuals) and western (80 individuals) regions of Ukraine, who constituted the first group of research. For various reasons and, primarily, because of financial problems, 77 individuals refused to receive allergy immunotherapy and were treated symptomatically. Among them, 20 persons represented a control group of the study. Following six months of therapy, "Rhinoconjunctivitis" symptom decreased by almost twice ( $1.4 \pm 1.2$ ) during the first seasonal period of pollination;  $P < 0.05$ ; and in 12 and 24 months of SLIT, the data were  $0.94 \pm 0.8$  and  $0.42 \pm 0.6$ ;  $P < 0.01$ , respectively. Other symptoms were also markedly reduced. Cough before the start of therapy was  $2.4 \pm 1.4$ , the presence of moderate to severe cough symptoms was clinically revealed in 57.1% and 57.5% of patients in both regions, particularly in pollination season; whereas in a dynamic monitoring it was possible to trace a reliable ( $p < 0.05$ ) regression of symptoms to  $1.5 \pm 0.07$  in 6 months,  $0.8 \pm 0.4$  in 12 months and  $0.3 \pm 0.2$  – in 24 months. Thus, minor or mild symptomatic manifestations had been detected in 49.5% and 50.0% of individuals, especially during the seasonal period by the end of the first year of therapy, and they almost disappeared by the end of the second year of therapy. Rhinorrhea, sneezing, itching of the nasal and eye mucosa, wheezing and cough were reduced in all patients who had undergone immunotherapy (Table 3). Besides, patients did not need any further medications after 2 years of immunotherapy. In the first group, there were no significant differences between mono- and polysensitized patients ( $p > 0.05$ ).

Table 3

**Data of visual analogue scale in patients who had SLIT and in control group**

Symptom, points (0-4)	1-st group (n=185)				Control group (n=20)			
	Before treatment	6 months	12 months	24 months	Before treatment	6 months	12 months	24 months
Rhinoconjunctivitis	$2.4 \pm 1.5^{**}$	$1.4 \pm 1.2^*$	$0.94 \pm 0.8^*$	$0.42 \pm 0.6^*$	$2.4 \pm 1.4$	$2.3 \pm 1.3$	$2.1 \pm 0.9$	$2.1 \pm 0.7$
Rhinitis	$2.3 \pm 0.9^{**}$	$0.8 \pm 0.4^*$	$0.6 \pm 0.6^*$	$0.3 \pm 0.5^*$	$1.9 \pm 0.9$	$1.5 \pm 0.9$	$2.4 \pm 1.3$	$2.3 \pm 1.2$
Sneezing	$1.85 \pm 1.3^{**}$	$0.6 \pm 0.6^*$	$0.4 \pm 0.4^*$	$0.36 \pm 0.6^*$	$1.7 \pm 1.3$	$0.9 \pm 0.4$	$0.8 \pm 0.4$	$1.2 \pm 0.9$
Upper palate itching	$0.3 \pm 0.9^{**}$	$0.09 \pm 0.9^{**}$	$0.05 \pm 0.3^{**}$	$0.05 \pm 0.2^{**}$	$0.05 \pm 0.3$	$0.05 \pm 0.3$	$0.04 \pm 0.2$	$0.04 \pm 0.2$
Wheezing	$1.9 \pm 1.4^{**}$	$1.5 \pm 1.09^{**}$	$0.7 \pm 0.4^*$	$0.5 \pm 0.11^*$	$2.3 \pm 1.09$	$1.4 \pm 0.6$	$1.7 \pm 0.6$	$2.3 \pm 0.8$
Cough	$2.4 \pm 1.4^{**}$	$1.5 \pm 0.07^{**}$	$0.8 \pm 0.4^*$	$0.3 \pm 0.2^*$	$2.7 \pm 1.2$	$1.5 \pm 0.7$	$1.6 \pm 0.4$	$2.3 \pm 0.9$

\* $P < 0.05$  – statistically significant differences between the first and second groups

\*\* $P > 0.05$  – statistically insignificant differences between the first and the second groups

In the performed research, we identified prevalent peculiarities of sensitization to Artemisia and Ambrosia in various regions of Ukraine. Thus, sensitization to Ambrosia was observed by 3.2 times more often in the central region of Ukraine, and, in contrast, sensitization to Artemisia was by 1.2 times more prevalent in the western region. This is obviously due to different climatic and geographical features of these regions. Among patients in central regions, age-specific characteristics were not observed in the prevalence of sensitization. Regarding the Western region, it is worth noting that monosensitization to Ambrosia was detected only in children who moved to the region from Crimea for a permanent residence because of military operation in the eastern part of the country. Another feature that was found predominantly in children under 6 years of age in two studied regions was a discrepancy between high levels of sensitization to Ambrosia and Artemisia and the presence of significant clinical manifestations of allergy.

According to the results of component studies, genuine sensitization to Artemisia and Ambrosia pollen has been confirmed in 94.4% and 85.7% of patients in the western region, respectively, and 93.0% and 90.5% of patients in the central regions, respectively. The obtained component data on the prevalence of allergy to Artemisia in the West, and to Ambrosia – in Central Ukraine coincided with SPT results. It should be mentioned that about 30% of examined patients and, largely, children had positive skin tests to

Ambrosia and Artemisia, in the presence of monosensitization associated with major allergen of Ambrosia. Apparently, this is due to the fact that the major allergen of Artemisia Art v 1 has little cross-reactivity with Ambrosia Amb v 4 allergen, but this cross-reaction is not clinically important. Another peculiarity of component investigations was the absence of complaints related to food allergy in anamnesis of patients with a detected major allergen of Artemisia Art v 3. It is known that Art v 3 is typically used to map primary sensitization to cross-reactions between nsLTPs of plant food. In many cases, it is an important diagnostic marker for patients suffering from polynucleotide syndromes associated with food allergy [12]. Thus, patients with the detected major component of Art v 3 (4.2% – Western region, 3.4% – Central region) received recommendations for avoiding consumption of celery, mustard, peaches, spices, etc.

In our study, we found that SLIT is an effective treatment for patients suffering from allergic respiratory diseases such as allergic rhinitis and asthma (fewer symptoms and less drug intake) compared to patients treated with symptomatic drugs alone. At the time of the study, patients in both groups had similar rates in VAS symptoms. In particular, such symptoms as rhinoconjunctivitis and coughing are described above. Thus, at the beginning of therapy, cough in the control group was  $2.7 \pm 1.2$  points and did not differ significantly ( $p > 0.05$ ) from that in the children of the first group –  $2.4 \pm 1.4$ . At the end of the second year of therapy, the results were significantly different between the groups:  $0.3 \pm 0.2$  (group I) and  $2.3 \pm 0.9$  (control group) ( $p < 0.01$ ). Recurrence of some symptoms in the control group indicated the need in SLIT. According to the literature and our study it has been concluded that improvement in clinical results was observed both in monosensitized and polysensitized patients [3]. The efficacy of SLIT treatment was not related to patients' age. At the time of the study, patients in both groups had similar indices in VAS symptoms.

One of the most important components of SLIT is the possibility of its safe use, taking into account the risks of development of possible anaphylactic reactions and their tolerance by patients [13]. SLIT tolerance was evaluated for patients of all ages in the first group using the linear scale as described above: 60.5% of patients (and their parents) rated tolerance for SLIT as "good", and 30.8% – "very good". Thus, the overall result of good and very good tolerance was 91.3%, indicating high safety of treatment and absence of serious side effects. Throughout observation period, no severe allergic / anaphylactic drug-related reactions were detected.

### Conclusions

1. Within a country there are regional peculiarities in the prevalence of sensitization to various types of weeds. Hidden sensitization to Ambrosia is often detected in patients in the western regions of Ukraine.
2. The use of SLIT with standardized medical allergens in atopic asthma and / or allergic rhinitis in patients of all ages is an effective and safe treatment and allows for rapid (during the first 6 months of SLIT) control of symptoms.
3. Data of comparative analysis in a group of patients who did not receive SLIT indicated a high incidence of disease symptoms after completion of basic therapy.

### References

1. Asero R, Bellotto E, Ghiani A, Aina R, Villalta D, Citterio S. Concomitant sensitization to ragweed and mugwort pollen: who is who in clinical allergy?. *Annals of Allergy, Asthma & Immunology*. 2014;113(3):307-13.
2. Bousquet J, Heinzerling L, Bachert C, Papadopoulos NG, Bousquet PJ, Burney PG, et al. Position paper EAACI practical guide to skin prick tests in allergy to aeroallergens. *Allergy*. 2012;67:18-24.
3. Douladiris N, Savvatiannos S, Roumpedaki I, Skevaki C, Mitsias D, Papadopoulos N. A molecular diagnostic algorithm to guide pollen immunotherapy in southern Europe: towards component-resolved management of allergic diseases. *International Archives of Allergy and Immunology*. 2013;162(2):163-72.
4. Gadermaier G, Hauser M, Ferreira F. Allergens of weed pollen: an overview on recombinant and natural molecules. *Methods*. 2014;66(1):55-66.
5. Gharib V, Zubchenko S, Chopyak V, Gajewska V, Gajewsky V. The molecular overview of sensitization to weed pollen allergens and its possible clinical application in Ukraine for the optimal allergoimmunotherapy. *Zhurnal vushnykh, nosovykh i horlovykh khvorib*. 2016;6:28-41.
6. Léonard R, Wopfner N, Pabst M, Stadlmann J, Petersen B, Dues J, et al. A new allergen from Ragweed (*Ambrosia artemisiifolia*) with homology to Art v 1 from Mugwort. *Journal of Biological Chemistry*. 2010;285(35):27192-200.
7. Linkov G, Toskala E. Sublingual immunotherapy. *Current Opinion in Otolaryngology & Head and Neck Surgery*. 2014;22(3):208-10.
8. Matricardi P. Molecular profile clustering of IgE responses and potential implications for specific immunotherapy. *Current Opinion in Allergy and Clinical Immunology*. 2014;13(4):438-45.
9. Movérare R, Larsson H, Carlsson R, Holmquist I. Mugwort-sensitized individuals from North Europe, South Europe and North America show different IgE reactivity patterns. *International Archives of Allergy and Immunology*, 2011;154(2):164-172.
10. Niederberger V. Allergen-specific immunotherapy. *Immunology Letters*. 2009;122(2):131-3.
11. Panzner P, Vachová M, Vítovcová P, Brodská P, Vlas T. A comprehensive analysis of Middle-European molecular sensitization profiles to pollen allergens. *International Archives of Allergy and Immunology*. 2014;164(1):74-82.
12. Sánchez-López J, Tordesillas L, Pascal M, Muñoz-Cano R, Garrido M, Rueda M, et al. Role of Art v 3 in Pollinosis of Patients Allergic to Pru p 3. *Journal of Allergy and Clinical Immunology*. 2014;133(4):1018-25.
13. Shupyk National Medical Academy of Postgraduate Education, Ukrainian Center for Scientific Medical Information and Patent License Activities. Algorithm for selecting patients for allergen specific immunotherapy (ASIT). Kyiv; 2011. 311 p.

## Реферати

**АНАЛІЗ ОСОБЛИВОСТЕЙ СЕНСИБІЛІЗАЦІЇ ДО ПИЛКУ БУР'ЯНИВ І ЕФЕКТИВНОСТІ АЛЕРГОІМУНОТЕРАПІЇ У ПАЦІЄНТІВ ЦЕНТРАЛЬНОГО І ЗАХІДНОГО РЕГІОНІВ УКРАЇНИ**

**Зубченко С.О., Шарикадзе О.В.**

На території України налічується понад 1,5 тис. видів бур'янистих рослин. Вони значно засмічують сільськогосподарські угіддя, а деякі з них володіють значними алергенними властивостями. Найпоширеніші в цілому світі клінічно значущі алергени бур'янів наявні в пиляках полину, амброзії, лободі, подорожника, кураю поташевому. Розвиток молекулярної діагностики дає можливість чітко визначити головний алерген пиляку бур'янів і на цій основі запропонувати пацієнту персоналізований вибір алергоімунотерапії з прогнозом її ефективності. За результатами наших досліджень виявлені регіональні особливості у поширенні сенсibilізації до різних видів бур'янів у Центральному та Західному регіонах України. Використання SLIT зі стандартизованими медичними алергенами для лікування хворих різного віку з пилковою алергією є ефективним і безпечним.

**Ключові слова:** полин, амброзія, молекулярна діагностика, VAS, ефективність SLIT.

Стаття надійшла 3.04.18 р.

**АНАЛИЗ ОСОБЕННОСТЕЙ СЕНСИБИЛИЗАЦИИ К ПЫЛЬЦЕ СОРНЯКОВ И ЭФФЕКТИВНОСТИ АЛЕРГОИМУНОТЕРАПИИ У ПАЦИЕНТОВ ЦЕНТРАЛЬНОГО И ЗАПАДНОГО РЕГИОНОВ УКРАИНЫ**

**Зубченко С.А., Шарикадзе Е. В.**

На территории Украины насчитывается более 1,5 тыс. видов сорных растений. Они приносят вред сельскохозяйственным угодьям, а некоторые из них обладают значительными аллергенными свойствами. Распространенные во всем мире клинически значимые аллергены сорняков имеются в пыльце полины, амброзии, лебеды, подорожника, чертополоха. Развитие молекулярной диагностики дает возможность четко определить главный аллерген пыльцы сорняков и на этой основе предложить пациенту персонализированный выбор алергоимунотерапии с прогнозом ее эффективности. Согласно результатов наших исследований выявлены региональные особенности в распространении сенсibilізації к различным видам сорняков в Центральном и Западном регионах Украины. Использование SLIT со стандартизованными медицинскими аллергенами для лечения больных разного возраста с аллергией на пыльцу является эффективным и безопасным.

**Ключевые слова:** полынь, амброзия, молекулярная диагностика, VAS, эффективность SLIT.

Рецензент Похилько В.І.

DOI 10.26724/2079-8334-2018-4-66-62-66

UDC 618.39-003.96-08

V.G. Kornienko

Danylo Halytsky Lviv National Medical University, Lviv

**PECULIARITIES OF GESTATION PROCESS WITH THREATENED MISCARRIAGE AND ITS CORRECTION**

E-mail: avfitkalo@gmail.com

Certain positive outcomes have been achieved recently in prevention and treatment of miscarriages. However, the rate of this pathology not only failed to decrease but also tends to increase. Current approaches to diagnostics and choice of adequate therapy for preventing the onset of preterm labour promote further progress of pregnancy, developing foetus in a safe intrauterine environment. The effectiveness of therapy with phytometabolic preparations for improving gestation process in women with threatened preterm labour was studied. Women from two main groups and the comparison group were admitted for inpatient treatment with threatened preterm labour: 55 (30,6 %) patients – at 22-27 weeks of pregnancy, 79 (43,9 %) patients – at 28-33 gestation weeks, 46 (25,6 %) women – at 34-35 pregnancy weeks. Pregnant patients with threatened miscarriage underwent complex therapy according to standards of obstetrical and gynaecological care and clinical protocols approved by Ministry of health care of Ukraine (micronized natural progesterone in vaginal tablets by 50 mg twice per 24 hours during observation period due to clinical manifestations, tocolytics were drip-fed once per 24 hours during 24-48 hours in case of available marked uterine tone). Pregnant women of the group II with marked signs of maladaptation syndrome were administered phytometabolic preparation Cratal by 1 tablet thrice per 24 hours additionally. Excretion levels of adrenaline and noradrenaline ranged within the following margins (adrenaline:  $52,1 \pm 3,3$  nmol/24 hours and noradrenaline:  $61,2 \pm 4,3$  nmol/24 hours) in women who underwent phytometabolic therapy. Characteristic considerable decreasing of adrenaline excretion level was observed in 61 (76,2 %) cases, increased level was noticed in 19 (23,7 %) cases. Changes in serotonin level were more noticeable in blood of pregnant women after therapy with Cratal (serotonine level ranged in margins characteristic for the control group –  $1,37 \pm 0,06$  mcmol/l). Decreasing serotonergic system function was observed in 36 (45,0 %) patients, increased serotonin level was noticed in 31 (38,7 %) cases.

**Key words:** preterm labour, catecholamines, phytometabolic preparation.

*The study is a fragment of the research project "Elaboration of individual-group supervising system for women with gynaecological and obstetric pathology and comorbid conditions for rehabilitation of reproductive health and preserving health quality at different age periods", state registration No. 0117U001075.*

According to World Health Organization (WHO) estimates, approximately 15 million of preterm labour (PL) occur annually worldwide. [4,5,6]. High rate of PL in Ukraine causes detrimental effects on both mothers and newborns. Preterm labour is an integral indicator of response to any changes in mother's body and foetus as well as to adverse effect of external factors – social and economic, ecological,