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Original scientific paper

Changing Pattern of Sensitization in Croatia to Aeroallergens in Adult Population Referring to Allergy Clinic during a Period of 15 Years

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A B S T R A C T

Published data indicate that during the last decades there is a possible change in the pattern of sensitization to different aeroallergens in adult population with atopy. The aim of this investigation was based on the hypothesis that during last 15 years there has been a change in the structure of prevalence of sensitization to different aeroallergens in adult population of Zagreb and its surroundings with atopy. Medical records from outpatient allergy clinic were screened for the period 1991.–2004. We included 794 patients during years 1991–1994, 814 patients during years 1995–1999, and 969 patients during years 2000–2004. Following data were analyzed: age, gender, education level, residence, referral diagnosis, dominant symptoms, results of skin-prick test (SPT), total and specific serum immunoglobulin E. As risk factors for allergic sensitization we determined the decade of birth ($p<0.0001$), male gender ($p<0.008$), level of education ($p<0.0001$), and place of residence ($p<0.05$). Proportion of sensitized individuals to pollen significantly increased from the period 1991–1994 towards 2000–2004 ($p<0.001$ for the trend) with a significant increase in the proportion of sensitized individuals to weed pollen ($p=0.002$ for the trend) while the proportion of sensitized to other two groups of pollen (grasses and trees) was not significantly different. A significant increase in the proportion of sensitized individuals was determined for sensitization to ragweed pollen ($p=0.004$ for the trend), and to mugwort ($p=0.005$ for the trend). Despite all its limitations primarily based on the selection bias the results of this study are conclusive about the significant change in the proportion of sensitization to different aeroallergens and different pollen groups and individual pollen species during the investigated 15-year time interval.

Key words: *hypersensitivity, allergens, pollen, ambrosia*

Introduction

Allergic disorders are noticeably gaining importance as disorders associated to modern lifestyle with increasing prevalence[1]. For their dramatic increase in prevalence during the second half of twentieth century we still have no distinctive explanation. The questions are raised about the cause for that increase in prevalence. There is a lot of scientific evidence that this is a consequence of many factors as global lifestyle changes, economic, political, cultural, meteorological, and ecological or other unknown factors[2–4]. Ecological/meteorological factors are best represented by the interaction between pollen concentration and distribution and adjuvant interaction with air pollutants[5–8]. There are also data of the changing pattern of exposure to aeroallergens specifically to ragweed pollen in Croatia[9] together with new sensitizations in the areas where this allergen was previously not present[10]. The changes in pattern of sensitization over time were evident also in some other countries[11,12].

Published and anecdotal data indicate that during the last decades there might be a change in the pattern of sensitization to different aeroallergens in adult population with atopy in the city of Zagreb and its surroundings[13,14]. To test this hypothesis, we performed a retro-

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spective study with specific goal to determine prevalence of sensitization to different inhalant allergens in adult population with respiratory symptoms referring to our Allergy Clinic during the 15-years period, with specific emphasis on the changes in pattern of sensitization to pollens, more specifically to ragweed pollen as the most aggressive allergen.

Patients and Methods

Medical records from outpatient allergy clinic (»Jordanovac« University Hospital for Lung Diseases, Zagreb) were screened for the period 1991.–2004. A total of 5591 patients were identified, mainly referred from their general practitioner, ENT specialist or pulmologist for definite allergy testing and evaluation because of suggestive respiratory symptoms. The flow chart of selection of patients is shown in Figure 1. After exclusion of patients with missing or incomplete data, we included 794 patients for time period 1991–1994 (group 1992), 814 patients for time period 1995–1999 (group 1997), and 969 patients for time period 2000–2004 (group 2002) as 3 time-dependent subgroups. These patients were included based on having all relevant data in their medical charts: age, gender, education level, residence, referral diagnosis, dominant symptoms, result of skin-prick test (SPT), total and specific serum IgE. Excluded patients were not significantly different concerning age and sex distribution from the patients that were included into analysis ($p>0.05$ for both).

Skin-prick tests (SPT) were performed using a standardized procedure according to EAACI guidelines[15–17] using allergic extracts from Imunološki zavod (Zagreb, Croatia). All patients were tested with a standard series of aeroallergens (*Dermatophagoides pteronyssinus,* cat and dog dander, moulds, mixtures of trees, grass and weeds pollen) together with a negative control (phosphate buffer solution) and a positive control (histamine hydrochloride, 1 mg/mL). Additional testing with individual allergen extracts of moulds (*Alternaria alternata, Aspergilus fumigatus, Chladosporium herbarum*) and pollens of grasses (*Alopecurus pratensis, Agrostis alba, Dactylis glomerata, Phleum pratensae, Lolium perenne, Poa pratensis, Secale cereale, Zea mayus, Tritacum sativa*), weeds (*Ambrosia elatior, Artemisia vulgaris, Rumex acetosa, Plantago lanceolata, Toraxacum officinale, Parietaria officinalis, Urtica dioica, Artemisia absintium, Humulus lupulus*) or trees (*Corylus avellana, Betula verrucosa, Quercus rubor, Alnus incana, Pinus nigra, Robinia pseudoacacia, Salix alba, Populus alba, Platanus acerifolia, Sambucus nigra, Aesculus hipocastanum*) was done in case of a positive or doubtful reaction to allergen mixtures of moulds, grasses, weeds or trees or in case of a suggestive medical history for a specific pollen season. SPT was done on the volar side of the forearm using a standardized lancet with the 1 mm tip by a vertical puncture through the drop of allergen extract into the skin. The reaction was read after 20 minutes. The mean wheal diameter ([largest diameter plus vertical to it at the half of it] divided by2) of 3 mm and over (with erythema) was assessed as a positive skin test (SPT+).

Serum total and specific immunoglobulin (IgE) levels were measured using the standardized immuno-enzymatic method (Pharmacia AB Diagnostics, Upsala, Sweden), and results were expressed as international units *per* mL of sera (IU/mL) for total IgE, and as kUA/L for specific IgE. Levels of 125 IU/mL and over for total IgE and of 0.35 kUA/L and over for specific IgE were considered as elevated (positive). Total or specific IgE was determined in patients with suggestive medical history for allergic disorder and a negative or doubtful SPT, or in patients with a positive SPT.

Statistics

Statistical analyses were performed using STATISTICA, version 6 (StatSoft, Inc. Tulsa, OK, USA). All results of quantitative measures were expressed as mean (SD) and for qualitative variables as number (%). Comparisons between groups for quantitative variables were performed using ANOVA, and for qualitative variables using chi-square test. Univariate and multivariate logistic regression was used to depict associations and risk factors for allergic sensitization. The results of the logistic regression analyses were presented as odds ratios (ORs) together with 95% confidence intervals (CIs). The level of statistical significance was set at $p<0.05$.

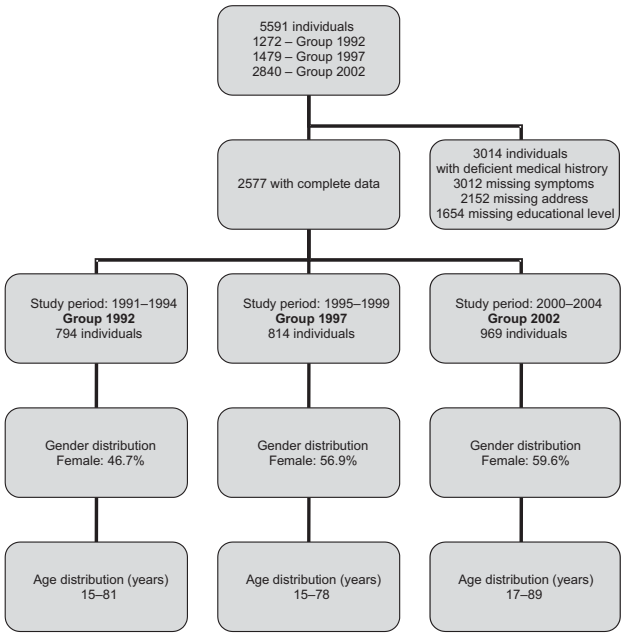

Fig.1. The flow chart of selection of patients.

Results

All the factors in clinical practice in studied period were constant, but the number of patients reporting to our outpatient clinic has considerably risen (318/year during 1991–1994 period up to 568/year during 2000–2004 period). The demographic data for examined groups are

summarized in Table 1. The proportion of female patients and patients with a higher degree of education increased significantly between time periods (gender distribution, χ^2=31.35, p<0.0001; education, χ^2=218.04, p<0.0001). Also the average year of birth and age were significantly different between groups (p<0.0001 for both). Patients from the group 1997 were younger than two other groups however they were born at the same time as the group 2002. There was also a significant difference in the distribution of total IgE and symptoms of referral between groups (high total IgE, χ^2=8.52, p=0.0141; symptoms, χ^2=156.72, p<0.0001). There was a significantly lower proportion of high total IgE in the group 2002 compared to other groups and a significantly higher proportion of patient referring for the symptoms of lower respiratory tract in the group 1992. Decrease in the proportion of high total IgE in group 2002 was most likely the consequence of the difference in age, gender and referral symptoms distributions (oldest, more women, less with lower respiratory tract symptoms) showing a statistically significant negative (age and gender) and positive (type of symptoms) associations with the high total IgE in investigated groups (age, OR for each decade, 0.83, 95% CI 0.76–0.90, p=0.00001; women, OR 0.64, 95% CI 0.51–0.81, p=0.00024; symptoms [skin to lower airways], OR for each step 1.20, 95% CI 1.04–1.38, p=0.0109).

Table 2 shows the results of SPTs and sensitization (individuals with the positive SPT and/or positive specific IgE) data in investigated groups. Proportions of sensitized patients to different groups of aeroallergens in the subgroup of allergic patients and proportions of sensitized individuals to different groups of pollen allergens are presented in Figures 2 and 3. We found decade of birth (from 1920s to 1980s) (OR for each decade, 1.43; 95 CI, 1.31–1.55; p<0.0001; Figure 4), male gender (OR, 1.67; 95% CI, 1.33–2.08; p<0.0001), level of education (OR for each level, 1.08; 95% CI, 1.02–1.14; p=0.00647), place of residence (from village to industrial area of

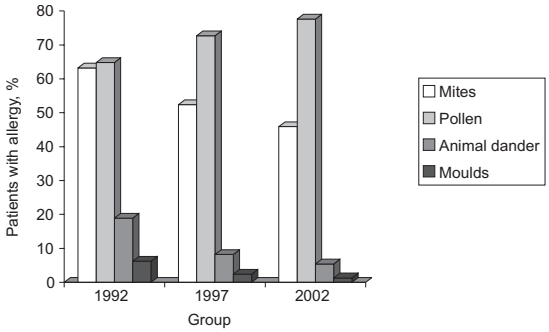

Fig. 2. Proportion of sensitized individuals to different groups of aeroallergens in the subgroup of allergic patients according to the time dependent groups (N=1204; group 1992, n=307; group 1997, n=450; group 2002, n=477); proportion of sensitized individuals to pollen significantly increased (p=0.00014 for the trend), while proportion of sensitized individuals to mites significantly decreased (p<0.00001 for the trend) during the 15-year period.

TABLE 1
GENDER, AGE, EDUCATION, TOTAL IGE AND ALLERGY SYMPTOMS DISTRIBUTIONS IN THREE TIME DEPENDENT GROUPS (N=2577)

Characteristics	Group 1992 N=794	Group 1997 N=814	Group 2002 N=969	p-value
Gender, female, No (%)	371 (46.7)	463 (56.9)	577 (59.6)	<0.0001
Age, mean (SD) [range], yrs	42.1 (15.2) [15–81]	39.1 (14.4) [15–78]	42.9 (15.5) [17–89]	<0.0001
Year of birth, mean, year	1950	1958	1959	<0.0001
Education level, No (%)				
I	3 (0.3)	6 (0.7)	0	
II	207 (26.0)	122 (14.9)	100 (10.3)	
III	187 (23.5)	171 (21.0)	117 (12.1)	<0.0001
IV	281 (35.4)	360 (44.2)	426 (44.0)	
V	21 (2.7)	80 (9.9)	92 (9.5)	
VI	95 (12.0)	75 (9.3)	234 (24.2)	
Total IgE >125 kU/L, No (%)*	195 (48.6) [n=401]	230 (52.9) [n=435]	138 (42.2) [n=327]	0.0141
Symptoms, No (%)				
LA	689 (86.8)	507 (62.5)	698 (72.1)	
PR	38 (4.8)	114 (14.1)	100 (10.3)	<0.0001
IR	50 (6.3)	165 (20.4)	147 (15.2)	
Eye	12 (1.5)	22 (2.7)	6 (0.6)	
Skin	5 (0.6)	1 (0.1)	17 (1.8)	

I – haven't finish primary school, II – finished primary school, III – finished 3-years high school, IV – finished 4-years high school, V – college degree, VI – university degree, LA – lower airways, PR – persistent rhinitis/rhinosinusitis, IR – intermittent rhinitis/rhinosinusitis

*The number of patients with total IgE was lower that total number for that subgroup because IgE was determined on indications described in »Methods« section.

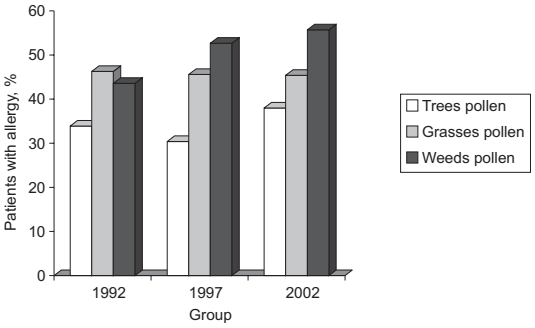

Fig. 3. Proportion of sensitized individuals to different groups of pollen allergens in the subgroup of allergic patients according to the time dependent groups (N=1204; group 1992, n=307; group 1997, n=450; group 2002, n=477); proportion of sensitized individuals to weeds pollen significantly increased (P=0.00188 for the trend)

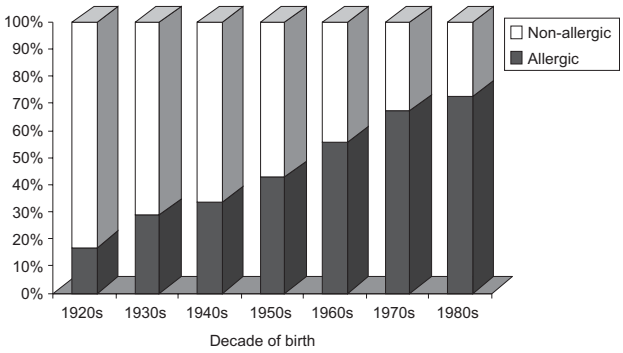

Fig. 4. Proportion of individuals with allergy according to the decade of birth (N=2577; p<0.0001 for the trend).

Zagreb) (OR for each residence area, 1.23; 95% CI, 1.09–1.38; p=0.00065) as statistically significant indipendent risk factors for allergic sensitization. As represented in Figure 4 starting with patients born in 1920s there was an evident increase in the proportion of allergic patients from 16.9% (OR, 1; reference), to 28.9% for born in 1930s (OR, 2), 33.6% for 1940s (OR, 2.49), 42.8% for 1950s (OR, 3.67), 55.5% for 1960s (OR, 6.12), 67.3% for 1970s (OR, 10.12), and 72.3% for 1980s (OR, 12.8) (p<0.00001 for linear trend). There were no significant diffences in these proportions between tested groups (p=0.5923). Linear trend of increase in proportion of allergic patients was also evident for the place of residence starting with the village/small town (N=456) with 42.9% (OR, 1; reference), to city of Zagreb (N=1685) with 51.4% (OR, 1.41), surroundings and suburbs of Zagreb (N=304) with 58.5% (OR, 1.88), industrial area of Zagreb (N=86) with 71.4% (OR, 3.33), and northern part of Zagreb (N=46) with 90.9% (OR, 13.33; p<0.00001 for linear trend). The lower risk in rural environment was concomitant for all allergens (p=0.007). As risk factors for sensitization to pollens of trees, grasses and weeds we determined the decade of birth (OR, 1.21; 1.62; 1.38; p<0.0001 for all), male gender (OR, 1.52; 1.56; 1.32; p<0.008 for all), level of education (OR, 1.19; 1.18; 1.17; p<0.0001 for all), and place of residence (OR, 1.23; 1.26; 1.16; p<0.05 for all).

The proportion of weed pollen sensitized patients was significantly increasing from the period 1991–1994 towards 2000–2004 (43.7% to 55.7%; p=0.002 for the trend; Figure 3) while the proportion of sensitized to other two groups of pollen (grasses and trees) was not significantly

TABLE 2
SKIN-PRICK TEST RESULTS AND SPECIFIC IGE POSITIVITY TO TESTED ALLERGENS AND NUMBER OF ALLERGIC PATIENTS IN THREE TIME DEPENDENT GROUPS (N=2577)

	Group 1992 N=794	Group 1997 N=814	Group 2002 N=969	p-value
SPT, positive to (%)				
Mites	194 (24.4)	235 (28.9)	202 (20.9)	0.00045
Tree pollen	104 (13.1)	137 (16.8)	170 (17.5)	0.02838
Grass pollen	142 (17.9)	202 (24.8)	201 (20.7)	0.00283
Weed pollen	134 (16.9)	236 (29.0)	249 (25.7)	<0.00001
Animal dander	58 (7.3)	37 (4.6)	21 (2.2)	<0.00001
Moulds	19 (2.4)	11 (1.4)	6 (0.6)	0.00679
Sensitized, number (%)*				
Mites	194 (24.4)	236 (29.0)	205 (21.2)	0.00066
Tree pollen	104 (13.1)	137 (16.8)	170 (17.5)	0.02838
Grass pollen	142 (17.9)	205 (25.2)	203 (21.0)	0.00158
Weed pollen	134 (16.9)	237 (29.1)	249 (25.7)	<0.00001
Animal dander	58 (7.3)	37 (4.6)	24 (2.5)	0.00001
Moulds	19 (2.4)	11 (1.4)	6 (0.6)	0.00679
Patients with allergy, number (%)	307 (38.7)	450 (55.3)	447 (46.1)	<0.00001

SPT – skin prick test.

*Sensitization represents individuals with the positive SPT and/or positive specific IgE

different (grasses, 46.3% to 45.4%; p=0.972 for the trend; trees, 33.9% to 38%; p=0.131 for the trend; Figure 3). There was a significant decrease in the proportion of mite sensitized patients (63.2% to 45.9%; p<0.001 for the trend; Figure 2).

A significant increase in the proportion of sensitized patients was determined for sensitization to ragweed pollen (21.82%, 39.56%, 34.23%, p=0.004 for the trend), and to mugwort (21.82%, 40.22%, 34.23%, p=0.005 for the trend). Pronounced and significant concomitant skin and specific IgE reactivity was determined for the sensitization between ragweed and mugwort (OR, $>10^6$; sensitivity, 99.25%; specificity, 100%; p<0.001) suggesting a possible crossreactivity.

Discussion

Allergic disorders can be named as an epidemic of the 21st century. During the last few decades an increase of asthma and other atopic disorders (allergic rhinitis and atopic dermatitis) has been recorded[18]. Asthma and other allergic disorders are today regarded as one of the most significant health problems, particularly in highly developed countries. Some 10 millions of adults and 5 millions of children are recorded in the USA as asthma patients[19]. However, due to a high number of presumed factors playing part in allergic disorders, it is not easy to collect all the evidence on real variability of their incidence. The increase in the incidence of allergic diseases could be caused by a higher social and professional awareness of these disorders. Although screening for allergy in asymptomatic population is not advocated, it has been recorded increasing number of studies on these patients. It has been shown that even asymptomatic people who are sensitized to allergens may demonstrate bronchial hyperresponsiveness[20]. Also, the specialized allergologic health care is more accessible, enabling patients to refer for an early allergologic medical evaluation[21].

This study was performed during the last 15 years in the very same institution taking care for the same population (City of Zagreb and its surroundings, approximately 1.000.000 inhabitants). In this period (1991–2004) the clinical allergology practice in the institution was not changed, the clinical staff, as well as the diagnostic methods for allergic disorders was the same. Our study was divided in three 5-year periods. Although epidemiological studies evaluating trend changes in chronic diseases require a long-term investigation, results from other studies have shown that the time-period we evaluated was long enough to perform valuable statistical expertise[22]. The number of inhabitants in the Republic of Croatia is relatively small (4.4 millions) compared to other European countries expecting the absolute number of patients with allergic diseases being considerably lower than in other countries and our group consisting of 2,577 patients was considered suitable for evaluation and statistical analysis.

Such grouping of patients enabled an evaluation of potential sensitization and atopic disorders trends, and was conformed to statistical evaluation of obtained results. In all groups, a high proportion of sensitized patients were found (38.7%, 55.3%, and 46.1% for groups 1992, 1997, and 2002 respectively). This finding was expected because the patients were referred for allergologic evaluation in our outpatient clinic due to their respiratory complaints presumably of allergic etiology (moderate pre-test probability for allergic sensitization).

It is known that the level of education is correlated with asthma morbidity, although the mechanisms of this association are still unclear. Cakmak et al. in their study[23] evaluated the association between the hospitalization in asthma patients and the daily pollen air concentration in 10 major Canadian cities. Their results showed a correlation of the level of aeroallergens and hospitalizations in subjects with a lower level of education. Also, younger males were more often hospitalized, a finding in concordance with previously published studies showing young males to be more prone to sensitization to aeroallergens and having asthma symptoms requiring hospitalization. Similar results were published by Ellison-Loschmann et al.[24] using data from the European Community Respiratory Health Survey Study comparing the socioeconomic status and asthma and chronic bronchitis incidence. The results clearly showed the connection between asthma and a lower education level. However, some studies showed the opposite association between atopy and the level of education. An 11-year study[25] conducted on 2,819 subjects aged 15–70 years in western Norway disclosed a decrease of respiratory symptoms connected with an increase in the level of education. The cumulative incidence of asthma was 5.3%, 4.1%, and 1.8% in subjects with primary, secondary, and academic level of education respectively, concluding that people with a lower level of education had higher risk for asthma and respiratory disorders.

In patients reporting respiratory symptoms, in our study we disclosed the highest proportion of sensitized patients being in their twenties (72.3%), while the lowest proportion (16.9%) was found in patients in their eighties with no significant differences in these proportions between studied groups. These data are in concordance with other studies evaluating atopic patients and their reasons for referral to an outpatient clinic. Allergies are distributed through all age groups, but the twenties seem to be the most affected age group, as many studies have shown. Similar data i.e. the increase in allergic disorders in younger populations have recently being published. Soti in his study[26] showed an average incidence of allergy in age group 19–29 being 135 average cases/year (4.495 cases/100,000 population/year), in age group 30–60 being 89 average cases/year (2.964 cases/100,000 population/year), and in age group 60–80 only 24 average cases/year (0.800 cases/100,000 population/year) (OR 5.6 in the youngest group) which is comparable to our results (OR 6.4). Dorner's study from Vienna[27] disclosed allergy incidence up to 27.6% for men, and 32.2% for women; just a year before the percentages were 19.6 and 22.4 for men and women respectively. Higher educated people living in urban areas are more frequently affected than people

from lower socioeconomic class living in rural areas. A study performed during army recruitment in Austria showed a two-fold increase in allergic rhinitis, 3.6-fold increase in asthma and a 4.6-fold increase in atopic eczema between two periods (1986 and 2003/4). Surprisingly, the highest risk (OR 13.33) for atopy was recorded in residents of northern Zagreb (hilly sub-mountainous area with rich vegetation) which was even higher than in residents from the industrial area (OR 3.33). A low number of patients from this area could bias these data, but we should not forget that exposure to pollen combined with traffic pollution (one of the main traffic routes in Zagreb) in this area could act as a potential trigger for sensitization and symptom induction. In recent decades, the northern part of the city of Zagreb had substantially increased the number of inhabitants and also traffic pollution.

As we had no data regarding pets in households of our studied subjects, we cannot compare our results with studies involving pets, but as a contribution to the hygiene theory we can add our findings of the lowest atopy risk in residents of small villages and/or little towns (OR 0.71 compared to the city of Zagreb). This lower risk was present for all allergens. The aim of Stevens's study[28] was to judge the relative incidence of hypersensitivity to four common aeroallergens in two separate atopic populations with asthma and/or rhinitis. The first population was studied in the period 1975–1979 and the second between 1992 and 1995. Patients with respiratory allergy showed an increased incidence of birch pollen hypersensitivity, showing a raise from 13% to 34%. In contrast, the incidence of hypersensitivity to dust mites, grass and weed pollen did not change. The recorded increase was not connected with an elevated number of birch pollen particles that failed to demonstrate significant changes through 15-year period. Our study with a similar 15--years-time period, showed a similar dust mite sensitization change, and an increase in weed pollen sensitization, more specifically to ragweed. This finding correlates with an increase in the number of ragweed pollen particles during the pollination period in the continental part of Croatia (Zagreb and surrounding area), expanding to other Croatian geographic areas. Peternel's study[29] confirmed increase in pollen count in Zagreb and surrounding area where percentage of ragweed pollen in total pollen count ranged from 6 to 24% in 2002, while these percentages were higher in 2003, ranging from 8 to 33%. It shows an increase compared with the period from 1973–1987, where *A. elatior* pollen represented from 8 to 15% in total pollen count[30]. Rapid expansion of ragweed pollen in Europe from 1989 to 1997 was also published[31,32] together with the fact that ragweed sensitisation rates correlate with the amount of inhaled airborne pollen[32].

A Scandinavian study[11] showed an elevated concentration of IgE antibodies to timothy grass and birch pollen comparing 1973 and 1994 showing a correlation of timothy grass pollen-specific serum IgE levels and the number of IgE reactivities to individual allergens. A cross-sectional survey[12] conducted in Denmark in 1990 and 1998, has found an increase in the prevalence of specific IgE positivity to aeroallergens in two studied periods.

The association between air pollutants and atopy can be studied through three different settings. *In vitro* exposure of pollen to air pollutants stimulates morphological changes and it seems that the presentation of allergens from pollen particles is facilitated[5]. In animal models, the pollutants, especially diesel exhaust particles can trigger the IgE response[33]. Also, epidemiological studies show that air pollutants can elucidate symptoms in allergic patients[34]. On the contrary, the prospect of air pollutants to trigger allergic diseases *de novo* is still a topic for a debate. Some investigations suggest air pollutants, especially diesel exhaust particles, as triggers for allergic hypersensitivity and development of allergic diseases[33].

It seems that our results are depicting a multifactorial risks for atopic disorders, including a lower risk for all allergens in people with rural residency with low air pollution, and an elevated risk in people with higher socioeconomic status (younger population) living in industrialized environment. Moreover, an even higher risk was found in those living in traffic polluted areas (downtown population, industrial areas, and northern part of Zagreb).

The manifestation and the severity of the allergic rhinoconjuctivitis and asthma are related to the pollen concentration in the air. An increase in the number of sensitized individuals was observed in the Osijek-Baranja County during the last few years. This finding was in a correlation with the high air pollen concentration and with ragweed exposure[35]. Prus et al. measured concentration of ragweed pollen through period 2001–2003. Results showed high concentration level in 2001 (6202 pollen counts/m^3) and during 2003 (5952 pollen counts /m^3). Our data are in concordance with the results from the Osijek-Baranja County, clearly showing an increase in weed pollen sensitization as well as an increase of ragweed pollen concentration in the City of Zagreb area and its surroundings[9]. In our country, Cvitanović et al. investigated the hypersensitivity to ragweed in patients from the southern part of Croatia (i.e. the Mediterranean part). Their results showed a considerable number of patients (56/120; 47%) with allergic symptoms in late summer/early autumn because of hypersensitivity to *Ambrosia elatior*[36]. These data emerged *A. elatior* as an important allergen even in these southern parts of Croatia where it didn't played an important role before. There is evidence that *A. elatior* can spread 6–20 km a year. Furthermore, *A. elatior* pollen grains have good aerodynamic properties and can migrate as far as 300 km. Climatic changes, global warming in particular, have influenced changes in the plant growth, distribution, and allergenic pollen emission. The second possible explanation for *A.elatior* hypersensitivity in places where its pollen counts is in minor concentration is clinical cross-reactivity with *Parietaria officinalis*. There is high rate of cross-reactivity among those sensitised to Ambrosia and Artemisia[37]. Significant but low antigenic cross-reactivity has been demonstrated among *Parietaria judaica* and *Artemisia vulgaris* by several *in vitro* techniques[38].

In the area of Lyon, France[39], the concentration of ragweed pollen increased from several hundred in 1987 up to 1200 granules/m^3 in 2000. Also, the number of days with the concentration of pollen high enough to provoke allergy symptoms in sensitive individuals, increased from 10 days in 1987 up to 30 days in 2002. Ragweed is the third most frequent type of pollen observed in the atmosphere of the central continental part of Croatia, with 14.3% of the total yearly spectrum in 2002 and 17.7% in 2003[9]. These data indicate an expansive spread of a very aggressive allergen, raising a number of sensitized individuals to ragweed as well as weed pollen showing a moderate to high cross reactivity in sensitized individuals in our study.

Despite all its limitations primarily based on the selection bias the results of this study suggest a significant change in the pattern of sensitization to different aeroallergens and different pollen groups and individual pollen species during the investigated 15-year time interval. These results have to be verified by the well planned epidemiological survey.

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PROMJENA PREOSJETLJIVOSTI NA POJEDINE INHALACIJSKE ALERGENE U ODRASLIH BOLESNIKA OBRAĐIVANIH U SKLOPU ALERGOLOŠKE AMBULANTE TIJEKOM 15-GODIŠNJEG PERIODA

SAŽETAK

Objavljeni radovi upućuju da tijekom posljednjih desetljeća postoji mogućnost za promjenu tipa senzibilizacije na različite inhalacijske alergene kod odraslih atopičara. Cilj rada temeljio se na hipotezi da je u zadnjih 15-tak godina došlo do promjene u strukturi učestalosti senzibilizacije na pojedine aeroalergene u odrasle populacije s atopijom u Zagrebu i široj okolici. Učinjena je retrogradna analiza zdravstvenih kartona alergološke ambulante u vremenu od 1991. do 2004. godine. U analizu je po skupinama uključeno 794 ispitanika u skupini 1991.–1994. god., 814 u skupini 1995.–1999. god., te 969 u skupini 2000.–2004. god. Analizirani su slijedeći podaci: dob, spol, stručna sprema, mjesto stanovanja, uputna dijagnoza, dominantni simptomi, nalaz ubodnog kožnog testa (SPT), ukupni i specifični imuno-

globulin E. Kao rizični čimbenici za senzibilizaciju utvrđeni su desetljeće rođenja ($p<0,0001$), spol ($p<0,008$), razina edukacije ($p<0,0001$) te mjesto stanovanja ($p<0,05$). Utvrđeno je da udio senzibiliziranih osoba na pelud statistički značajno raste od perioda 1991.–1994. prema periodu 2000.–2004. godine ($p<0,001$) uz značajan porast udjela senzibiliziranih na pelud korova ($p=0,002$) dok se udio senzibiliziranih na druge dvije grupe peluda (trava i stabala) nije statistički značajno povećavao. Statistički značajan porast udjela zabilježen je za senzibilizaciju na pelud limundžika ($p=0,004$ za trend), i divljeg pelina ($p=0,005$ za trend). Usprkos svim ograničenjima ove studije koja prvenstveno proizlaze iz selekcijske pristranosti temeljem rezultata ove studije moguće je zaključiti da je vidljiva značajna promjena u udjelu senzibilizacije na različite alergene te na različite skupine peludnih alergena uz značajnu promjenu spektra senzibilizacije u ispitivanom 15-godišnjem razdoblju. Navedene rezultate je potrebno provjeriti provođenjem odgovarajuće epidemiološke studije.