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OCCURRENCE AND CONTRIBUTING FACTORS OF FOOD-RELATED HYPERSENSITIVITY SYMPTOMS IN ADULTS WITH SEASONAL IMMUNE REACTIVITY

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SUMMARY – A community investigation explored how often individuals with seasonal nasal allergy symptoms also experience food-related allergic reactions in the mouth, and what characteristics might predict this condition. The study focused on patients confirmed to have seasonal rhinitis in a defined regional sample. Survey and clinical data were collected on symptoms, coexisting conditions, and lifestyle. Approximately half of the participants reported oral allergy symptoms. Significant associations were observed with preexisting metabolic conditions and symptom severity. These findings suggest that mouth-related allergic symptoms are common among those with seasonal nasal allergies and may be predicted by specific health or symptom patterns.

Key words: *Oral allergy syndrome, risk factors; Rhinitis, allergic, seasonal; Croatia*

Introduction

Oral allergy syndrome (OAS) represents a set of localized oral symptoms such as itching, tingling, and swelling of lips, tongue, palate and pharynx in patients suffering from seasonal allergic rhinitis (SAR), asthma, or both. These symptoms are usually self-limiting and last for only a few seconds to a few minutes[1] .

Symptoms occur as a consequence of specific food allergies caused by cross-reactivity between pollen and protein from fresh fruits and vegetables[1-4]. Allergic reactions to proteins in fruit and vegetables, which show cross-reactivity with pollen antigens in sensitive individuals, behave according to hypersensitivity type I and are mediated by immunoglobulin E (IgE)[1-3]. In contrast to other types of food allergy in which drivers are specific IgE to antigens from food, in OAS drivers are specific IgE to antigens from grass pollens, trees and weeds[3,5]. In addition to food, OAS can also occur in patients who are hypersensitive to latex the basic origin of which is also vegetable (rubber)[6,7]. Due to the fact that incriminated antigens for the pathogenesis of OAS are mostly thermo labile and subjected to decomposition by digestive enzymes, dominant symptoms occur in the upper gastrointestinal tract (mouth and throat) and immediately after eating the offending fruit and vegetables. Even though systemic reactions are very rare, OAS has a considerable potential for anaphylaxis[1]. Diagnosis is based on the history of SAR and typical symptoms that occur immediately after eating certain food of plant origin.

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Differential diagnoses include many diseases (such as burning mouth syndrome, angioedema, hay fever, various other oral diseases, etc.), and for this reason a multidisciplinary approach is necessary, as different specialists need to be involved in the diagnostic procedure[2]. Prevention and treatment are carried out through avoiding certain fruits and vegetables and/or their thermal processing, and antihistamines. The frequency of OAS is difficult to estimate. Many patients have mild symptoms that are eliminated by simply avoiding the incriminated food and have no need for further consultation with the physician[3]. Therefore, data in the literature significantly vary (by 8%-70%)[8-14]. It is also unclear in which patients with SAR we can expect OAS. For these two reasons, this study was conducted to estimate the prevalence of OAS in patients with SAR and to identify the possible risk factors for its development.

Patients and Methods

This cross-sectional study was conducted in primary care offices in the Split-Dalmatia County in the period from March 1 to September 30, 2012. The study was approved by the Ethics Committee of the Split University School of Medicine. A total of 600 questionnaires were distributed, of which 284 were not filled out or were filled out partially and were excluded from the study. There were 316 completed questionnaires, of which 16 were excluded because the respondents were under age 18 (n=15), and one was filled out by a pregnant woman. The final sample for analysis included 300 questionnaires.

The survey included 300 adult patients with SAR, which was confirmed by skin-prick test to seasonal inhalant allergens (grass, tree and weed pollens) and by symptoms of allergic rhinitis according to ARIA guidelines (runny nose, nasal obstruction, itchy nose and eyes, sneezing, watery and red eyes)[15,16]. Exclusion criteria were positive skin-prick test for perennial allergens (dust mites, feathers, and dander) and food allergy. Data were collected through a questionnaire that quantified the severity of nasal and ocular symptoms of SAR (0 – no symptoms, 1 – mild, 2 – moderate, and 3 – severe) and oral symptoms of OAS in the same manner[14,15] . A score of individual symptoms of OAS more than 3 is noted as positive in terms of the diagnosis of OAS.

Anthropometric parameters, other chronic diseases and lifestyle as the possible risk factors for OAS were also noted in the questionnaire (age, gender, weight, height, presence of asthma, diabetes, high blood pressure or some other chronic disease, smoking habits, positive family history of allergy, and duration of SAR/asthma symptoms).

Statistical analysis

We analyzed differences between the frequency of different categories and frequencies between categorical variables (different symptoms) using the χ^2-test. Of statistical tests, we used Pearson χ^2-test to determine correlation between the Total Nasal Symptom Score (TNSS) and Total Ocular Symptom Score (TOSS), TNSS and Total Oral Symptom Score (TORSS), and correlation between TOSS and TORSS. The same test was used to determine the possible association of anthropometric parameters, presence of asthma, diabetes, high blood pressure, smoking, family history, and duration of suffering from SAR/asthma as the possible risk factors for the development of OAS. Spearman's rho correlation coefficient was used to determine the association among TNSS, TOSS and TORSS. Kolmogorov-Smirnov test was used to determine normality of distribution. Odds ratios and 95% confidence intervals were estimated. Differences were considered significant at $p<0.05$.

Results

In our study, 300 adult patients with SAR, 168 (56%) male and 132 (44%) female, completed the survey. All investigated clinical characteristics and demographic data on patients with and without OAS were compared (Table 1).

The average age was 42 (18-85) years, average weight 78 (±13.98) kilograms and average height 175 (±11.24) cm. Of all patients, 127 (42.3%) were active smokers and 54 (18%) former smokers. Elevated blood pressure was present in 87 (29%) patients. Diabetes mellitus was present in 25 (8.3%) patients with SAR but 17 (68%) of them had OAS, which was statistically significant ($p<0.001$). Other chronic illnesses were present in 38 (12.7%) patients, mostly gastrointestinal (n=11; 3.7%) and cardiovascular (n=7; 2.3%) diseases. Asthma was diagnosed in 65 (21.7%) patients, while

Table 1. Comparison of patients with and without oral allergy syndrome

	SAR n=300	OAS positive n=137	OAS negative n=163	Odds ratio	95% Confidence interval	
Gender:				0.93		**
male	168	78 (46.4%)	90 (53.6%)		0.59-1.47	**
female	132	59 (44.7%)	73 (55.3%)			
Smoker:						
yes	127	61 (48.0%)	66 (52.0%)			**
no	119	51 (42.9%)	68 (57.1%)			**
ex	54	25 (46.3%)	29 (53.7%)			**
Positive skin-prick test:						
grass pollen	191	103 (53.9%)	88 (46.1%)	0.38	0.23-0.63	**
Parietaria	145	83 (57.2%)	62 (42.8%)	0.39	0.25-0.63	**
weed pollen	163	84 (51.5%)	79 (48.5%)	0.59	0.37-0.94	**
Mediterranean area tree pollen	216	107 (49.5%)	109 (50.5%)	0.56	0.33-0.95	**
Hypertension	87	39 (44.8%)	48 (55.2%)	1.04	0.63-1.73	**
Diabetes mellitus	**25**	**17 (68%)**	**8 (32%)**	**0.36**	**0.15-0.87**	**p<0.001**
Asthma	65	36 (55.4%)	29 (44.6%)	0.60	0.34-1.05	**
Atopic diathesis	166	81 (48.8%)	85 (51.2%)	0.75	0.47-1.19	**
Suffered from asthma or SAR:						
up to one year	9	3 (33.3%)	6 (66.7%)			**
more than one year	47	18 (38.3%)	29 (61.7%)			**
up to 5 years	74	28 (37.8%)	46 (62.2%)			**
more than 5 years	170	88 (51.8%)	82 (48.2%)			**

**Pearson χ^2-test (nonsignificant); OAS = oral allergy syndrome; SAR = seasonal allergic rhinitis

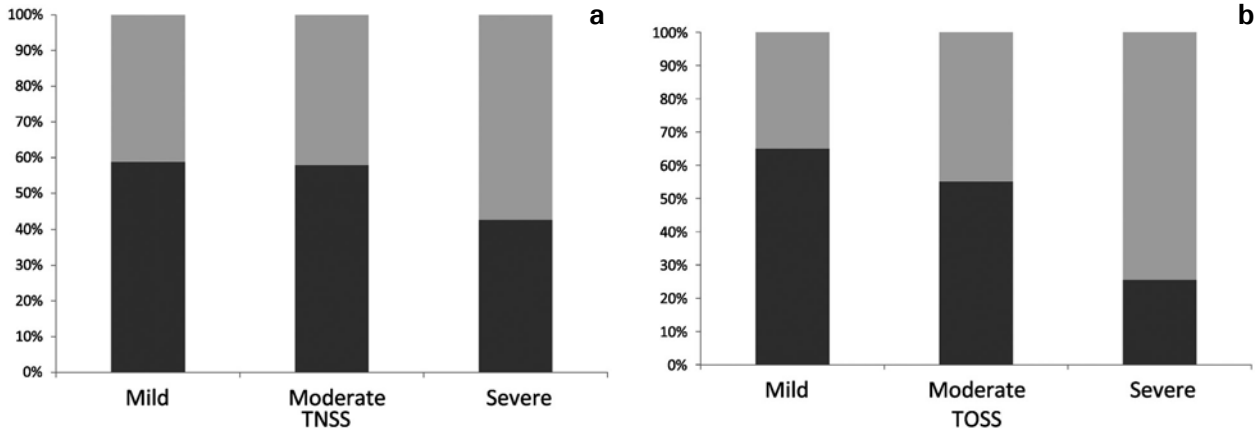
166 (55.3%) patients had atopic diathesis (positive family history). At the time of survey, 170 (56.7%) respondents had suffered from SAR or asthma for more than 5 years. The majority of patients were allergic to Mediterranean area tree pollen (n=216; 72%), grass pollen (n=191; 63.7%), weed pollen (n=163; 54.3%) and *Parietaria* (n=145; 48.3%). There were 78 (26%) monosensitized subjects and the others were polysensitized. The leading nasal symptom was sneezing, which occurred in 276 (92%) patients. The most common ocular symptom was watery eyes that occurred in 254 (84.7%) patients. The frequency of OAS in our study was 45.7% (n=137). The leading oral symptom of tingling throat, palate and mouth after eating offending raw plants was present in 176 (58.7%) patients.

The severity of nasal and ocular symptoms was assessed by TNSS and TOSS (mild (0-4), moderate (5-8) and severe (9-12). The incidence of OAS symptoms increased with the severity of TNSS (rs=0.115; p<0.05) (Fig. 1a) and severity of TOSS (rs=0.260; p<0.001) (Fig. 1b). Patients with more severe nasal symptoms had more severe ocular symptoms (rs=0.248; p<0.001).

Of the potential risk factors for developing OAS in patients with SAR investigated in the present study, only three parameters were statistically significant: 1) diabetes (Pearson χ2-test); 2) severity of nasal symptoms (Spearman's rho correlation coefficient); and 3) severity of ocular symptoms (Spearman's rho correlation coefficient).

Discussion

Oral allergy syndrome is caused by cross-reactivity between proteins from fresh fruits or vegetables and pollens. That is why it can develop only in patients



TNSS = Total Nasal Symptom Score mild (0-4), moderate (5-8) and severe (9-12); Spearman's rho correlation coefficient (r_s=0.115; p=0.047)
TOSS = Total Ocular Symptom Score mild (0-4), moderate (5-8) and severe (9-12); Spearman's rho correlation coefficient (r_s=0.260; p<0.001)

Fig. 1. (a) Incidence of oral allergy syndrome due to severity of nasal symptoms; (b) incidence of OAS due to severity of ocular symptoms.

with SAR. It is common, but not all pollen allergic patients develop OAS. The prevalence of OAS has not been precisely established (i.e. varying across very wide ranges). It is affected by many factors including the form of making it more sensitive in certain geographic areas and the increasing prevalence of allergic rhinitis[1]. Therefore, literature data on the frequency of OAS significantly differ (by 8%-70%)[8-12,17-19]. According to our results, the prevalence was 45.7%.

Since the symptoms of OAS are usually mild and transient, many patients do not associate them with pollen allergy and rhinitis, and do not report it to physician on visiting the office. For this reason, OAS symptoms should be interviewed in all patients with rhinitis due to pollen allergy. If the diagnosis of OAS is established, patients should be informed about the possibility of hypersensitivity to certain fruits and vegetables[14]. In our study, gender was not a statistically significant risk factor for developing OAS symptoms. Men were slightly predominant, which is in contrast to literature data, where female gender seems to be the risk factor for OAS[14,20,21].

In this study, the severity of ocular and nasal symptoms was associated with OAS occurrence, i.e. the more severe ocular/nasal symptoms implied greater likelihood for the patient to develop OAS. It was the most striking result with great influence on everyday allergology practice and patient education; however, it should be noted that correlations were low but significant. We can speculate that the same pattern of neuro-regulatory mechanisms included in ocular symptoms, like naso-ocular reflex, is involved in oral symptoms throughout the trigeminal nerve mediated reflexes on oral mucosa. Eyes and oral mucosa share the same innervation pattern and it can be proper explanation of our results. Further investigations are needed to exclude or confirm our speculations.

In spite of all the possible risk factors for OAS that we expected to be statistically significant, such as asthma, smoking or atopic diathesis, only diabetes was a statistically significant risk factor for developing OAS in patients with SAR. We found no literature data on this issue and have no idea on the possible mechanisms of this type of association.

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