

Oral allergy syndrome in children

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Oral allergy syndrome (OAS) is an allergic reaction that occurs after consumption of fresh fruits and vegetables in patients with allergy to pollen. It is mediated by immunoglobulin E (IgE) antibodies and symptoms arise as a result of cross-reactivity between pollen and plant-derived food. OAS is rarely seen in young children, but the prevalence increases with age. The objectives of the study were to identify the prevalence of OAS and probable risk factors in children and adolescents with seasonal allergic rhinitis (AR). One-hundred and twenty patients with seasonal AR were included. Patients were diagnosed based on their clinical history, skin prick test outcome and specific IgE. In patients describing OAS, prick-by-prick tests with fresh fruit or vegetables were carried out. Thirty-two patients had OAS and it was more frequent in female patients than in male patients. OAS was more frequent in adolescents than in small children and in patients with higher total IgE. OAS was significantly more prevalent in patients with AR and asthma ($P = 0.0016$), as was the case in patients with AR and atopic dermatitis ($P = 0.0004$). OAS is rarely diagnosed in small children, partly because of an inadequate clinical history. Patients with OAS may have some risk factors in addition to pollen allergy, and those with more severe atopy are more likely to develop OAS.

Key words: Allergic rhinitis, oral allergy syndrome, children, pollen food allergy syndrome

INTRODUCTION

Oral allergy syndrome (OAS) is a condition characterised by symptoms of early allergic reactions mediated by immunoglobulin E (IgE) antibodies. It is a singular allergic reaction to food, caused by the cross-reactivity between pollen allergens and food of plant origin^{1,2}. It occurs after consumption of fresh fruits and vegetables in patients with allergy to pollen. The prevalence of OAS depends on many factors, but primarily on the pattern of sensitisation in different geographical regions, as well as on the increasing prevalence of allergic rhinitis (AR) and allergy to pollen. According to various reports, 47–70% of adults with AR have OAS and it is more common in women^{3,4}. In central and northern Europe, grass (*Dactylis glomerata* and *Phleum pratense*) and ragweed (*Ambrosia elatior*) are the main causes of OAS, whereas in the Mediterranean countries, the most frequent causes of OAS are sensitisation to grass, ragweed and pellitory (*Parietaria officinalis*)⁵. OAS is rarely seen in young children, but the incidence increases with age and it is the most frequently occurring expression of food allergy in adolescents and adults⁶. Symptoms usually occur between 2 and 15 minutes after eating smaller amounts of

fresh fruits and vegetables and are usually manifested as numbness of the lips or mouth, itching or oedema of the lips, itchy throat, palate or gingiva, erythema of the face and tightness of the throat. Sometimes, generalised symptoms, such as urticaria, rhinitis, conjunctivitis, asthma attack or even anaphylaxis, may develop^{7–9}. Gastrointestinal symptoms, such as pain, nausea, vomiting and diarrhoea, are less common, and they usually occur after consuming large quantities of food. Symptoms of OAS are caused only by fresh food, and not by boiled, chemically treated or frozen foods. Although the symptoms of OAS can occur at any time, they are most common during the pollination season.

The symptoms of OAS can sometimes be very worrying and confusing for patients with pollen allergy, leading them to seek help from a dentist. General dental practitioners must be aware of this syndrome in order to be able to recognise typical symptoms located in the oral cavity in patients with hay fever. Awareness of this condition can facilitate diagnosis, and a first line of therapy by allergen avoidance can be advised to the patient by their general dental practitioner. In serious and refractory cases, referral to an allergist is thereby suggested much sooner.

METHODS AND MATERIALS

Study design and subjects

The research was conducted in full accordance with the World Medical Association Declaration of Helsinki. The study included 120 patients who were sent by their primary care physician to the outpatient clinic of the Department of Pulmonology, Allergology, Immunology and Rheumatology of the Children's Hospital Zagreb, with the diagnosis of seasonal AR. Written consent was obtained from parents of all participants for the use of demographic and laboratory data for research purposes. The Ethics Committee of the Children's Hospital Zagreb reviewed and approved the study protocol. Demographic data, as well as personal and family histories of atopic diseases, were obtained for each patient.

Diagnosis and *in vitro* tests

Diagnosis and classification of AR were made according to allergic rhinitis and its impact on asthma guidelines¹⁰, and a diagnosis of asthma was established based on the international guidelines global initiative for asthma and practical allergy^{11,12}. Allergic sensitisation was confirmed by the skin prick test (SPT; presence of wheal ≥ 3 mm), using a standard set of common aeroallergens, including house-dust mites, trees, grasses, weeds, moulds, feathers and cat and dog dander (Alyostal Prick; Stallergenes, Antony, France). The results were compared with those obtained with a positive control (histamine 10 mg/ml, Alyostal Prick; Stallergenes) and a negative control (phenolated glycerol 0.9% sodium chloride; Alyostal Prick; Stallergenes), to exclude false-negative and false-positive results. Patients who reported symptoms of OAS underwent prick-by-prick testing with fresh fruit and vegetables, according to the individual patient's history. Total and specific IgE in serum were determined using a monoclonal-based immunoassay (Uni-Cap-system; Pharmacia-Upjohn Diagnostics, Uppsala, Sweden).

Statistics

The results are given as median or number (percentage). Pearson's chi-square test, Fisher's exact test and the *t*-test were used to compare data obtained from patients with OAS with those without OAS. Odds ratio (OR) and 95% confidence interval (95% CI) were estimated where appropriate. Differences were considered significant when $P < 0.05$.

RESULTS

One-hundred and twenty patients (78 girls and 42 boys), median age (range) 10.9 (3.4–18.6) years, were

included in the study. OAS was more prevalent in girls, but the difference was not statistically significant. A comparison was made between the clinical characteristics of patients with and without OAS, and the results are listed in *Table 1*. OAS was present in 32 (26.7%) patients, and was more common in adolescents than in small children, but the difference was not significant. Most ($n=119$) patients had only oral symptoms, mostly numbness of the lips and itching of the lips and throat or palate; four patients also had a feeling of tightness in the throat; and only one patient reported extra-oral symptoms, such as nausea and abdominal pain, along with previously described oral symptoms. None of the patients had generalised symptoms. Among patients with OAS, the most pronounced symptoms were found in patients allergic to birch pollen. Foods reported to cause symptoms of OAS in study patients are shown in order of frequency in *Table 2*. Our results show that OAS was more prevalent in patients with both AR and asthma ($\chi^2 = 9.94$, $P = 0.00167$, OR = 3.85, 95% CI: 1.621–9.139) as well as in patients with AR and atopic dermatitis ($P = 0.000419$). The median total IgE level was higher in OAS-positive patients, as were the median levels of specific IgE against pollens, although the differences were not statistically significant.

DISCUSSION AND CONCLUSION

OAS was first used in 1987 to describe symptoms that occur in patients hypersensitive to food and who have a positive SPT to specific nutritive allergens¹³. Ortolani *et al.*¹⁴ describe OAS as the group of symptoms that occur after ingestion of fresh fruits and vegetables in patients with pollen sneeze and allergy to pollen¹⁴. To distinguish these symptoms from other symptoms caused by allergic reactions to food, the name pollen-food allergy syndrome was proposed^{15,16}. OAS has attracted particular interest during the last few decades because of the rising occurrence of inhaled allergies¹¹. It is increasingly common and should always be considered in patients with pollinosis. As the symptoms of OAS are usually mild and transient, patients often do not associate them with pollen allergy and rhinitis, and do not report them to their physician. For this reason, all patients with AR and/or allergic conjunctivitis caused by pollen allergy should be questioned regarding whether they have experienced any symptoms of OAS^{4,6,16}. If the diagnosis of OAS is confirmed, patients should be informed about the possibility of reactions to certain fruits and vegetables^{16,17}.

Very limited data are available on the prevalence of OAS in children^{6,18,19}. Our results reveal that the prevalence of OAS in children could be higher than estimated, and we believe that OAS is underdiagnosed in children. According to our data, self-reported

Table 1 Comparison of patients with and without oral allergy syndrome (OAS)

Clinical characteristics	OAS		P-value
	Negative(<i>n</i> = 88)	Positive(<i>n</i> = 32)	
Age			
≤7 years	36 (40.9)	10 (31.3)	0.3348
>7 years	52 (59.1)	22 (68.7)	
Gender			
Male	33 (37.5)	9 (28.1)	0.8414
Female	55 (62.5)	23 (71.9)	
Asthma	32 (36.4)	22 (68.8)	0.0016
Allergic conjunctivitis	80 (90.9)	30 (93.8)	0.7281
Atopic dermatitis	6 (6.8)	11 (34.4)	0.0004
Family history of atopy	52 (59.1)	21 (65.6)	0.5169
Allergen (SPT)			
House-dust mite	20 (22.7)	6 (18.8)	0.6390
Trees	72 (81.8)	23 (71.9)	0.2350
Grass	28 (31.8)	11 (34.4)	0.7913
Weed	14 (15.9)	7 (21.9)	0.6801
Cat/dog dander	8 (9.1)	3 (9.4)	0.6038
Total IgE (IU/ml)	266	482	0.4199
Eosinophil count (/l)	455 × 10 ⁶	498 × 10 ⁶	0.3745
Rhinitis duration (years)	2	2.8	0.0936

Values are given as *n* (%) or median. AR, allergic rhinitis; SPT, skin prick test. Bolded *P*-values are statistically significant.

Table 2 Foods provoking oral allergy syndrome (OAS) in our patients

Allergen	Food
Birch	Apple, cherry, peach, carrot, hazelnut
Grasses	Apple, peach, carrot, kiwi
Ragweed	Watermelon, banana

symptoms of OAS were recorded only for a fraction of children with AR over 7 years of age, but after targeted interviewing the OAS symptoms in this age group were documented in 29.7% of patients with AR. Based on our results, the prevalence of OAS in children is lower than that reported for adults (up to 70%)^{4,6,15}, which could be caused by failure to recognise the syndrome in younger children. As the symptoms of OAS, when limited to the oropharyngeal mucosa, may not be visible and cannot be objectively measured, and because young children are often unable to describe them accurately, it is likely that in some patients OAS remains unrecognised or masked in the form of rejection of fresh fruits and vegetables because the child 'does not like it' or 'doesn't want to eat it'.

In our study, OAS was more common in girls than in boys, and similar results have been published for adults^{3,15}. This finding can be explained by the already well-known higher prevalence of atopic diseases in female adolescents^{20–24}. Wheeze and asthma are more prevalent in boys than in girls, but this pat-

tern changes in adolescence²⁰. Hormonal changes in puberty could be one of the possible explanations for this switch in susceptibility, according to gender, to develop asthma and AR. Sex hormones possibly have an important role in the development of the allergic immune response²³. The most common sensitising allergen in study patients with OAS was birch pollen, and the main foods responsible for the symptoms of OAS were apple, peach, carrot and melon, which again are compatible with most of the published results^{6,17,25–28}.

Patients with both seasonal AR and asthma were more predisposed to develop OAS, and similar results have been reported for adults⁴. OAS was more frequent in patients with higher levels of total and specific IgE. It seems that patients with severe atopy are more likely to develop OAS. Based on our results, severe atopy in children is a risk factor for OAS. Pollen allergen-specific immunotherapy (SIT), although performed successfully in patients with pollen allergy, seems to have different effects on patients with pollen-food allergy syndrome. Some authors report excellent performance in patients allergic to birch pollen with symptoms of OAS to apple, whereby in 84% of cases symptoms of OAS disappeared after an allergen-SIT with birch pollen²⁹. An advantageous, although not as impressive, effect of SIT on the symptoms of OAS was described by some other authors, although usually on a small number of individuals and with a questionable long-term effect^{30,31}. However, studies in the paediatric population have not confirmed these results³². There is a risk of development of new allergies to other components of the allergen during SIT, and some authors reported on the appearance of symptoms of OAS after treatment of AR with pollen-specific immunotherapy^{32,33}. Patients with OAS are advised to avoid fresh foods that cause symptoms, although thermally processed foods can be consumed. However, caution is required in patients with atopic dermatitis, as, in such patients, the consumption of thermally processed fruits and vegetables can cause a late, T-cell-mediated reaction and worsening of eczema. Antihistamines can partially reduce the symptoms of OAS^{16,17}. Patients who have experienced generalised symptoms or anaphylaxis are advised to follow a strict elimination diet, and they must carry an adrenaline auto-injector, antihistamines and oral glucocorticoids and a medical certificate, as well as an identification card with a diagnosis and guide for the emergency procedure in the event that anaphylaxis occurs.

In conclusion, the OAS is increasingly common and should always be considered in patients with seasonal allergic rhinoconjunctivitis. Detailed medical history and targeted questions are mandatory, especially in younger children. If the diagnosis is established,

patients should be instructed to avoid the fresh fruits and vegetables that cause symptoms, although such foods, if cooked, can be consumed. Caution is required in patients with atopic dermatitis, in whom the consumption of thermally processed fruits and vegetables can cause a late, T-cell-mediated response and worsening of eczema³⁴. Patients who have experienced generalised symptoms or anaphylaxis are advised to follow a strict elimination diet and must be instructed to carry an adrenaline auto-injector, antihistamine and glucocorticoids, as well as their medical certificate and identity card with diagnosis and instructions on the emergency procedure in the event that anaphylaxis occurs.

General dental practitioners should be aware of this syndrome in order to be able to recognise, in a timely manner, typical symptoms located in the oral cavity in patients with hay fever and thereby facilitate diagnosis and therapy.

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The Ethics Committee of the Children's Hospital Zagreb has reviewed, and thereupon approved, the study protocol. The manuscript does not include clinical trials. All subjects involved in the study were regular patients sent by their primary care physicians for the evaluation to the outpatient clinic of the Department of Pulmonology, Allergology, Immunology and Rheumatology, Children's Hospital Zagreb.

Conflict of Interest

The author declares that no conflict of interest exists.

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