

EXPERIENCE OF OCULAR SYMPTOMS AMONG ALLERGIC RHINITIS PATIENTS DEPENDING ON THE TYPE OF AEROALLERGENS

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ISPOLJAVANJE OKULARNIH SIMPTOMA U ZAVISNOSTI OD TIPOVA INHALATORNIH ALERGENA

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REMARK

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ABSTRACT

The aim of this study was to determine the frequency of ocular symptoms and compare the demographic and clinical characteristics in AR patients depending on sensitisation to various types of aeroallergens.

Allergic rhinitis is defined as an IgE-mediated inflammation of the lining of the nose that is characterized by nasal symptoms, including nasal congestion, sneezing, itching of nose and runny nose. Patients suffering from allergic rhinitis frequently experience ocular symptoms such as ocular redness, eye itching and tears. The frequency of ocular symptoms in our study population was 27,6%. No statistical significance was found in the mean ages of the patients who did or did not experience ocular symptoms $p > 0,05$ ($p = 0,243$). Our results indicated that there were no statistical differences ($p > 0,05$) among the groups of allergic rhinitis patients based on experiencing nasal symptoms according to the types of aeroallergens. Our results indicated that there were significant experiences of ocular symptoms in patients who were sensitised to outdoor aeroallergens ($p < 0,001$) and significant sensitisation to both outdoor and indoor aeroallergens ($p < 0,05$). Experiencing the examined ocular symptoms, including ocular redness, eye itching and tears, demonstrated highly statistical significance ($p < 0,001$) among the groups of allergic rhinitis patients who were sensitised to indoor aeroallergens and outdoor aeroallergens, and there was statistical significance ($p < 0,05$) among the groups of allergic rhinitis patients who were sensitised to indoor aeroallergens and both types of aeroallergens (indoor and outdoor).

Ocular symptoms are more common in patients who are sensitised to outdoor aeroallergens.

Keywords: Allergy, rhinitis, ocular symptoms, aeroallergens.

SAŽETAK

Cilj našeg istraživanja bio je da se utvrdi zastupljenost okularnih simptoma i korelacija u ispoljavanju okularnih simptoma kod obolelih od alergijskog rinitisa u zavisnosti od senzibilizacije na alergene spoljašnje, unutrašnje sredine ili obe grupe inhalatornih alergena.

Alergijski rinitis je IgE posredovana inflamacija sluzokože nosa koja karakterišu nazalni simptomili: kongestija, kihanje, svrab i curenje nosa. Oboleli od alergijskog rinitisa često ispoljavaju i okularne simptome: crvenilo očiju, svrab i suzenje. U ispitivanoj populaciji prisustvo okularnih simptoma uočeno je kod 26,27% obolelih od alergijskog rinitisa. Ispoljavanje okularnih simptoma nije povezano sa starošću ispitanika $p > 0,05$ ($p = 0,243$). Naši rezultati ukazuju da ne postoji statistički značajna razlika između ispitanika koji su senzibilisani na inhalatorne alergene spoljašnje, unutrašnje sredine i senzibilisanih na oba tipa inhalatornih alergena u ispoljavanju svih nazalnih simptoma ($p > 0,05$). Ispoljavanje okularnih simptoma je statistički visoko značajno u grupi ispitanika senzibilisanih na inhalatorne alergene spoljašnje sredine ($p < 0,001$) i statistički značajno kod senzibilisanih na oba tipa inhalatornih alergena ($p < 0,05$). Kod naših ispitanika u pogledu ispoljavanja crvenila, svraba očiju i suzenja postoji visoko statistički značajna razlika među senzibilisanim na inhalatorne alergene unutrašnje i spoljašnje sredine ($p < 0,001$) i statistički značajna razlika među senzibilisanim na inhalatorne alergene unutrašnje sredine i na obe vrste inhalatornih alergena ($p < 0,05$).

Ispoljavanje okularni simptomi kod obolelih od alergijskog rinitisa je u neposrednoj povezanosti sa senzibilizacijom na inhalatorne alergene.

Ključne reči: Alergija, rinitis, okularni simptomi, inhalatorni alergeni.



ABBREVIATIONS

AR- allergic rhinitis
OS- ocular symptoms
SIA- sensitised to indoor aeroallergens

SMA- sensitised to both outdoor and indoor aeroallergens
SOA- sensitised to outdoor aeroallergens

INTRODUCTION

Allergic rhinitis (AR) is defined as inflammation of the lining of the nose and is characterized by nasal symptoms that may frequently be followed by ocular symptoms (OS), particularly in patients who are allergic to outdoor allergens. Allergic rhinitis is a common chronic disease that affects 10-40% of the population worldwide (1-5) and is characterised by the following nasal symptoms: rhinorrhoea, nasal congestion, sneezing and nasal itching. It is often accompanied by OS such as tearing, ocular redness and itching (3).

Allergic rhinitis is a major chronic respiratory disease due to its prevalence, impact on quality of life, impact on work/school performance and association with asthma. Allergic rhinitis is also associated with co-morbidities such as allergic conjunctivitis (3,6). Additionally, AR is one of the top ten reasons for patients visiting their general practitioner (7).

Allergic rhinitis is a multifactorial disease that is induced by gene–environment interactions (8). It is well established that aeroallergens cause AR. Aeroallergens have traditionally been subdivided into indoor and outdoor allergens. Major outdoor allergens include various types of pollens and outdoor moulds. Major indoor allergens include mites, animal dander and indoor moulds. Patients with AR can be sensitised to indoor, outdoor or both types of aeroallergens (mixed sensitisation). Aeroallergens as risk factors for AR may occur at all ages of life (3).

Based on the types of aeroallergens, AR is divided into seasonal AR and perennial AR. Seasonal AR is associated with outdoor aeroallergens, whereas perennial AR is most frequently caused by indoor or mixed aeroallergens (8,9). The Allergic Rhinitis and its Impact on Asthma workshop, in collaboration with the World Health Organization, introduced a new classification for AR based on the duration of symptoms, i.e., as either intermittent or persistent, and on the severity of symptoms, i.e., ranging from mild to moderate to severe (3).

The ocular symptoms experienced in AR, which is usually referred to as conjunctivitis, are multifactorial and can be caused by allergic agents, with various mechanisms, symptoms and signs and degree of severity (10,11). One mechanism is an acute hypersensitivity reaction with hyperaemia and chemosis accompanied by intense tearing, itching and burning of the eye following exposure to aeroallergens; alternatively, conjunctivitis may be due to the parasympathetic naso-ocular reflex (12,13).

The aim of this study was to determine the prevalence of ocular symptoms and compare the demographic and clinical characteristics in AR patients depending on sensitisation to various types of aeroallergens.

PATIENTS AND METHODS

We analysed 312 male and female consecutive patients older than 12 years who had a documented clinical diagnosis of AR at the Department of Otorhinolaryngology, Health Centre Kragujevac, Serbia, from March 2012 to 2014. All patients with OS were referred for an ophthalmological examination.

The diagnosis was based on anamnesis according to an AR questionnaire (14), clinical otorhinolaryngologic and ophthalmologic examination that included slit-lamp examination. All enrolled subjects had a positive skin prick test (weal 3 mm larger than the diluted control- histamine 1 mg/1 ml) to at least one of following aeroallergens: cat fur, moulds (indoor and outdoor), tree pollen, house dust, dog fur, weed pollen, grass pollen, *Dermatophagoides pteronyssinus*, plumage and cockroaches and/or serum-specific IgE. Patients who had undergone nasal surgery in the previous 6 months and patients with nasal polyps, significant deviation of the nasal septum or acute upper respiratory infection were excluded.

This population was divided into three managed groups based on the following criteria: sensitised to outdoor aeroallergens - SOA (sensitised to at least one of these aeroallergens: tree pollen, weed pollen, grass pollen), sensitised to indoor aeroallergens - SIA (sensitised to at least one of these aeroallergens: cat fur, moulds, house dust, dog fur, *Dermatophagoides pteronyssinus*, plumage and cockroaches) and sensitised to both outdoor and indoor aeroallergens or mixed group - SMA (sensitised to at least one of the indoor and one of the outdoor aeroallergens).

Statistics were generated using the standard statistical package SPSS (Statistical Package for the Social Sciences, version 19.0). P values less than 0,05 were considered significant, and those less than 0,001 were considered to be highly significant for all of the above tests. To describe the parameters of interest, we used the methods of descriptive analysis, chi-square test, Mann Whitney U test and ANOVA model.

We used the Mann Whitney U test to compare the experience of OS and mean ages in patients with and without OS.

The study was conducted in compliance with the Declaration of Helsinki and was approved by the local ethics committee. All participants or parents or legal guardians gave their written consent to participate in the study.

RESULTS

During the study period, a total of 312 patients had a clinical diagnosis of AR, and most of them were females



Table 1: Frequency of aeroallergens

Aeroallergens	Males N=104 n (%)	Females N=208 n (%)	Total N=312 n (%)
Weeds pollen	57(54.81)	112(53.85)	169 (54.2)
Dermatophagoides pteronyssinus	48(46.15)	97(46.63)	145 (46.5)
Plumage	44(42.31)	91(43.75)	135 (43.3)
Grass pollen	32(30.77)	67(32.21)	99 (31.7)
House dust	23(22.11)	48(23.08)	71 (22.8)
Cat fur	11(10.58)	24(11.54)	35 (11.2)
Trees pollen	11(10.58)	23(11.06)	34 (10.9)
Dog fur	10(9.61)	23(11.06)	33 (10.6)
Moulds	11(10.58)	22(10.58)	33 (10.6)
Cockroaches	6(5.77)	15(7.21)	21 (6.7)

(66,7%). The average age was $27,9 \pm 12,7$; the ages ranged from 12 to 59 years.

The majority age group was 12–25 years, accounting for 158 (50,6%) of all cases. Based on the sensitisation to aeroallergens, the groups were SOA (30,4%), SIA (20,2%) and SMA (43,3%). No significant difference was found in the mean ages of the patients with and without experience of OS $p > 0,05$ ($p = 0,243$).

The frequencies of aeroallergens are shown in Table 1. Most patients were sensitised to weed pollen (54,2%), followed by Dermatophagoides (46,5%) and plumage (43,3%). The presence of sensitisation to one aeroallergen was 15,38% (48 patients), that to 2-4 aeroallergens was 52,88% (165 patients) and polysensitized (5 or more) occurred in 31,74% (99 patients).

The most common nasal symptoms were nasal congestion in 97,1% of all patients. Overall, 27,6% of all patients had OS, of which eye itching was the most common OS symptom by affecting 19,2% of the cases.

The distribution of the main demographic and clinical patient characteristics in the observed groups SOA, SIA and SMA is presented in Table 2. Our results indicated that there were no significant differences ($p > 0,05$) among

Table 2: Patients demographic and clinical characteristics

	SIA (N=81)	SOA (N=63)	SMA (N=168)
Gender (males)	27 (33.33)	22 (34.92)	55 (32.74)
Mean age ($\pm$ sd)	28.7 ± 10.1	27.23 ± 12.2	27.69 ± 11.9
Nasal congestion N (%)	81(100)	61(92.82)	161(95.83)
Sneezing N(%)	30(37.04)	23(36.51)	63(37.50)
Itching of nose N (%)	23(28.39)	20(31.74)	57(33.93)
Runny nose N (%)	19(23.46)	15(23.81)	38(22.62)
Ocular redness N(%) ^{a,b}	1(1.23)	12(19.05)	20(11.90)
Eye itching N(%) ^{a,b}	2(2.47)	19(30.16)	39(23.81)
Tearing N(%) ^{a,b}	0 (0.00)	6(9.52)	12(7.14)

SIA patients sensitised to indoor aeroallergens;

SOA patients sensitised to outdoor aeroallergens;

SMA patients sensitised to outdoor and indoor aeroallergens; N, number of subjects;

a Highly statistically significant difference between SIA and SOA ($p < 0,001$).

b Statistically significant difference between SIA and SMA ($p < 0,05$).

the SOA, SIA and SMA groups regarding gender, mean age, nasal congestion, sneezing, itchy nose and runny nose. Additionally, our results indicated that there was a highly significant difference ($p < 0,001$) in ocular redness, eye itching and tearing in the SIA and SOA patients and a significant difference ($p < 0,05$) between the SIA and SMA groups.

A significant finding was noted in the SOA and SMA groups and experience of OS. We found a highly significant presence of OS ($p < 0,001$) ($\chi^2 = 29,747$; $df = 1$; $p = 0,000$) in patients who were sensitised to outdoor aeroallergens. In the group sensitised to mixed aeroallergens, OS were positively correlated ($p < 0,05$) ($\chi^2 = 10,085$; $df = 1$; $p = 0,002$). Only three patients had OS in the group sensitised to indoor aeroallergens (not significant; $p > 0,05$).

DISCUSSION

Allergic rhinitis represents a global health problem and has considerable prevalence, especially in children and young people (15,16). Half of the patients in this study were 12-25 years old, which is comparable with previous studies conducted elsewhere (17,18).

In this study, a predominance of females was observed, which is in agreement with other studies (19), but other studies reported a male (20) predominance and no gender predilection (21).

In our study, the existence of OS was not correlated with age. According to data from the literature (22), patients under 50 years of age have more frequent combined nasal and OS. This finding might be partly due to other ocular conditions that could develop later in life contributing to this result, such as tear film dysfunction, which appears to increase with age, whereas atopy decreases with age (23).

Most patients presented with sensitisation to weed pollen, followed by Dermatophagoides and Plumage, in our study. These data depend on the flora and climate of the region and environmental conditions (24-26).

Generally, “polysensitisation” means “more than one sensitisation” (i.e., anything other than monosensitisation). According to Jong et al. (27), the term “polysensitisation” describes 2 to 4 sensitisations, and “polysensitisation” describes 5 or more sensitisations. Clinical symptoms were more severe in polysensitized patients than in monosensitized patients (28). In our study, the majority were sensitized to 2-4 aeroallergens, which was similar to the results of recently published studies (29). Establishing mono- and polysensitisation may be clinically significant because polysensitisation is correlated with disease severity (9).

Allergic rhinitis is a complex and multifactorial IgE-mediated disorder that is associated with the epithelial accumulation of effector cells, such as mast cells, eosinophils and basophils, and with the formation and release of various inflammatory mediators that are responsible for the early symptoms of rhinitis, such as nasal itch, sneezing and



rhinorrhoea (7). Pathophysiologically, the disease is characterized by a two-phase process that involves an initial sensitization phase (allergen exposure resulting in IgE over-expression), with subsequent allergen exposure provoking an allergic response. Clinically, the allergic response can be divided into the following two phases: the early phase inflammatory response, which is initiated within minutes of re-exposure to the allergen and is primarily caused by mast cell degranulation, and the release of preformed mediators such as histamine and a newly generated different type of mediators. For the patient, the clinical manifestations are early symptoms of AR such as sneezing, itching and rhinorrhoea. Additionally, they stimulate the production, adhesion and infiltration into local tissue of circulating inflammatory cells such as eosinophils, basophils, monocytes, and lymphocytes (7,30). The late-phase inflammatory response begins 2–4 h after allergen exposure and involves the activated inflammatory cells which release further mediators, thus promoting local oedema and tissue damage and the continuation of the overall inflammatory process. Symptomatically, the late-phase allergic reaction is characterized by nasal congestion and obstruction (30).

All patients in this study had nasal symptoms, and nasal congestion was found in most patients. Nasal congestion is a symptom that characterises both the early and late phases of AR, and it often persists long after allergen exposure. The same observation was also reported in another study (31). Rhinorrhoea was also reported as the most frequent symptom, but the difference in the data was likely due to different methodological approaches and the different characteristics of the population and environmental milieu (including children younger than 12 and examined patients suffering from seasonal AR). Rhinorrhoea is common in small children and is commonly accompanied by viral and bacterial infections, particularly in children under five years of age, who were the majority in this study (32).

Allergic conjunctivitis is the typical conjunctival reaction in allergic rhinitis or following exposure to allergens. The pathophysiology underlying OS remains to be elucidated. The symptoms probably arise via a combination of mechanisms that include direct contact of the conjunctiva with natural pollen and reflex mechanisms originating in the nose. Pollen exposure can result from the direct transfer of pollen to the conjunctiva from the blowing of air or nasal secretions that contain the antigen up the nasolacrimal duct. In support of direct contact of pollen as a source of ocular symptoms in patients with allergic rhinitis, pollen can be washed out of the conjunctiva on windy days, although the amount is 10-fold less than the amount of pollen recovered simultaneously from the nose (33).

Ocular symptoms occur in a large proportion of patients with AR. The rate of OS found in this study (27,6%) is lower than the rate presented in the literature, which is higher than 40% (34–36). Traditionally, allergy investigations have focused on nasal symptoms, but recent studies have highlighted the prevalence and significance of OS. Evidence suggests that OS are particularly prevalent in

seasonal AR sufferers (37) who were sensitised to outdoor aeroallergens (9). Despite previous opinions, OS are not only common but also distressing for sufferers (36).

The present study was performed to establish a correlation among the demographic characteristics in AR patients who were sensitised to various types of aeroallergens: SIA, SOA and SMA. There were no significant differences in regard to gender, age and nasal symptoms, which were equally represented in the observed groups. Our results indicate significant differences in the ocular redness, eye itching and tearing among the observed groups. These results indicate that the main risk factor for experience of OS is sensitisation to outdoor aeroallergens. Our results are similar to the results of recent studies (9,38).

Our present study demonstrated a lower presence of OS than did the data from the other studies, which may indicate that the majority of the patients with AR who also have OS either seek care from their general practitioner or do not recognise their symptoms to be a disease at all. Some of them also act as their own doctors. In AR sufferers, it is necessary to address all symptoms, especially OS, which are more common in patients who are sensitised to outdoor aeroallergens. These patients must be referred to an ophthalmologist for examination and adequate treatment because currently, the ophthalmologic examination is not part of the AR diagnostic protocol.

Conflict of Interest

There is no financial interest and no other conflict of interest.

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