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Allergic rhinitis in the etiology of obstructive sleep apnea

Allergic rhinitis with sleep apnea

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Abstract
Aim: In this study, it was aimed to determine the prevalence of allergic rhinitis in patients with obstructive sleep apnea syndrome and to investigate the effect of allergic rhinitis on the severity of obstructive sleep apnea (OSA).
Material and Methods: In our study, patients who applied to our outpatient clinic with complaints of snoring and excessive daytime sleepiness and underwent polysomnography (PSG) and skin prick test (SPT) between 2014-2017 were retrospectively evaluated. The relationship between OSA and allergic rhinitis was evaluated.
Results: The study included 519 cases, 162 females (31,2%) and 357 males (68,8%), with a mean age of 49,26 ± 12,21 (19–85), who were diagnosed with simple snoring and OSA. The prevalence of allergic rhinitis among the OSA groups was 20.8%. Statistically, significant correlation was found when the OSA groups were compared according to age, body mass index and Epworth values (p<0,001, p<0,001, p=0,004, respectively). When the distribution of allergens was examined according to the prick test results performed on the patients, while most common sensitivity was detected to house dust mites (42%), and the second most common sensitivity was detected to grass pollen (39%) in atopic patients, sensitivity to fungal spores and animal hair/epithelium was detected less commonly (9,5%).
Discussion: As a result of our study, we think that allergic rhinitis may contribute to the development of snoring and OSA, and therefore, allergy treatment may improve the clinical picture of snoring and OSA.

Keywords
Sleep Apnea, Allergic Rhinitis, Skin Prick Test

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Introduction

Obstructive sleep apnea (OSA) is a clinical disease characterized by recurrent episodes of upper airway collapse during sleep. When the study algorithm was established based on patient complaints and clinical+polysomnography (PSG) data, the prevalence of OSA was observed to be 4% in men and 2% in women [1,2]. There are many predictive causes identified for OSA. Obesity, male gender, age, race, genetics, smoking and alcohol addiction are the most common known causes [3]. Disorders or anatomical variations formed in the upper respiratory tract are also among important factors that can cause OSA. Changes in the upper respiratory tract, especially in the connective tissues, play an important role in the pathophysiology in patients with OSA [4].

Primary symptoms of allergic rhinitis (AR) result from inflammation in the upper respiratory tract after allergen exposure. Nasal congestion is the most disturbing symptom in AR patients and usually occurs with perennial allergens. This complaint, which continues especially at night, causes deterioration in respiratory airflow in the upper respiratory tract and snoring may occur in patients [5].

In a review published in 2014, the prevalence of AR was 10% to 30% in adults and 40% in children [6].

Treatments of inflammation/congestion that develops in the nasal region and causes flow restriction reduce the existing barrier [7].

It is known that Obstructive Sleep Apnea and Allergic Rhinitis are frequently encountered and significantly affect the quality of life of people who are exposed to them. These are diseases to be considered because they are treatable. In our study, we also aimed to investigate the relationship between the current situation and AR, and the structure of the correlation between AR and OSA severity, while including patients who were admitted to our outpatient clinic with complaints of sleep apnea, snoring, and daytime sleepiness in the PSG program to evaluate them in terms of OSA.

Material and Methods

In our study, we retrospectively examined patients over the age of 18 who applied to the Chest Diseases outpatient clinic of our hospital between February 2014 and November 2017 with complaints of snoring and excessive daytime sleepiness, and who underwent PSG. Patients with central apnea and patients with a history of malignancy were excluded from the study.

In order to make a differential diagnosis with OSA for each patient, some tests were performed to exclude other diseases that cause similar symptoms. For this reason, pulmonary function test, skin prick test, hemogram and biochemistry analyses, posterior-anterior chest X-ray were requested from the patients.

The patients were divided into groups according to the severity of OSA and whether they were allergic or not. The prevalence of allergic rhinitis in OSA patients and the relationship between diseases were evaluated.

This study was carried out with the permission of Balıkesir University Faculty of Medicine, Health Practice and Research Hospital Ethics Committee, dated 16.11.2016 and decision number 2016/115.

Skin prick test

The skin prick test is a frequently used method in clinical practice, as it is both inexpensive and easy to apply [8]. The skin prick test was applied to the inner forearm by using standard allergens (Allergopharma, Reinbek, Germany). The test was evaluated 15 minutes after its application. Sensitivity to any allergen was defined as an atopic body.

Polysomnography

The standard PSG process was performed with the 62-channel Embla N7000 vehicle (Medcare Flage, Iceland). Polysomnographic records were scored using the American Academy of Sleep Medicine manual scoring criteria [9]. The patients were categorized in terms of OSA severity as follows: AHI <5 was considered normal (control groups), 5 and <15 were considered mild OSA, 15 and <30 moderate OSA, and 30 and above were considered severe OSA. Patients diagnosed with OSA were divided into 4 groups; simple snoring (114 persons) Group I, mild OSA (125 persons) Group II, moderate OSA (132 persons) Group III, severe OSA (148 persons) Group IV.

Statistical Method

SPSS 23.0 program was used in the analysis of the variables. The conformity of the data to the normal distribution was evaluated using the Shapiro-Wilk test, and the homogeneity of variance was evaluated using the Levene test. While the Independent-Samples T-test was used together with the Bootstrap results in the comparison of two independent groups with each other according to the quantitative data, the Mann-Whitney U test was used with the Monte Carlo simulation technique. In the comparison of independent multiple groups with each other according to quantitative data, the Kruskal-Wallis H Test, one of the nonparametric tests, was used with the results of the Monte Carlo simulation technique, and Dunn's Test was used for Post Hoc analyses. In a comparison of categorical variables with each other, Pearson's Chi-Square and Fisher-Freeman-Holton tests were tested with the Monte Carlo Simulation technique and column ratios were compared with each other and expressed according to Benjamini-Hochberg corrected p-value results. Quantitative variables were shown in the tables as mean ± std (standard deviation) and median range (maximum-minimum), while categorical variables were shown as n (%). The variables were analyzed at a 95% confidence level, and a p-value of <0.05 was considered significant.

Results

The study was performed on 519 cases diagnosed with simple snoring and OSA. The mean age of the patients was 49,26 ± 12,21 years, with 162 (31,2%) females and 357 (68,8%) males; One hundred and six (20,4%) of all patients were evaluated as allergic (Table 1). In OSA groups, the prevalence of allergic rhinitis was 20,8%.

A statistically significant difference was found between OSA severity and gender (p=0,011). The rate of male patients was higher in all groups (p=0,011) (Table 1).

When assessing the severity of OSA and the presence of comorbidity, a significant difference was found between the groups (p<0,01) (Table 1).

When atopy, smoking history and nasal obstruction were compared in all groups according to the severity of OSA, no

Table 1. Distribution of demographic characteristics between groups

Demographic data		OSA groups				p
		Group I n (%)	Group II n (%)	Group III n (%)	Group IV n (%)	
Gender	Female	48 (42,1)	38 (30,4)	42 (31,8)	34 (23)	0,011
	Male	66 (57,9)	87 (69,6)	90 (68,2)	114 (77)	
Atopy status	Non-Allergic	92 (80,7)	98 (78,4)	102 (77,3)	121 (81,8)	0,783
	Allergic	22 (19,3)	27 (21,6)	30 (22,7)	27 (18,2)	
Comorbidiy	No	93 (81,6)	89 (71,2)	74 (56,1)	83 (56,1)	<0,001
	Yes	21 (18,4)	36 (27,9)	58 (43,9)	65 (43,9)	
Smoke	Non-smoker	85 (74,6)	80 (64)	80 (60,6)	94 (63,5)	0,078
	Smoker	29 (25,4)	45 (36)	52 (39,4)	54 (36,5)	
Nasal congestion	Non-mild	10 (45,5)	12 (44,4)	17 (56,7)	12 (44,4)	0,751
	Moderate-Severe	12 (54,5)	15 (55,6)	13 (43,3)	15 (55,6)	

Table 2. Allergen distributions between groups

Allergens		OSA groups				p
		Grop I n (%)	Group II n (%)	Group III n (%)	Group IV n (%)	
Herbs	None	103 (90,4)	112 (89,6)	118 (89,4)	133 (89,9)	0,998
	Exist	11 (9,6)	13 (10,4)	14 (10,6)	15 (10,1)	
Meadow Grasses	None	110 (96,5)	116 (92,8)	127 (96,2)	141 (95,3)	0,519
	Exist	4 (3,5)	9 (7,2)	5 (3,8)	7 (4,7)	
Wild Herbs	None	112 (98,2)	119 (95,2)	131 (99,2)	145 (98)	0,218
	Exist	2 (1,8)	6 (4,8)	1 (0,8)	3 (2)	
Tree Pollen	None	108 (94,7)	119 (95,2)	123 (93,2)	139 (93,9)	0,912
	Exist	6 (5,3)	6 (4,8)	9 (6,8)	9 (6,1)	
House Dust	None	102 (89,5)	110 (88)	115 (87,1)	135 (91,2)	0,723
	Exist	12 (10,5)	15 (12)	17 (12,9)	13 (8,8)	
Animal	None	113 (99,1)	120 (96)	127 (96,2)	146 (98,6)	0,254
	Exist	1 (0,9)	5 (4)	5 (3,8)	2 (1,4)	
Fungi	None	109 (95,6)	123 (98,4)	129 (97,7)	145 (98)	0,565
	Exist	5 (4,4)	2 (1,6)	3 (2,3)	3 (2)	

OSA: Obstructive sleep apnea

Table 3. Laboratory and biochemistry values of allergic and non-allergic patients

		Atopy		p
		Non-allergic	Allergic	
Age		49,73 ± 12,37	47,43 ± 11,46	0,063
Gender	Male	279 (67,6%)	78 (73,6%)	0,23
	Female	134 (32,4%)	28 (26,4%)	
BMI		31,10 (18,40/57,10)	29,50 (18/46,5)	0,15
Comorbidity	Yes	151 (36,6%)	29 (27,4%)	0,76
	No	262 (63,4%)	77 (72,6%)	
AHI		16,20 (0/115)	16,05 (0/87,30)	0,481
O2 min		85 (50/96)	87 (50/94)	0,08
Epworth		9 (0/24)	8 (0/24)	0,18
Total IgE		38 (0,87/1.977,19)	115,61 (8,57/1.701,83)	<0,001

BMI: Body mass index, AHI: Apnea hypopnea index

statistically significant correlation was found (p=0,783, p=0,078 and p=0,751, respectively) (Table 1).

No significant correlation was found between the groups in terms of atopy, smoking history and nasal obstruction when comparing the severity of OSA (p=0,783, p=0,078, p=0,751, respectively) (Table 1).

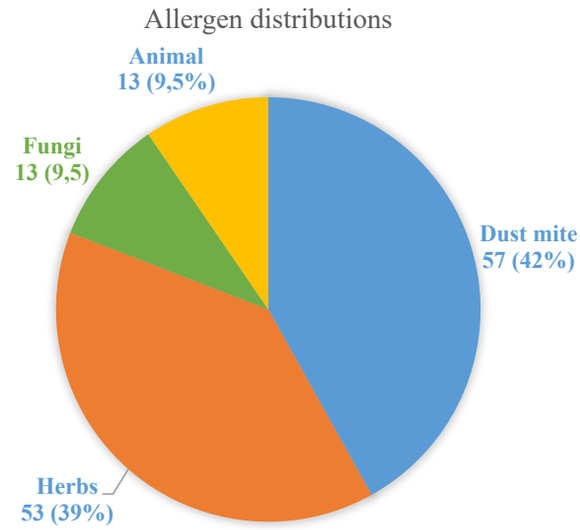

Figure 1. Allergen distribution according to the prick test result

It was observed that the mean age increased as the severity of OSA increased among the groups (median age was 46 years in Group I, 49 in Group II, 51 in Group III, 52 in Group IV) (p<0,001). When Epworth and BMI values were compared between groups; while median Epworth was 7 in group I, it was found as 10 in group IV; while the median BMI was found 28,10 in group I, the median was found as 32,4 in group IV (p=0,004, p<0,001, respectively).

When the allergen types were compared according to the severity of OSA, no significant correlation was found (Table 2).

27,4% of allergic patients and 36,6% of non-allergic patients had comorbidities, and the difference between them was not significant (p=0,076) (Table 3). A history of cardiac and pulmonary disease was found in 19 patients in the non-allergic group and in 1 patient in the allergic group (4,6% vs. 0,9%, respectively).

When the patients were evaluated according to their allergy status; no statistically significant correlation was found between allergic and non-allergic subjects in terms of age, BMI, AHI, lowest nighttime oxygen saturation, Epworth, values (Table 3).

When the total IgE levels of the patients were compared, the total IgE values (115,61) of the allergic patients were found to be higher than in non-allergic patients (n=38), and this highness was found to be statistically significant (p<0,001) (Table 3).

When the distribution of allergens was examined according to the prick test results performed on the patients, the most common sensitivity was detected to house dust mites (42%), and the second most common sensitivity was detected to grass pollen (39%) in atopic patients. Sensitivity to fungal spores and animal hair/epithelium was detected lesser (9,5%). The distribution of allergens is shown in Figure 1.

Discussion

The main event in OSA is the closure of the airway. Agreed predisposing factors for OSA are obesity, male gender, smoking, craniofacial abnormalities, family history, increased pharyngeal soft tissue, and nasal obstruction. Especially male gender and obesity come to the fore [10]. Also in our study, the severity of

OSA was found to be higher, especially in males and in patients with high BMI. This situation is explained by the neck structure of the male gender and the increase in pharyngeal adipose tissue in overweight patients.

The prevalence of allergic rhinitis is observed with a frequency varying between 15% and 40%, depending on the population and the methods used [11]. Also in our study, it was similarly found that the prevalence of allergic rhinitis was 20,4% in the entire patient population.

It was reported that hypoxemia caused by OSA and subsequent sympathetic stimulation are risk factors especially for cardiovascular and cerebrovascular diseases [2]. Our study also showed that the severity of OSA increased even more in patients with comorbidities.

One of the predisposing factors for OSA is smoking. Many studies showing a higher prevalence of smoking in OSA patients have attempted to demonstrate the relationship between OSA and smoking [12,13]. In our study, the prevalence of smoking was found to be 34,7% and no significant effect of smoking on the severity of OSA was found. This may be attributed to the multifactorial components of the OSA pathophysiology rather than the inflammatory effect of smoking.

Nasal obstruction was stated as a risk factor especially for OSA. Nasal congestion significantly blocks airflow during sleep and disrupts the normal physiological functions of the nasal cavity, a possible primary factor leading to pharyngeal collapse [14]. In the study by Bozkurt et al., the presence or absence of allergic rhinitis symptoms in patients with Sleep breathing disorder symptoms did not cause significant change in PSG parameters. In the same study, the mean AHI value was found to be higher in the non-allergic group, but this highness was not statistically significant [15]. Also in our study, no relationship was found between the degree of nasal obstruction and the severity of AHI in the absence or presence of nasal obstruction in allergic patients.

The Epworth sleepiness scale is commonly used for screening and distinguishing between individuals with versus without OSA [16]. In the NASAL study, patients with allergic rhinitis reported that they had more difficulty falling asleep (24% vs 8%), woke up more frequently during the night (31% vs 13%), and did not sleep well (26% vs 11%) compared to the general population [17]. However, in another study performed, allergic and non-allergic patients were evaluated, Epworth results were found to be similar between the groups [15]. In our study, there was no difference between allergic and non-allergic patient groups in terms of Epworth values.

AR has been defined as a clinical form accompanied by an IgE-related immune response [18]. Also in our study, the total IgE ratio was higher in the allergy group. No significant difference was found between OSA and non-OSA, and the grade of AHI, in terms of total IgE level. In our study, the total IgE ratio was found to be higher in the allergic group, which is consistent with the literature.

The skin prick test has become routinely used today, due to its ease of application, fast results and cost effectiveness [19]. In a recently published article, the sensitivity and specificity of the skin prick test to aeroallergens were found to be approximately 70-97% [20]. In a study performed, prick test was carried out on patients with a high risk for OSA, and the test was found to be positive in 72,5%. Afterwards, PSG was performed on the patients and OSA was detected in 69,2% of the patients [21]. In a meta-analysis by Yuan Cao et al., the prevalence of AR in adults was found to be 23% and 35% in Sleep disordered breathing/OSA patients [22]. In our study, the prevalence of allergic rhinitis in OSA patients was 20,8%, and in atopic patients in allergen distribution, house dust mite (42%) was the most common, while sensitivity to herbs (39%) was the second most common. However, the effect of house dust mite or grass pollen on the severity of OSA could not be demonstrated.

Conclusion

In our study, the prevalence of allergic rhinitis in OSA patients was 20,8%, and the highest sensitivity was found in relation to house dust mites. Therefore, we concluded that especially perennial allergic rhinitis may be associated with snoring and OSA. As a result of our study, we think that with the treatment of allergic rhinitis, snoring and clinical picture of OSA may be improved. Along with this relationship, we suggest that allergic rhinitis symptoms be questioned within the questions directed to patients with snoring complaints and patients with OSA.

Our study had some limitations. No comparison was made with the healthy population without simple snoring/OSA. Nasal inspiratory flow measurements and rhinomanometry measurements were not performed for the evaluation of nasal obstruction. Non-allergic rhinitis group was not determined among the patients and this group was not evaluated separately. Further and larger studies are needed to determine the relationship between OSA and allergic rhinitis.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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