



Evaluation of olfactory function in children with seasonal allergic rhinitis and its correlation with acoustic rhinometry

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ABSTRACT

Objectives: Seasonal allergic rhinitis (SAR) is common in children and hyposmia is a major symptom affecting the quality of life. The aim of the present study is to assess olfactory dysfunction in pediatric patients with SAR and correlate the results with acoustic rhinometry measurements.

Methods: Forty children, diagnosed as moderate and severe SAR based on clinical findings, ARIA (Allergic rhinitis and its impact on asthma) classification and prick test results were enrolled in the study. Endoscopic nasal examination, acoustic rhinometry, total nasal symptom score (TNSS) and Connecticut Chemosensory Clinical Research Center (CCCRC) tests were performed 'in season' (May–August) and 'out season' (November–February). Three patients who did not show up in 'out season' examinations were excluded from the study.

Results: The ages of the children ranged between 8 and 18 years with a hyposmia increased and odor identification decreased ($p < 0.005$, $p = 0.003$, respectively), whereas no differences were found between odor thresholds and the discrimination values ($p > 0.05$). Mean CCCRC value was obstruction score ($r = -0.340$, $p = 0.04$), subjective hyposmia ($r = -0.44$, $p = 0.007$) and TNSS ($r = -0.494$, $p = 0.02$). Although some of the acoustic rhinometry parameters were lower during allergy season, there were no correlations between acoustic rhinometry parameters and CCCRC values.

Conclusion: Nearly half of the children with AR reported a mild to moderate hyposmia during pollen season and there was a decrease in odor identification, which can be easily shown using a CCCRC test.

1. Introduction

Allergic rhinitis (AR) is an inflammation of the nasal membranes caused by an Ig-E mediated hypersensitivity reaction to sensitized antigens with a prevalence reaching up to 40% in children worldwide [1]. Common symptoms of AR include sneezing, nasal congestion, nasal itching, rhinorrhea, coughing, a sore throat and itchy eyes. Seasonal allergic rhinitis (SAR) usually occur during the spring and fall season and are typically in response to outdoor allergens like pollens from grass, trees and weeds, whereas perennial allergies occur year round, or at any time during the year in response to indoor substances, like dust mites, pet dander, cockroaches or mold. Although AR itself is not life-threatening, it might be associated with asthma, sinusitis and anaphylaxis, and thus has further important health implications. The quality of life might be compromised by frequent night awakenings, easy fatigue, defects of language and irritability, and limited outdoor activities.

Smell disorders can result from a physical blockage of the nose, such as a deviated septum, nasal allergies, and swelling of the mucosa caused by chronic rhinosinusitis, nasal polyps or from damage to the olfactory cleft or nerve or upper-airway inflammation by physically obstructing access to the smell nerves or damaging the special cells and nerves of the smell pathway [2]. Hyposmia is a fairly common complaint in patients with long-standing allergic or nonallergic rhinitis [3–8]. In a systematic review, smell disorders were shown to be present in 20–40% of the adult patients with AR [9]. However, they are often neglected by the patients and overlooked by the physicians. Both obstruction of airflow across the olfactory epithelium secondary to inflamed mucosa or enlarged polyps and nasal inflammation without obstruction were suggested to cause olfactory dysfunction in AR.

In the literature, there are limited number of studies about olfactory dysfunction in pediatric patients with SAR. In a recent study [10], using a subjective scale, odor dysfunction was reported in 44% of the AR

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children with ages between 6 and 12 years and loss of smell frequency and intensity was found to be related to disease duration and severity. However, in another study, olfactory function was found to be normal in children aged 6–18 years with AR and non-AR [11]. The aim of this study is to evaluate the changes in olfactory function in pediatric patients with SAR using both subjective and objective scales in allergy season, compare the findings with out season measurements and correlate the results with acoustic rhinometry parameters.

2. Materials and methods

2.1. Patient selection

The study was approved by the Ethics Committee of Selcuk University with the protocol no 2016/4. Written informed consent was obtained from parents of the children who participated in the study.

Forty children with ages between 8 and 18 years who were admitted to the Department of Otorhinolaryngology-Head and Neck Surgery or referred from the Department of Pediatric Allergy-Immunology with symptoms of SAR between May 2016 and August 2016 were enrolled in the study.

SAR was diagnosed based on clinical findings, ARIA classification [12] and prick test results. The children were tested with a panel of common inhalant allergens including house dust mites, a mixture of 12 grass pollens, a mixture of four grain pollens, tree pollens, molds, *Cladosporium* mixture, animal epithelium and cockroach (*Stallergenes* SA, 92160, Antony, France). A mean wheal diameter greater than 3 mm was considered positive. According to skin prick test, children who had only pollen allergy were included in the study.

Inclusion criteria were a history of seasonal nasal symptoms for at least 2 years, diagnosed as moderate and severe AR based on ARIA criteria and positive skin prick test to only pollens. Exclusion criteria were anatomical deformities causing airway obstruction, such as adenoid hypertrophy, tumor or choanal atresia, nasal polyps, upper respiratory tract infection or acute rhinosinusitis within 2-weeks, asthma, treatment with steroids, antihistamines, thyroid medications and/or antidepressants for a month or longer, immunotherapy, previous nasal surgery, history of head trauma and smoking.

2.2. Study design

Pollen season was determined according to Konya's pollen map for 2010 (www.aid.org.tr/aid.polen.konya). The period from May to July was considered 'in season' for tree pollens and from May to August for grass and grain pollens. A general medical history was taken for every child. The children were asked if they have hyposmia and a subjective scoring was performed on a scale from 0 to 3 (0 = no smell loss, 1 = mild, 2 = moderate and 3 = severe/no smell). Endoscopic nasal examination, nasal obstruction score, total nasal symptom score (TNSS), acoustic rhinometry, and Connecticut Chemosensory Clinical Research Center (CCCRC) tests were performed both during pollen season (May–August) and out season (November–February) and 3 patients who did not show up in 'out season' examination were excluded from the study.

2.2.1. Total nasal symptom score (TNSS)

Nasal symptoms were assessed using the total nasal symptoms score (TNSS) by calculating the sum of scores for nasal obstruction, rhinorrhea, nasal itching, and sneezing. Each nasal symptom was scored on a scale from 0 to 3 (0 = no symptoms; 1 = mild; 2 = moderate; 3 = severe) according to TNSS. Any symptom not causing significant discomfort was considered mild. Any symptom causing discomfort but not interfering with daily activity and/or disturbing sleep was considered moderate. Any symptom that interfered with daily activity and sleep pattern was considered severe. The scores for each symptom were summed and the total nasal symptom score was obtained. Loss of the

sense of smell of the patients were also questioned.

2.2.2. Endoscopic nasal examination

Both sides of nasal cavities were evaluated endoscopically using the Storz 0° pediatric endoscope. Concha hypertrophy, nasal mucosal edema, paleness, rhinorrhea were recorded.

2.2.3. Acoustic rhinometry

Using acoustic rhinometry, the nasal volume from 0 to 2.2 cm (VOL1), the nasal volume from 2.2 cm to 5.4 cm (VOL2), total nasal volume from 0 to 5.4 cm (TVOL), the minimum cross-sectional area of the anterior (MCA1) and the minimum cross-sectional area of the posterior (MCA2) were measured from each nasal cavity within the distance of 5.4 cm from the nostrils. The test was repeated 3 times and the mean value was recorded.

2.2.4. Olfactory function

Olfactory function testing was performed by means of a modified Connecticut Chemosensory Clinical Research Center test [13] consisting of a threshold, identification, and discrimination test. The results of 3 tests were summed to calculate the CCCRC score. The validity of this test in the Turkish adult population was confirmed before [14].

Threshold testing was performed with solutions of 1-butanol in deionized water, decreasing in 8 steps. The strongest butanol concentration (bottle 0) was 4% butanol in deionized water. Each subsequent dilution (bottles 1–8) was a 1:3 dilution with deionized water. Possible scores ranged from 0 to 8. Starting with the lowest concentration, the patients received a bottle with odorant and a bottle filled with deionized water and had to decide which smelled stronger. In this test, 60 ml of the odorant was presented in a squeezable polyethylene bottle. The bottles were of identical appearance and presented simultaneously. Subjects were instructed to occlude one nostril and place the tip of the bottle immediately beneath the other nostril. If the choice was incorrect, the next stronger concentration of butanol was presented along with a bottle containing only water. A concentration was defined to be the threshold concentration if it was correctly identified four times for that nostril. The other nostril was then tested separately, and the scores for both nostrils were averaged to arrive at the final score. The test result was expressed as threshold score from 0 to 8.

In the identification testing 8 well-known odorants which contains Peanut butter, soap, mothballs, Vicks, chocolate, coffee, cinnamon and baby powder were presented within 180 ml opaque jars to the test person in the same manner. Subjects chose from a printed list containing the correct items as well as an equal number of distractor items. The forced choice items included the following: Vicks, burnt paper, wood shavings, coffee, baby powder, peanut butter, spearmint, cinnamon, soap, chocolate, mothballs, grape jam, ketchup, black pepper, and rubber. The ability to sense Vicks indicates intact trigeminal nerve function. Possible scores ranged from 0 to 7 items correctly identified. Scores for both nostrils were averaged to arrive at the final score.

In the discrimination testing the subject received three different odorants. Two were identical and the third was a different odor. The differing bottle had to be identified. A total of seven triplets were tested in this manner. The person received one point for each correct answer, with a possible maximum of seven points.

Scores for the butanol threshold test, identification tests and discrimination tests were subsequently averaged to arrive at a CCCRC score.

2.3. Statistical analyses

All analyses were performed using SPSS 21.0 (SPSS for Windows, USA). Values for categorical variables were provided in numerals and percentages of the total. Data are presented as the means $\pm$ standard deviation, IQR (interquartile range). Categorical variables were compared using chi-square test. The correlation between two continuous

Table 1

Comparison of the total nasal symptom score (TNSS), odor scores and acoustic rhinometric measurements between “in season” and “out season”.

Parameter (Mean $\pm$ SD)	In season	Out season	P
TNSS	5.9 $\pm$ 2.5	2.6 $\pm$ 1.9	0.00
Odor threshold	7.9 $\pm$ 0.16	7.9 $\pm$ 0.16	–
Odor identification	0.76 $\pm$ 0.14	0.87 $\pm$ 0.12	0.003
Odor discrimination	0.92 $\pm$ 0.22	0.91 $\pm$ 0.24	0.32
CCRC	1.62 $\pm$ 0.16	1.72 $\pm$ 0.12	0.00
Right MCA1 (cm ²)	0.38 $\pm$ 0.13	0.43 $\pm$ 0.13	0.01
Right MCA2 (cm ²)	0.36 $\pm$ 0.12	0.57 $\pm$ 0.62	0.04
Right Vol1 (cm ³)	1.52 $\pm$ 0.39	1.60 $\pm$ 0.51	0.3
Right Vol2 (cm ³)	3.32 $\pm$ 1.02	3.78 $\pm$ 1.58	0.05
Right TVol (cm ³)	4.85 $\pm$ 1.23	5.39 $\pm$ 1.77	0.044
Left MCA1 (cm ²)	0.34 $\pm$ 0.11	0.39 $\pm$ 0.15	0.05
Left MCA2 (cm ²)	0.42 $\pm$ 0.19	0.48 $\pm$ 0.21	0.03
Left Vol1 (cm ³)	1.37 $\pm$ 0.30	1.40 $\pm$ 0.44	0.01
Left Vol2 (cm ³)	3.28 $\pm$ 1.35	3.65 $\pm$ 1.17	0.2
Left TVol (cm ³)	4.65 $\pm$ 1.43	5.06 $\pm$ 1.38	0.245

TNSS, Total nasal symptom score; CCRC, Connecticut Chemosensory Clinical Research Center Test; MCA1, minimum cross-sectional area of the anterior; MCA2, minimum cross-sectional area of the posterior; Vol1, nasal volume from 0 to 2.2 cm; Vol2, nasal volume from 2.2 cm to 5.4 cm; TVol, Total nasal volume from 0 to 5.4 cm.

variables was evaluated by either Pearson's or Spearman's coefficient based on normality tests. Paired-t test was used to compare the parameters taken during and out season. A p value of < 0.05 was considered as statistically significant.

3. Results

Thirty-seven patients (23 boys and 14 girls) with a mean age of 13 ± 2.4 years (range 8–18 years) were included in the study. Subjective hyposmia was found to be significantly higher in pollen season compared to out season. ($p < 0.05$) There was mild to moderate loss of smell in 43.2% of the children during pollen season (27% mild, 16.2% moderate) and 32.4% of the children reported mild loss of smell even in out season.

TNSS was 5.9 ± 2.5 in pollen season and 2.6 ± 1.9 in out season. ($p < 0.01$) (Table 1) The range was 0–5 in out season and 1–11 in pollen season. In endoscopic examination, nasal mucosal edema, paleness and rhinorrhea were remarkable during pollen season. ($p < 0.01$) There were no statistically significant differences in mean odor thresholds and discrimination values between in and out season ($p > 0.05$). Odor identification decreased during allergy season (0.76 ± 0.14) compared to out season (0.87 ± 0.12) ($p = 0.003$). Mean CCRC value was lower during allergy season (1.62 ± 0.12) compared to out season (1.72 ± 0.16). ($p < 0.001$) (Table 1) The right nasal cavity MCA1, MCA2, VOL2, total volume and left nasal cavity MCA1, MCA2 and VOL1 decreased significantly in allergy season. ($p < 0.05$) (Table 1).

Among the acoustic rhinometry parameters, only right VOL2 ($r = -0.39$; $p = 0.017$) and right TVOL ($r = -0.367$; $p = 0.025$) showed a negative significant correlation with nasal obstruction score. Mean CCRC showed a negative correlation with subjective hyposmia ($r = -0.44$, $p = 0.007$), nasal obstruction score ($r = -0.340$, $p = 0.04$) and TNSS ($r = -0.494$, $p = 0.02$), whereas no correlations were found between acoustic rhinometry parameters and TNSS ($p > 0.05$) and acoustic rhinometry parameters and CCRC scores ($p > 0.05$). (Table 2).

4. Discussion

Hyposmia is a common finding in patients suffering from AR. However, the mechanism of olfactory dysfunction in AR remains poorly understood. Mechanical obstruction of the airway secondary to nasal

congestion and coassociated nasal polyps/sinusitis might block odour particles to reach the olfactory neuroepithelium and lead to loss of smell in AR. Persistent AR patients with diminished smell function frequently have nasal polyps or sinusitis [6,7,15]. In the study of Apter et al. [6] on 62 subjects with chronic rhinitis and olfactory loss, the mean olfactory score for rhinitis group without polyps and sinusitis was 4.35, consistent with moderate hyposmia and 0.61 in subjects with polyps and chronic sinusitis, consistent with anosmia, which indicate that both obstruction and inflammation might play a role in smell dysfunction. Cowart et al. [7] found a clinically significant loss of smell in 23.1% of the patients with AR. Although nasal resistance was significantly higher among AR patients compared to controls ($p < 0.001$), it was not related to olfactory threshold. Clinical or radiographic evidence of sinusitis or nasal polyps was found to be significantly associated with hyposmia ($p < 0.006$).

In recent years, direct inflammatory damage of the olfactory receptor cells and a change in the surrounding milieu were also supposed to lead an olfactory dysfunction. In the study of Rydzewski et al. [3] the incidence of smell and taste disorders in patients with AR was 21.4% and 31.2%. The olfactory thresholds showed a significant correlation with number of eosinophils in blood and in nasal discharge, nasal polyps and X-ray changes in the ethmoid sinuses. Pharmacotherapy, desensitization and surgery were shown to have a positive influence on the impairment of the sense of smell in AR. In their prospective controlled study, Klimek and Eggers [4] found a remarkable decrease in threshold and identification in patients with AR from the 7th day of allergy season compared to preseason period using a modified CCRC. These changes were found to be better correlated to eosinophilic cationic protein (ECP) in nasal secretions than to nasal volume flow. The authors concluded that inflammation in AR can affect the olfactory cleft, implicating a direct role for allergic inflammation in smell loss. In the study of Becker et al. [8] patients with AR (seasonal and perennial) showed impaired olfactory functions with Sniffin'Sticks test in comparison with the control group. Nasal secretion analysis of SAR group showed increased values of ECP and trypsinase, whereas rhinomanometry showed no differences in nasal flow between AR and control groups, supporting the hypothesis that inflammation rather than obstruction seems to play in olfactory dysfunction. In the study of Guilemany et al. [16], most patients with persistent AR (67%) presented self-reported hyposmia and smell detection, identification, and forced choice tests were significantly worse and nasal nitric oxide, a marker of nasal inflammation, correlated remarkably with loss of smell. In the study of Guss et al. [17], even in the absence of mucosal disease on CT scan, half of the patients with AR exhibited hyposmia, mostly to a mild or moderate degree. In an experimental model of AR [18], both of odor detection ability test and local field potential showed that olfactory function was impaired in mice with AR, correlated with a prominent infiltration of eosinophils, plasma cells, neutrophils, mast cells, and macrophages in lamina propria of olfactory mucosa. These studies suggest a potential role for inflammatory changes in nasal mucosa to cause the olfactory dysfunction in AR.

Antiinflammatory treatment with nasal steroids might improve smell dysfunction in allergic patients [5,19]. Sivam et al. [5] performed a randomized, double-blind, placebo-controlled, parallel clinical trial in 17 patients with SAR who had symptoms of impaired olfaction. Treatment with intranasal steroids for 2 weeks was shown to be associated with improved nasal symptoms ($p < 0.015$), nasal peak inspiratory flow ($p < 0.04$), reduced nasal inflammation ($p < 0.05$), and chemosensory-specific quality of life ($p < 0.03$). The presence of eosinophils in the olfactory area might indicate a direct, deleterious effect of inflammation on olfactory epithelium and loss of smell in SAR. Similarly, in a double-blind, randomized study by Meltzer et al. [19], SAR patients 12 years of age or older received either steroid nasal spray or placebo spray once daily for 2 weeks and both subjective nasal symptoms and objective measures of eosinophil, basophil, neutrophil counts, mucociliary clearance, eosinophilic cationic protein, trypsinase and

Table 2

The correlation between TNSS, CCCRC and acoustic rhinometric measurements.

		R MCA1	R MCA2	R VOL1	R VOL2	R TVOL	L MCA1	L MCA2	L VOL1	L VOL2	L TVOL
TNSS	r	-.119	-.038	-.100	-.256	-.245	.207	.019	-.042	-.124	-.125
	p	.484	.824	.555	.126	.143	.218	.909	.807	.466	.461
CCCRC	r	.094	-.028	.171	.142	.173	-.108	-.180	.213	.060	.101
	p	.582	.869	.311	.401	.305	.526	.288	.205	.726	.553

TNSS Total nasal symptom score; CCCRC Connecticut Chemosensory Clinical Research Center Test; r Spearman's correlation coefficient; R Right nasal cavity; L Left nasal cavity; MCA1 minimum cross-sectional area of the anterior; MCA2 minimum cross-sectional area of the posterior; VOL1 nasal volume from 0 to 2.2 cm; VOL2 nasal volume from 2.2 cm to 5.4 cm; TVOL Total nasal volume from 0 to 5.4 cm.

albumin levels, nasal airway resistance and odor identification were better in steroid group.

The evaluation of olfactory function in children is different from adults. Schriever et al. [20] modified “Sniffin’ Sticks” odor identification test for children in which 14 odors out of 16-items, which were identified at a high rate by children were used. In this study 537 children between 6 and 17 years of age were included and “Sniffin’ Kids” test was able to discriminate between normosmia and anosmia with a cutoff value of > 7 points on the odor identification test. Dalton et al. [21] reported that children as young as 3 years of age can perform olfactory testing as they were perfectly capable of understanding the instruction and question of the tests, but take longer than do older children and adults.

There are only a few studies about the olfactory dysfunction in children with AR [10,11]. In an observational, cross-sectional and multicentre study which evaluated the sense of smell in untreated 1260 pediatric AR patients aged 6–12 years using a subjective scale, 44% of the children reported smell dysfunction, with both loss of smell frequency (52.1%, $p < 0.001$) and intensity (0.75 ± 0.84 , $p < 0.001$) being more frequent in patients with persistent than intermittent AR (38.0% and 0.51 ± 0.73 , respectively) [10]. Therefore, the authors concluded that loss of smell can be considered as a clinical marker of disease severity. In contrary, in the study of Kutlug et al. [11], using Sniffin’ Sticks test, there were no significant differences among AR, non-AR and healthy children with respect to odor scores and no association was found between odor scores, severity of rhinitis and laboratory results. Odor identification and total odor scores of the patients with rhinitis lasting for longer than 3 years were significantly lower than those lasting for one to three years.

In this study, we assessed olfactory function in children with AR using both subjective and objective scales. TNSS was 5.9 ± 2.5 (range 1–11) during season and 2.6 ± 1.9 (0–5) out season, which means that there were some differences among the children included in the study; some had more severe and/or chronic symptoms with acute exacerbations during pollen season. According to subjective scale, mild to moderate loss of smell was reported by 43.2% of the children during pollen season and 32.4% of the children reported mild loss of smell even in out season. There was a significant decrease in most of the acoustic rhinometry parameters in season compared to out season ($p < 0.05$).

All children were able to perform the CCCRC smell test successfully. We found that odor identification and CCCRC scores decreased significantly during allergy season ($p < 0.05$) and the scores seem to be correlated with subjective hyposmia scores ($r = -0.44$, $p = 0.007$). As expected, there was no deterioration in olfactory discrimination in pollen season, since olfactory discrimination is influenced mainly by disorders of the central nervous olfactory system rather than by disorders of the nose and olfactory epithelium [22]. None of the children had mechanical obstruction, such as adenoid hypertrophy, nasal polyps, previous nasal surgery or recent upper respiratory tract infection or rhinosinusitis, which might lead to smell disorder. Although there was a significant correlation between CCCRC scores and TNSS ($r = -0.494$, $p = 0.02$), no correlation was found between CCCRC scores and acoustic rhinometry parameters ($p > 0.05$). Although nasal

volume and cross sectional area values decreased in pollen season, these parameters did not have a remarkable effect on olfactory function, which supports the hypothesis that nasal inflammation rather than nasal obstruction lead to hyposmia in AR. A limitation of our study was that inflammatory parameters in terms of histology or nasal specimens were not studied. Further studies are needed to evaluate the effect of inflammatory mediators on olfactory function in AR.

In conclusion, nearly half of the children with AR reported a mild to moderate hyposmia during pollen season and there was a decrease in odor identification, which can be easily shown using a CCCRC test.

Declarations of interest

None.

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