

Nasal and bronchial response to exercise in children with seasonal allergic rhinitis out of the pollen season

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Background: Allergic rhinitis is a type I allergic disease of the nasal mucosa, and is characterized by paroxysmal sneezing, watery rhinorrhea, and nasal blockage. In seasonal allergic rhinitis subjects, even subthreshold allergen doses have been found to cause inflammatory cell infiltration in the nasal mucosa. This study aimed to investigate the presence of nasal obstructions and symptoms in seasonal allergic rhinitis subjects by assessing an exercise challenge test (ECT) outside of the pollen season.

Methods: Twenty patients and 20 healthy children who were admitted to the Osmangazi University Medical School Pediatric Allergy Clinic were included in the study in a pollen free season. The total nasal airflow and visual analog scale (for rhinorrhea, nasal congestion, sneezing, and itching) and pulmonary function tests were evaluated before and after each ECT. The nasal airflow and resistance changes were evaluated with anterior rhinomanometry.

Results: Eight patients and one healthy child had nasal obstructions after the ECT. There was a significant difference in the exercise-induced nasal obstructions between

the 2 groups ($p = 0.02$). Eighteen children with exposure to tobacco smoke in the patient and control groups had lower forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), and forced expiratory flow 25% to 75% (FEF₂₅₋₇₅) values than the children without exposure to tobacco smoke.

Conclusion: The prevalence of exercise-induced nasal obstruction in children with seasonal rhinitis out of the pollen season is 40%. We showed that minimal persistent inflammation and nasal symptoms can also be diagnosed in rhinitis children in a symptom-free period. © 2014 ARS-AAOA, LLC.

Key Words:

allergic rhinitis; children; exercise; nasal airflow; nasal resistance

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Rhinitis is an inflammatory disorder of the nasal mucosa that is characterized by nasal congestion, rhinorrhea, and itching, and is often accompanied by sneezing and conjunctival irritation.¹ It affects ~25% of adults in Europe and up to 40% of children globally.^{2,3} Rhinitis can be classified according to its etiology, allergic (immunoglobulin E [IgE]-mediated) and nonallergic symptoms, and its clinical presentation, which includes intermittent/persistent or mild/moderate/severe classifications (Allergic Rhinitis and its Impact on Asthma [ARIA] classification).¹ It is well known that exercise induces a marked decrease in nasal

resistance in the human nose. This relationship between exercise and nasal patency was first described by Richerson and Seeböhm.⁴ Hyperosmolar airway fluid formed by evaporation of airway water during exercise is the pathophysiological trigger and possibly triggers exercise-induced rhinitis as well. The nose protects the lower airway by filtering, humidifying, and warming inspired air; therefore, nasal congestion places the lower airway at an increased risk.⁵ Autonomic reflexes affect nasal congestion by regulating glandular secretions and mucosal blood vessel dilation and permeability. Dynamic exercises stimulate α -adrenoceptors, which vasoconstrict and reduce nasal resistance.⁶ The aim of this study was to assess the response of the nose during exercise in the presence of seasonal allergic rhinitis outside of the pollen season.

Subjects and methods

Subjects

A total number of 20 children with allergic rhinitis and 20 healthy nonatopic children, as the control group, were

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enrolled in the study. Both groups were studied outside of the pollen season. Rhinitis was diagnosed as having symptoms such as sneezing, nasal itching, rhinorrhea, and nasal obstruction over a period of 2 years during the pollen season. All of the 20 patients with allergic rhinitis sensitive to pollens were diagnosed by their histories and skin-prick tests (SPTs). An SPT was performed on all children. The SPTs were negative in the control group. All of the children had positive results for pollens in the patient group; however, none of them had a positive result for dust mites. All of the children's parents gave informed consent for their children's participation. The study was approved by the local ethics committee.

The inclusion criteria for the patient group were as follows:

1. A positive SPT for pollens;
2. Over 10 years of age, so that they were cooperative during testing;
3. No evidence of vasomotor rhinitis, chronic rhinitis, structural defects (eg, polyposis and septum deviation), or rhinitis medicamentosa;
4. No respiratory infections during the last 4 weeks;
5. No treatment with nasal or systemic corticosteroids during the last 4 weeks;
6. No treatment with antihistamines or nasal vasoconstrictors during the last 2 weeks;
7. No cardiac or respiratory disease.

All patients had allergic rhinitis symptoms, including sneezing, nasal itching, rhinorrhea, and nasal obstructions during the pollen season and mild intermittent rhinitis, as characterized by the ARIA classification.

Inclusion criteria for the control group were as follows:

1. No rhinitis symptoms;
2. Negative SPT and Phadiotop (UniCAP; Phadia, Uppsala, Sweden) test;
3. No chronic disease.

The subjects' age, gender, family history of atopy, and presence of asthma and conjunctivitis were questioned. Each subject's complete blood count, total serum IgE, and Phadiotop were evaluated. The total symptom score (TSS) and visual analog scale (VAS) of the patients were recorded after each exercise challenge test (ECT). A 10-cm VAS was used to evaluate the patients' obstruction, rhinorrhea, itching, and sneezing symptoms. The TSS, according to the Gosepath symptom scoring scale, was recorded before and after the ECTs.⁷

The ECT

The ECT was conducted using a standard protocol based on the American Thoracic Society guidelines.^{8,9} The patients withheld their rhinitis medications for the appropriate time before the challenge. Caffeine and beverages or food containing caffeine were not taken before the study. Subjects

did not indulge in vigorous exercise for at least 4 hours prior to arriving at the laboratory. None of the subjects had suffered from clinically apparent upper respiratory tract infections over the previous 4 weeks. All of the children had a physical examination before the testing. The patients underwent an ECT for 6 to 8 minutes on a treadmill, which achieved 80% of their maximum heart rate (220 minus age in years) or 40% of their predicted maximum voluntary ventilation level (35× forced expiratory volume in 1 second [FEV1]). Spirometric measurements were carried out before running and repeated at 0-, 2-, 5-, 10-, 15-, and 30-minute time points after the end of the exercise. Forced vital capacity (FVC), FEV1, and the maximum mid-expiratory flow (MMEF) were measured in triplicate before the challenge and in duplicate after the challenge at each of the time points. All of the patients could reproducibly perform the spirometry. A positive ECT was defined as a maximum percentage fall in FEV1 $\geq 10\%$ from baseline.

Rhinomanometry

After a 30-minute acclimatization period, the subjects were examined in a sitting position, breathing room air. The temperature was constant at 26°C, with 60% humidity. The patients were asked to close their mouths and breathe through their noses. No nasal decongestants were used. Pressure was recorded in each subject's nasal cavity via a catheter that was connected to a pressure transducer while flow was monitored in the other nasal cavity by a pneumotachograph. All measurements were made at a reference pressure of 150 Pa, according to the guidelines of the recommendations of the International Committee on Standardization of Rhinomanometry. The resulting pressure (Pa/cm³/second) measurements were analyzed offline for total resistance and low/high resistance passages, which are related to the nasal cycle.¹⁰ Nasal airflow was measured before and after the completion of the exercise test. Rhinomanometric evaluations were made immediately before the spirometric tests at approximately the 0-, 5-, 10-, 15-, 30-, and 60-minute time points. During exercise and/or after nasal obstruction development, a 40% decrease in the total nasal flow and/or a 100% increase in the total nasal resistance in each patient were considered a positive test.

The SPT

The SPTs were performed with house dust mites (eg, *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*), grass pollens (eg, poa, phleum, and lolium), a cereal mix, a tree mix, cockroaches, molds (*Alternaria*, *Aspergillus*), and cat and dog epithelial antigens (92160; Stallergenes SA, Antony, France). The results were evaluated after 15 minutes. The test was considered positive if it elicited a wheal at least 3mm greater in diameter than a negative control.

TABLE 1. Demographic and clinical data of the groups*

	Patients (n = 20)	Controls (n = 20)	p
Age, years	13.2 ± 1.6	13.3 ± 1.7	0.989 ^a
Weight, kg	47.4 ± 10.1	48.4 ± 11.1	0.903 ^a
Height, cm	157.9 ± 9.8	158.1 ± 9.9	0.957 ^a
BMI, kg/m ²	18.8 ± 2.1	19.2 ± 2.7	0.677 ^a
Family history of atopy	15 (75%)	2 (10%)	<0.001 ^b

*Values are mean ± SD or n (%).

^at test.

^bFisher's exact test.

BMI = body mass index; SD = standard deviation.

Statistical analyses

All statistical analyses were performed with SPSS for Windows 17.0 (SPSS Inc., Chicago, IL). The descriptive statistics were expressed as the means ± standard deviation, median, frequency, and percent. Statistical *t* tests were used between 2 independent groups of normal distribution, and Fisher's exact tests were used for abnormal distributions. Correlations were performed with the Spearman correlation test.

Results

Twenty patients and 20 healthy control subjects were included in the study. Table 1 shows the demographic and clinical data of the groups. The mean values for age, weight, height, body mass index (BMI), and sex distribution were not different between the 2 groups. There was a significant association between family history of atopy and rhinitis ($p < 0.001$).

Table 2 shows the laboratory data of the groups. The associations between rhinitis, total IgE levels and blood eosinophil counts were analyzed. There was no significant association between rhinitis and total IgE levels; however, a significant association was found between blood eosinophil counts and rhinitis ($p < 0.001$).

Eighteen children with exposure to tobacco smoke in the patient and control groups (9 patients and 9 healthy group subjects) had lower FEV₁, FVC, and forced expiratory flow 25% to 75% (FEF₂₅₋₇₅) values than the children without exposure to tobacco smoke. Additionally, exposure to tobacco smoke in the patient and healthy groups was not associated with PEF (Table 3).

The rhinomanometry results showed that 18 children who were exposed to tobacco smoke in the patient and control groups had similar total nasal resistance and air-flow levels.

No differences were found between the weights, heights, BMIs, total IgE levels, blood eosinophil counts, or the rhinitis durations between the patients who were and those who were not administered the ECT.

There were no differences in the baseline FEV₁, FVC, PEF, FEF₂₅₋₇₅, total nasal airflow, nasal resistance levels, or VASs between the patient and control groups before the ECTs ($p > 0.05$). The mean nasal airflow and resistance levels were not related to any of the baseline characteristics (eg, age, sex, and height).

Three patients (15%) and one healthy child (5%) had exercise-induced bronchoconstriction (EIB). No differences were found in the EIB levels between the children with rhinitis and those without rhinitis (Table 4).

Eight patients and one healthy child had nasal obstructions after the ECT. There was a significant difference in the exercise-induced nasal obstructions between the 2 groups ($p = 0.02$) (Table 4).

Significant total nasal resistance differences between the patient and healthy subjects were observed at 15, 30, and 60 minutes after the ECT ($p < 0.05$). However, there was no significant difference in total nasal resistance between the 2 groups at 5 or 10 minutes after the ECT (Fig. 1).

Discussion

Our study demonstrates that physical exercise is associated with a decrease in nasal resistance in healthy subjects and patients with rhinitis. It has been thought that these changes could largely be caused by a vasoconstrictive phenomenon that reduces the volume of the venous sinusoids. This vasoconstriction results from an increase in sympathetic activity, but it is possible that other factors, such as dilatation of the nasal valve due to an increase in muscular activity, contribute to this phenomenon. Vasoconstriction occurs for breathing through both the nose and the mouth; therefore, it does not seem to be motivated by local reflexes or by the increase in ventilation found during exercise as isocapnic hyperventilation does not in itself alter nasal resistance.¹¹

Serra-Batlles et al.¹² studied the nasal response by means of posterior rhinometry in a group of healthy subjects and other groups with rhinitis, asthma, and concomitant asthma and rhinitis after exercise on a bicycle. They found

TABLE 2. Laboratory data of the groups*

	Patients (n = 20)	Controls (n = 20)	p
Total IgE levels (U/mL)	81.7 (47.9–104.1)	47.7 (34.8–67.7)	0.062 ^a
Blood eosinophil count (mm ³)	200 (200–320)	120 (100–145)	<0.001 ^a

*Values are median (minimum–maximum).

^aMann-Whitney U.

IgE = immunoglobulin E.

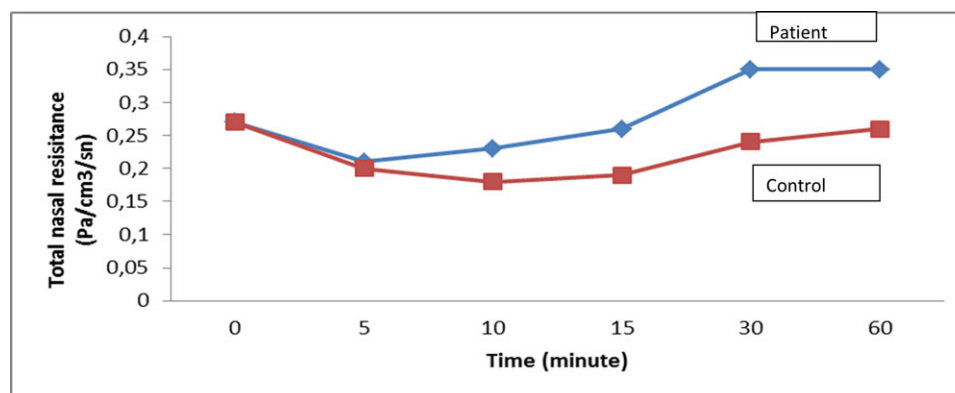
TABLE 3. Lung function parameters of the children with smoking parents and those without a smoker in the family*

Lung function parameters	Allergic rhinitis (n = 20)			Control group (n = 20)		
	Smoking parents (n = 9)	Nonsmoking parents (n = 11)	p	Smoking parents (n = 9)	Nonsmoking parents (n = 11)	p
FEV1 (%)	92.0 ± 4.8	97.5 ± 6.0	0.040 ^a	90.7 ± 2.0	97.9 ± 4.8	<0.001 ^a
FVC (%)	93.1 ± 3.5	97.3 ± 4.3	0.031 ^a	93.8 ± 1.4	99.4 ± 4.5	0.002 ^a
PEF (%)	90.9 ± 5.0	90.5 ± 4.0	0.832 ^a	88.4 ± 3.0	90.8 ± 2.9	0.086 ^a
FEF ₂₅₋₇₅ (%)	88.3 ± 3.0	91.7 ± 3.6	0.036 ^a	88.9 ± 2.6	93.4 ± 3.8	0.008 ^a

*Values are mean ± SD percentage.

^at test.FEF₂₅₋₇₅ = forced expiratory flow 25% to 75%; FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity; PEF = peak expiratory flow; SD = standard deviation.**TABLE 4.** Frequency of exercise-induced bronchoconstriction with and without exercise-induced nasal obstruction in children

	Allergic rhinitis (n = 20)		Control group (n = 20)	
	Children with exercise-induced nasal obstruction (n = 8)	Children without exercise-induced nasal obstruction (n = 12)	Children with exercise-induced nasal obstruction (n = 1)	Children without exercise-induced nasal obstruction (n = 19)
Children with exercise-induced bronchoconstriction	3	–	–	1
Children without exercise-induced bronchoconstriction	5	12	1	19

**FIGURE 1.** The total nasal resistance change pattern in the groups after the exercise challenge test.

that the decrease in nasal resistance was similar in all 4 groups, which returned to baseline values after 30 minutes. When a separate analysis was conducted on those who had and those who had not developed a bronchospasm, they verified that the nasal resistances remained decreased for longer in the patients with bronchospasms after exercise, which would suggest that the existence of a bronchio-nasal reflex mechanism was responsible for increasing the nasal response in the patients with EIB.

Stroh et al.¹³ used posterior rhinomanometry to study the nasal response to exercise in healthy subjects and others with asthma or rhinitis and asthma. They concluded that the nasal response is not related to the bronchial response

or the temperature and humidity of the air breathed in through the mouth during the exercise test.

In the present study, the total nasal resistance changes showed a different profile than those of previous studies. The nasal resistance decreased immediately after exercise, subsequently returned to the pre-exercise level, and then surpassed it within 30 minutes after exercise. This observation substantiates the result reported by Syabbalo et al.¹⁴ and Ohki et al.¹⁵

There were no differences between the groups regarding age, gender, weight, height, or BMI. However, the family history of atopy in the patient group was higher than that of the control group. In many studies, it has been

emphasized that the most important risk factor for allergic disease development seems to be family history of atopy.¹⁶

In our study, there was no significant association between rhinitis and total IgE levels in children, and the normal total IgE values increased gradually until prepuberty, when they reached adult levels.^{17,18} A normal total IgE level does not rule out a specific allergy.

The Phadiatop test was shown to be highly sensitive and specific in differentiating individuals who are sensitized to common inhalants from those who are not. Its clinical sensitivity and specificity were 85% to 98% and 85.5% to 100%, respectively, in one report.¹⁹ In contrast to the results of previous studies, we found the Phadiatop test sensitivity to be 75%. However, we cannot compare our findings with those of previous studies because of the differences in the study times (within pollen season) and the study populations (seasonal allergic rhinitis).

There was no relationship between allergic rhinitis and passive smoking in our study. Studies on environmental tobacco smoke and rhinitis in children are scarce. One recent study showed that exposure to tobacco smoke in early infancy can increase the risk for IgE sensitization to indoor inhalants and food allergens.²⁰ No evidence for an interaction between passive smoking and asthma risk during the first 2 years of life was found in a Swedish study, but prenatal smoking had independently negative effects.²¹ Postnatal parental smoking or maternal smoking during pregnancy seems to be associated with increased risk of asthma, wheezing, reduced lung function, and respiratory infections in children aged <3 years; however, this was not observed with asthma symptoms in children aged 4 to 10 years or with allergic sensitization or allergic rhinitis.²² Our study demonstrated that paternal smoking was associated with deficits in FVC, FEV₁, and FEF₂₅₋₇₅ values in the observed healthy and rhinitis groups.

We found no difference in nasal resistance or airflow between the children with smoking parents and those without smokers in the family. However, insufficient data exist regarding passive smoking and allergic rhinitis symptoms; thus, the effect of passive smoking on nasal resistance in children remains unexplored. Similar to our findings, Virkkula et al.²² reported that smoking in the family was not associated with increased nasal resistance in the children with allergic rhinitis. The prevalence of EIB varies between 5% and 20% in the general population and 50% to 90% in known asthmatics. Among children with rhinitis, the prevalence of EIB is controversial. Valdesoiro

et al.²³ performed a retrospective study and found that 13 of 54 allergic rhinitis patients had positive exercise stress test results. In contrast to the results of a previous study, Custovic et al.²⁴ found that none of 17 observed children with allergic rhinitis had a positive free-running exercise test. Like this previous study, we found no difference in EIB between allergic rhinitis and healthy children. This may be explained by the timing of the study, which was conducted outside of the pollen season.

In this study, the nasal resistance was 0.27 ± 0.03 Pa/cm³/second and the total nasal airflow was 554 ± 79 mL/second in the allergic rhinitis group. In comparison, the nasal resistance was 0.28 ± 0.03 Pa/cm³/second and the total nasal airflow was 538 ± 60 mL/second in the healthy group. Our data were similar to the reference values in the literature.^{25,26} We found no difference in nasal resistance or airflow between the healthy children and children with rhinitis before the ECT because our study was conducted outside of the pollen season and none of the subjects had nasal symptoms. No gender differences were observed in the studied nasal airflow or resistance values in either the healthy children or the children with rhinitis.

We found a significant association between the total nasal airflow and VAS in the children with EIB. Bousquet et al.²⁷ showed that the VAS was a simple and quantitative method that can be used for the quantitative evaluation of severity of allergic rhinitis. Additionally, Marseglia et al.²⁸ reported that the VAS may be considered a useful tool for measuring decongestion in adolescents. We believe that children can use the VAS in a manner similar to adults. There were limitations in our cross-sectional study. We did not observe statistically significant differences for our clinical results because of the small number of patients. Additionally, we could not find new studies for reference values in the literature for data comparisons. Therefore, there is a need for comprehensive studies.

Conclusion

We have demonstrated that there is an increase in nasal obstruction after exercise in subjects with seasonal allergic rhinitis who were observed outside of the pollen season. We did not find any relationship between the pre-exercise and postexercise nasal obstruction values in the healthy group, which suggests that minimal persistent inflammation and nasal symptoms can also be diagnosed in children with rhinitis during symptom-free periods. ④

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