

Pulmonary Arterial Pressure in Children with Allergic Rhinitis

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ABSTRACT

Background: Chronic upper airway obstruction may lead to increased pulmonary arterial pressure in childhood. Allergic rhinitis is one of the frequent causes of upper airway obstruction by nasal blockage. The aims of the study were to evaluate the pulmonary arterial pressures in children with allergic rhinitis and the effect of topical corticosteroid therapy.

Methods: Forty-nine children composed of 27 subjects with seasonal and 22 subjects with perennial allergic rhinitis were enrolled in this study. The pulmonary arterial pressures were measured by using Doppler echocardiography.

Results: The pretreatment pulmonary arterial systolic, mean, and diastolic pressures of study group were significantly higher than in healthy controls ($p < 0.05$). The pulmonary arterial systolic and mean pressures of the patient group significantly decreased at the end of study ($p < 0.05$), whereas the decrease of the diastolic pressure was not statistically significant ($p > 0.05$) after the treatment of a topical corticosteroid, mometasone furoate (100 µg per day), for 8 weeks.

Conclusion: Our results showed that children with allergic rhinitis have higher pulmonary arterial pressure levels compared with healthy controls and that increased pulmonary arterial pressure levels due to allergic rhinitis are reversible by using nasal topical corticosteroids. Further studies are needed

to determine the clinical aspect of increased pulmonary arterial pressure. (American Journal of Rhinology 18, 227-232, 2004)

Allergic rhinitis is an extremely common disease worldwide affecting 10 to 25% of the population.¹ Moreover, an increasing prevalence of allergic rhinitis over the last decades has been recognized.² It has also been recently noticed that allergic inflammation does not necessarily limit itself to the nasal airway. Multiple co-morbidities have been associated with rhinitis such as asthma, sinusitis, conjunctivitis, otitis media with effusion and polyps.^{1,3,4} It was also demonstrated earlier that chronic upper airway obstruction such as adenotonsillar hypertrophy may lead to increased pulmonary arterial pressure in childhood and it could successfully be reversed after relief of upper airway obstruction.⁵⁻⁷ Similarly, increased pulmonary arterial pressures were reported in children with allergic rhinitis compared with their healthy age-matched controls in a study.⁸ One of the impacts of allergic rhinitis in children may be possible upper airway resistance syndrome and increased pulmonary arterial pressure due to nasal blockage.

In this study, the children who were affected by upper respiratory obstruction due to seasonal or perennial allergic rhinitis were evaluated by clinical and laboratory investigations. The aims of the study were to evaluate the pulmonary arterial pressures in children with symptomatic allergic rhinitis and to assess whether it varies with the treatment of allergic rhinitis.

MATERIALS AND METHODS

Forty-nine children diagnosed with allergic rhinitis and followed-up in our Pediatric Immunology and Allergy outpatient clinic were enrolled in the study. They were composed of 27 subjects with seasonal and 22 subjects with perennial allergic rhinitis according to their history and clinical and laboratory criteria. In both subgroups, the definition of allergic rhinitis was made by using the International Consensus Statement on the management of allergic

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TABLE I

Scoring Nasal Obstruction Symptoms of Children with Allergic Rhinitis

Symptom	0	1	2	3	4	5
Nasal blockage	No	Rarely	Mild	Moderate	Severe	Very serious
Mouth breathing	No	Rarely	Mild intermittent	Moderate intermittent	Frequently	Always
Hyponasal voice	No	Rarely	Occasionally	Intermittant	Frequently	Always
Snoring	No	Almost never	Rarely	Intermittant	Frequently	Every day
Restless sleeping	No	Rarely	Occasionally	Rather frequently	Frequently	Every day

rhinitis.⁹ Therefore, the patient group was diagnosed as those individuals with a characteristic history of perennial or seasonal symptoms of allergic rhinitis (rhinorrhea, sneezing, nasal obstruction, and pruritus) and who also had skin sensitization to perennial or seasonal allergens. All our patients had seasonal or perennial symptoms of allergic rhinitis for at least one year. Exclusion criteria included presence of other causes of nasal obstruction such as nasal polyps and rhinosinusitis. Children who were using nasal topical or systemic corticosteroids, anti-histamines or other anti-allergic drugs within the previous 2 months were not included in the study. Twenty children served as control group. All the controls were healthy, non-atopic, sex- and age-matched children with no evidence of any infectious and systemic disorder. The study was carried out after obtaining a written informed consent from the parents of all subjects.

The allergy skin tests were done using the prick-puncture method by a pediatric immunologist. Histamine and saline controls were used in all patients. Wheal and flare reactions were read 20 minutes after placement, and responses were measured in millimeters. A positive skin test was defined as any wheal and flare reaction at least one half the size of histamine control. All patients had positive skin-prick test responses to pollen extracts of grass mix, tree mix, weed mix as seasonal allergens, and *Dermatophagoides pteronyssinus* and *farinae* as perennial allergens (Allergopharma JGK, Reinbek, Germany). The allergy skin tests were not done in the control group.

To score nasal obstruction symptoms of the patient group, parents and subjects were asked by using standard criteria, which are presented in Table I.¹⁰ The criteria included upper airway obstruction symptoms such as nasal blockage, snoring, mouth breathing during sleep and daytime, and hyponasal voice. Scores of symptoms were between 0 and 5 points.

All children were evaluated considering the respiratory difficulty and tachycardia before and after treatment. Chest roentgenogram and electrocardiogram were obtained for all children. Cardiac diagnosis was confirmed by echocardiographic investigation in the Pediatric Cardiology Section. A sonos-1000 system ultrasonic imager (Hewlett-Packard, Miami Lakes, FL) with 2.5 MHz transducer was used for echocardiographic assessments. After routine cardiovascu-

lar examination, continuous-wave Doppler echocardiography was used to estimate pulmonary arterial pressure and to measure right ventricular pre-ejection period, ejection time, acceleration time, and corrected acceleration time. In all the patients, mean pulmonary arterial pressure was estimated by measuring peak systolic acceleration time of pulmonary artery described by Li Wan-zhem, et al¹¹ as: pulmonary arterial systolic pressure = $(55 \times \text{pre-ejection period/acceleration time}) - 0.8$; pulmonary arterial diastolic pressure = $(35.5 \times \text{pre-ejection period/acceleration time}) - 10.8$; pulmonary arterial mean pressure = $(43.2 \times \text{pre-ejection period/acceleration time}) - 4.6$. Standard precordial short-axis view of the heart was used for this echocardiographic examination. The children were examined in the supine position with the right shoulder slightly raised during echocardiographic investigation. Instantaneous measurements were made over three cardiac cycles and the mean values obtained. The measurements were obtained using the published standards recommended by the American Society of Echocardiography.¹²

After the inclusion and exclusion criteria were examined, the baseline symptom score was noted and echocardiographic investigations were performed. On this visit, families and children were instructed to administer one-a-day nasal corticosteroid, mometasone furoate (Nasonex Aqueous Nasal Spray 0.05%, Schering-Plough Co., Kenilworth, NJ), by using a dose of 100 μg per day (one puff in each nostril), in the evening for 8 weeks. At the end of the therapy, their symptoms scores and echocardiographic values were re-evaluated. All subjects were warned to admit to the clinic when there was any exacerbation in their symptoms.

Statistical analysis was done by SPSS for Windows computer program. Parameters and variables in the two groups were compared using the *t* test and the Mann-Whitney *U* test for non-parametric data. Pearson's correlation between the parameters was determined and compared by using paired *t* test. The effect of multiple factors on parameters was evaluated by Spearman's correlation test. Pre- and post-treatment symptom scores of the study group were compared by using Wilcoxon Signed Ranks test. Logistical regression analysis was used for multiple correlations and for evaluating the effect of the therapy on symptom scores. $p < 0.05$ was considered statistically significant.

TABLE II

Demographic and Clinical Characteristics of the Subjects

	Patients (n = 49)	Controls (n = 20)	p
Age (years)*	9.7 ± 2.9 (9)	9.0 ± 2.7 (9)	> 0.05
Age distribution	2.5–15	3–14	> 0.05
Gender			
Male	34	10	
Female	15	10	
Atopy	49	—	
Seasonal allergic rhinitis	27	—	
Perennial allergic rhinitis	22	—	
Having asthma	20	—	
Symptom duration (years)*	3.28 ± 2.1 (3)	—	
Positive family history of atopy	28 (57.1%)	—	
Total IgE (IU/ml)*	402.2 ± 369.9 (256)	ND	
High serum IgE	38	ND	
Positive SPT**	49	ND	
Eosinophilia (×10 ⁹ /L)*	0.48 ± 0.38 (0.3)	ND	

*Mean ± SD (median). **SPT, Skin-prick test. ND, Not done.

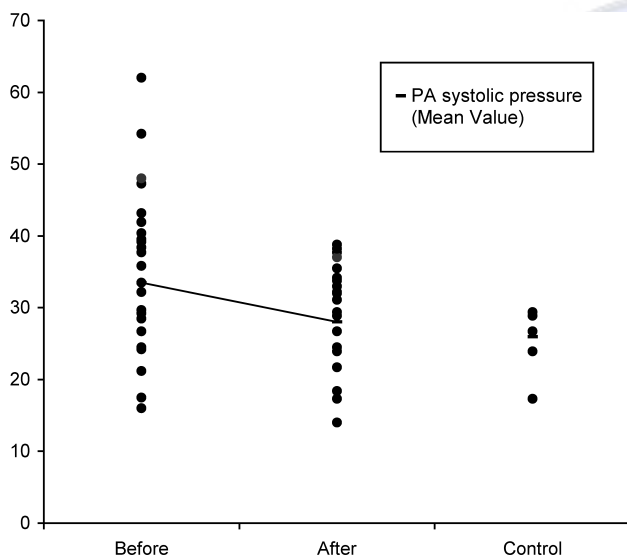


Figure 1. The pulmonary arterial systolic pressures in patient group and controls. PA, pulmonary arterial; P, pressure; before, before therapy; after, after therapy.

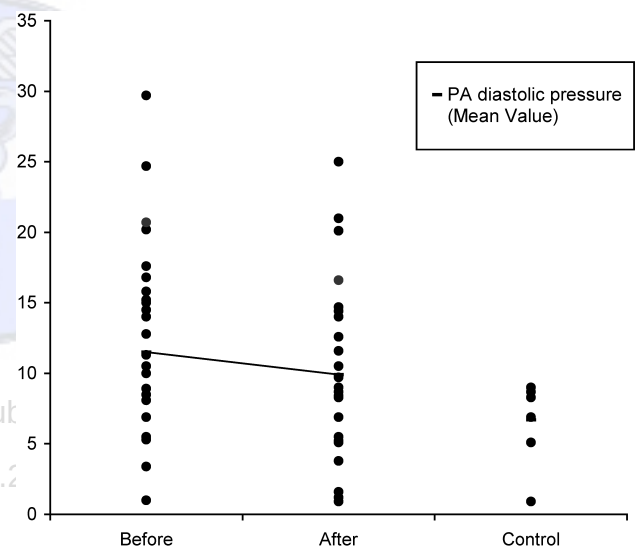


Figure 2. The pulmonary arterial diastolic pressures in patient group and controls. PA, pulmonary arterial; P, pressure; before, before therapy; after, after therapy.

RESULTS

Characteristics of patient and control groups enrolled in this study are summarized in Table II. Mean pretreatment symptom score of the patient group was 3.53 ± 0.94 and significantly decreased to 1.49 ± 0.61 at the end of eight weeks of therapy ($p < 0.05$). The chest roentgenograms and electrocardiograms obtained from all children were normal, and there was no change after 8 weeks of treatment.

Mean pretreatment pulmonary arterial systolic, diastolic,

and mean pressures of the study group were significantly higher than in healthy controls (Figs. 1–3), which were 33.48 ± 9.22 , 11.5 ± 5.73 , and 22.37 ± 7.13 mmHg in the patient group versus 26.12 ± 3.7 , 6.94 ± 2.02 , and 16.53 ± 2.9 mmHg in the control group, respectively ($p < 0.05$). When pulmonary arterial pressure of the children with seasonal and perennial allergic rhinitis were compared, there were no significant differences between both sub-groups ($p > 0.05$). The pulmonary arterial systolic and mean pressures of patient group significantly decreased to $28.87 \pm$

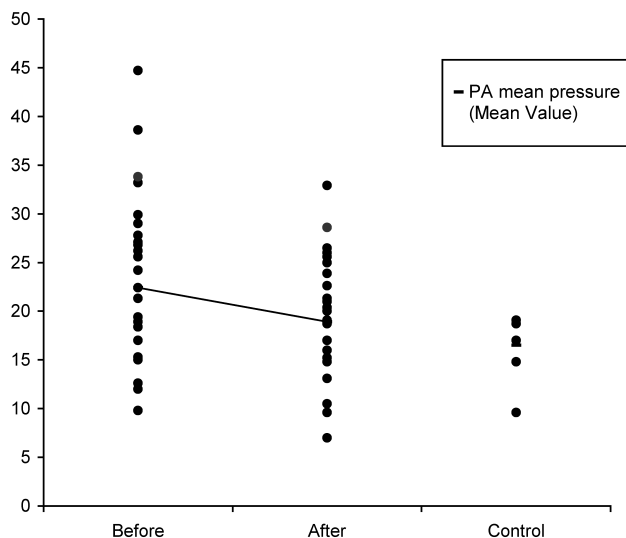


Figure 3. The pulmonary arterial mean pressures in patient group and controls. PA, pulmonary arterial; P, pressure; before, before therapy; after, after therapy.

5.77 and 18.9 ± 5.1 mmHg at the end of the study ($p < 0.05$) whereas the decrease of the pulmonary arterial diastolic pressure (9.98 ± 5.7 mmHg) was not statistically significant ($p > 0.05$). Also, pulmonary arterial pressure values of children with seasonal allergic rhinitis and those with perennial allergic rhinitis were significantly decreased by nasal topical therapy in both sub-groups. After the treatment, pulmonary arterial pressures of the patient group were slightly higher than those of healthy controls, the difference was not statistically significant ($p > 0.05$). No significant correlation was obtained between pulmonary arterial pressures (systolic, diastolic, mean) and each of the symptoms ($p > 0.05$) before and after the therapy, whereas pulmonary arterial pressures and the symptoms scores were decreased after 8 weeks of treatment. The decrease of pulmonary arterial systolic pressure was found to be correlated with the decrease of the symptom score after the treatment ($p < 0.05$), but this correlation was not observed between the symptom scores and pulmonary arterial mean and diastolic

pressures. The patients with higher symptom scores after the therapy also had the higher pulmonary arterial systolic pressure.

The echocardiographic measurements of right ventricular systolic time intervals of the study and control groups are demonstrated in Fig. 4. The corrected acceleration time was 100 ± 17.56 ms in the study group and 104.5 ± 8.87 ms in the control group ($p > 0.05$). The corrected acceleration time significantly increased with nasal topical therapy (107.67 ± 10.87 ms, $p < 0.05$). The pre-ejection period of the patient group was significantly higher than that in healthy controls (60.53 ± 11.2 in the patient group and 51.5 ± 7.45 in the control group, $p < 0.05$). It decreased (58.37 ± 9.24 ms) after nasal topical therapy ($p > 0.05$). The ratio of pre-ejection period to acceleration time was significantly higher in the study group than in healthy controls (59.6% in the patient group and 45.5% in the control group, $p < 0.05$). This ratio decreased (51.4%) with nasal topical therapy ($p < 0.05$). The ratio of acceleration time to ejection time was not found to be statistically significant between the study group and healthy controls (34.9% in the patient group and 35.6% in the control group, $p > 0.05$). This ratio increased (37%) with nasal topical therapy, but this was not found to be statistically significant ($p > 0.05$). The acceleration time, the ratio of pre-ejection period to acceleration time, and the ratio of acceleration time to ejection time were found to be correlated with the decrease of pulmonary arterial pressures, and pre-ejection period was found to be correlated with the decrease of pulmonary arterial systolic pressure in multiple regression analysis for evaluating the effect of therapy. The pulmonary arterial pressure levels were not found to be correlated with the age, gender, atopy, serum total IgE levels, association of asthma, allergy of house-dust mite or pollen, eosinophilia, and duration of the allergic symptoms.

DISCUSSION

Chronic upper airway obstruction may lead to increased pulmonary arterial pressure, and adenotonsillar hypertrophy is the most common cause of this entity in child-

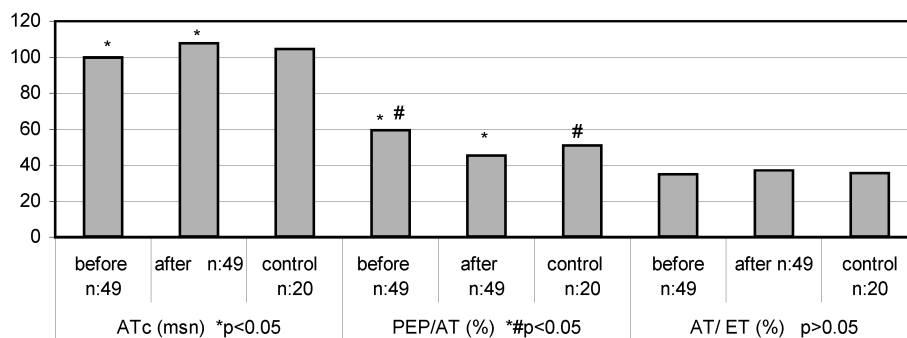


Figure 4. Echocardiographic measurements of right ventricular systolic time intervals in patient group and controls. PEP, pre-ejection period; before, before therapy; after, after therapy; msn, millisecond; ET, ejection time; AT, acceleration time; ATc, corrected acceleration time.

hood.^{5,7,13} It was also reported that children with allergic rhinitis had increased levels of pulmonary arterial systolic pressures compared with their healthy matched controls, and that the increased systolic pulmonary arterial pressures decreased to normal levels after resolving nasal obstruction by treatment with a nasal topical corticosteroid (budesonide 200 µg per day in the morning and evening).⁸ In the present study, mometazon furoat, another topical corticosteroid, 100 µg per day in the evening, was used to evaluate the impact of treatment on pulmonary arterial pressures in children with allergic rhinitis. Similarly, this study showed that children with symptomatic allergic rhinitis had increased levels of pulmonary arterial pressure compared with their healthy matched controls. The increased pulmonary arterial pressures significantly decreased to the levels of healthy controls at the end of therapy ($p < 0.05$).

Children with nasal obstruction related to allergic rhinitis may develop mandatory mouth breathing, snoring, and nasal hyponasal voice as observed in children with adenotonsillar hypertrophy.^{4,13–15} That adults with symptomatic allergic rhinitis may develop obstructive sleep apnea syndrome was also reported.¹⁶ Moreover, that the nose accounts for half of total respiratory system resistance is known.¹⁷ In this regard, difficult nasal airflow, which raises the resistance along the upper airway, results in upper airway resistance syndrome. Increased upper airway resistance contributes to lower airway obstruction and impairs the physiologic ventilation in the lung.^{4,7,17,18} Hypoxia and hypercarbia are formed^{4,7,13} and these may lead to hypoxic pulmonary vasoconstriction and also increased pulmonary arterial pressure if the disease persists.¹⁹ These pressure elevations are a result of chronic and much longer-standing degrees of airway obstruction than is suggested for the patient population described in this study. In the present study, we observed an increase of pulmonary arterial pressure levels in children with symptomatic allergic rhinitis, and the increased pressure level was not found to be correlated with the duration of the disease. We speculate that allergic rhinitis might lead to alveolar hypoventilation resulting in increased pulmonary arterial pressures in the early stage of the disease.

We are unaware of any report about pulmonary arterial pressure in children with allergic rhinitis except the study of Yuksel et al.⁸ They reported that the pulmonary arterial systolic pressure levels were higher in children with perennial allergic rhinitis than in children with seasonal allergic rhinitis. On the contrary, we have not found any difference between the sub-groups. This may be due to the higher number of subjects in our study and the distribution of the patients into sub-groups. They reported that there was no relation between symptom scores and pulmonary arterial pressures. We have found that the decrease of pulmonary arterial systolic pressure was correlated with the decrease of the symptom score after the treatment, whereas there was no correlation between pulmonary arterial pressures and each of the symptoms. The patients with higher symptom scores

after the therapy also had higher pulmonary arterial systolic pressure. We have shown that there was no correlation between the pulmonary arterial pressures and having asthma, age, gender, atopy, serum total IgE levels, allergy of house-dust mite or pollen, eosinophilia, or duration of the allergic symptoms. It was surprising that none of these factors was found to be correlated with pulmonary arterial pressures. The correlation between pulmonary arterial systolic pressure and post treatment symptom score shows the effect of the therapy. We suggest that multiple factors may contribute to increased pulmonary arterial pressure in children with allergic rhinitis and that the nasal topical therapy is an effective approach to decrease the pressures to normal levels.

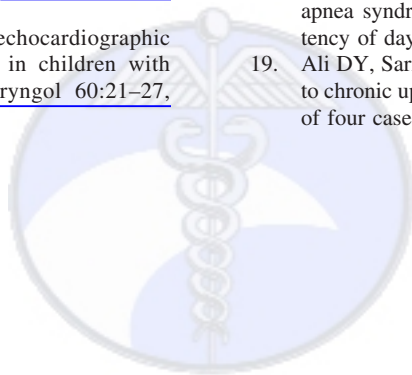
In the present study, we also evaluated the right ventricular systolic time intervals and the effects of nasal topical corticosteroid therapy in children with allergic rhinitis by echocardiography. Also, to our knowledge, this is the first report evaluating the systolic time intervals in children with allergic rhinitis by using echocardiography. The increased pulmonary arterial pressures decreased to the normal levels as the corrected acceleration time significantly increased and the pre-ejection period decreased after the treatment. The ratio of acceleration time to ejection time increased with nasal topical therapy, but the increase was not statistically significant. The measurement of right ventricular systolic time intervals may be affected by many of the same factors as the M-mode time intervals. Heart rate, ventricular function, right ventricular preload, the presence of bundle branch block, cardiac output, right atrial pressure, and Doppler sampling site all may affect measurement of Doppler time intervals. Several authors have examined the relationship between the Doppler flow pattern and pulmonary artery pressure. In general, the acceleration time and the ratio of the acceleration time to ventricular ejection time have been used to estimate the presence and degree of pulmonary arterial pressure.^{11,12} We have also found that the acceleration time, the ratio of pre-ejection period to acceleration time, and the ratio of acceleration time to ventricular ejection time were correlated with the decrease of pulmonary arterial pressures, and that the pre-ejection period was correlated with the decrease of pulmonary arterial systolic pressure.

In conclusion, children with allergic rhinitis have higher pulmonary arterial pressure compared with healthy controls, and increased pressure levels due to allergic rhinitis are reversible by using nasal topical corticosteroids. So, we speculate that allergic rhinitis may cause upper airway resistance syndrome, and the evaluation of pulmonary arterial pressure level might be useful in the follow-up and in planning the therapy of children diagnosed with allergic rhinitis. In this regard, Doppler echocardiography is a useful, non-invasive, and reliable method for the evaluation of pulmonary arterial pressures. We also speculate that particularly children with association of severe pulmonary hypertension and allergic rhinitis should be more carefully fol-

lowed because nasal blockage due to allergic rhinitis may contribute to the severity of the disease by increasing the already increased pulmonary arterial pressure. Further studies are needed to determine the clinical aspect of increased pulmonary arterial pressure.

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