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Is Pulmonary Arterial Pressure Affected by Allergic Rhinitis with Nasal Obstruction?

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SUMMARY Obstructive pathologies of the pulmonary tract may cause various levels of hypoxia. To compensate for the hypoxia, pulmonary arterial pressure and pulmonary arterial flow may increase. We investigated 35 patients with seasonal allergic rhinitis (AR) whether hypoxia caused by AR with a high level of obstruction in the airways may lead to an increased pulmonary arterial pressure. An echocardiographical evaluation was made following the determination of the symptomatic and non-symptomatic symptom scores. We found a positive correlation between the symptom scores both in the symptomatic and non-symptomatic periods, nasal obstruction scores and the mean pulmonary arterial pressures during these periods. Further studies with more cases are needed in order to determine the cardiac effects of hypoxia in AR, mainly pulmonary arterial hypertension.

Allergic rhinitis (AR) is a chronic disease of the nasal mucosa induced by an IgE mediated inflammation. Symptoms of AR include: rhinorrhea, nasal obstruction, nasal itching and sneezing. Asthma and AR are common co-morbidities and AR is considered a risk factor for the development of asthma.[1] According to epidemiological data, 38-60% of patients with AR were found to suffer from coexisting asthma and nearly 90% of asthmatic patients also showed upper respiratory tract symptoms.[1-4] Allergic inflammation does not limit itself to the nasal airways, but upper and lower airways, together recently named "united airways", are both affected by a common inflammatory process.[1]

Pulmonary hypertension (PHT) is defined as a pulmonary arterial systolic pressure above 30 mmHg at rest. The main reasons for PHT are an increase in the pulmonary vascular resistance, left atrial pressure and chronic obstructive pulmonary disease.[5] It is one of the main complications of diseases with respiratory obstructions and hypoxia.[4-6] Studies carried out since 1970 showed that obstructions of the upper airways cause pulmonary hypertension and affect the functions of the right ventricle.[5] The studies also proved that pulmonary arterial pressure increases in chronic obstructive pulmonary disease with evident obstructive pathologies and hypoxia in adults, in obstructive sleep apnea syndrome and in asthmatic cases.[7] This has been supported by experiments with animals showing that hypoxic pathological conditions result in PHT.[8]

In spite of the fact that obstructive pathologies in the lower airways cause PHT, there is no evi-

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dence whether obstruction of the upper airways cause PHT or not. Thus, in this study we aimed to investigate if there is an increase in pulmonary arterial pressure in patients with AR.

MATERIALS AND METHODS

We evaluated 35 patients diagnosed with seasonal AR. Seasonal AR was diagnosed by physical examination and laboratory tests carried out in our allergy-immunology outpatient clinic. We evaluated demographic characteristics of our patients on the basis of sex, mean age, occupation and duration of symptoms.

In order to support the diagnosis of AR and determine the allergen and/or allergens causing the disease, skin prick tests were performed according to the EAACI guidelines,[12] using extracts including grass (*Hulcus lanatus, Lolium perenne, Fectuca pratensis, Phleum pratense, Poa pratensis, Dactylis glomerata*), cereal (*Hordeum vulgare, Avena sativa, Secale cerela, Triticum sativum*), weed (*Artemisia vulgaris, Urtica dioica, Taraxacum vulgare, Plantago lanceolata*), and tree pollens (*Olea europaea, Fraxinus excelsior, Ulmus scabra, Alnus glutinosa, Quercus robur*), as well as allergen extracts of *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* (Allergopharma Ltd, Reinbek, Germany).

Seasonal AR symptom scores (SS) were employed during the symptomatic and the non-symptomatic period of the disease. Briefly, 4 major nasal symptoms (sneezing, itching, rhinorrhea, and nasal obstruction) were recorded according to a scale ranging from 0 (no symptoms), to 1 (mild), 2 (moderate) and 3 (severe). A total nasal symptom score was calculated by adding these scores; the maximum possible score was 12 for each subject. In addition, nasal obstruction scores (NOS) were determined alone, simultaneously with SS during the symptomatic and non-symptomatic periods.

After the nasal symptom scoring, assessment by echocardiography was done using an echocardiographical device (Esaote Biomedica Genoe, Italy). The patient was made to lie down in a lateral decubitus position during which parasternal long axis, parasternal short axis, apical two and four chambers were viewed by 2-D echocardiography and Doppler, recorded on a videotape. Pulmonary arterial systolic flow in the parasternal short axis was printed by Doppler and the pulmonary arterial mean systolic pressure (MPAP) was calculated by taking acceleration time into consideration. The right ventricular end-diastolic volume (RVEDV) and right ventricular end-systolic volume (RVESV) were calculated by the ellipsoidal Shell method. The right ventricular ejection fraction (RVEF) was formulated as (RVEDV-RVESV) / RVEDV.

All echocardiographical inspections were done by the same cardiologist. All parameters were recorded during both, the symptomatic and non-symptomatic periods; MPAP, pulmonary arterial late velocity (AVELOC), left ventricular end diastolic volume (LVEDV), right ventricular ejection fraction (RVEF), stroke index (SI), left ventricular systolic diameter (LVSD), stroke volume (SV) and ejection fraction (EF) were used to illustrate pulmonary arterial pressure differences.

For a correlation of differentiations, the differences of the levels of SS (SSD), NOS (NOSD) and MPAP (MPAPD) from the symptomatic period to the non-symptomatic period were calculated.

Informed consent for the described investigations was obtained from all patients. Approval for the study was given by the ethics committee of our hospital.

Statistical analyses used the Unpaired *Student t test* to evaluate the differences of variables between two groups and *Pearson's correlation test* to evaluate correlations. P values ≤ 0.05 were considered to be statistically significant.

RESULTS

All demographical data pertaining to the patients are summarized in Table 1. When comparing the symptom scores, symptomatic SS was higher than non-symptomatic SS (10.23 ± 1.63 *vs.* 2.54 ± 1.01; $p < 0.0001$). In addition, symptomatic NOS was higher than non-symptomatic NOS (2.41 ± 0.94 *vs.* 0.66 ± 0.94; $p < 0.0001$).

When the patients were compared in the symptomatic and non-symptomatic periods, statisti-

cally significant differences were determined for the MPAP, RVEF, LVSD, LVEDV, AVELOC, SV and SI ($p = 0.045$, $p = 0.0001$, $p = 0.003$ $p = 0.038$, $p = 0.016$, $p = 0.0001$, $p = 0.0044$, $p = 0.038$, respectively). The results are collectively shown in Table 2.

A positive correlation was found between the NOS and MPAP during the symptomatic period (Fig. 1a) ($r = 0.394$, $p = 0.019$). Additionally, a tendency towards a positive correlation was determined between the SS and MPAP during the symptomatic period (Fig. 1b) ($r = 0.320$, $p = 0.061$).

A positive correlation was documented between the SS and MPAP during the non-symptomatic period (Fig. 1c) ($r = 0.635$, $p < 0.0001$).

A negative correlation was observed between the SS and SI, SV and LVEDV during the symptomatic period ($r = -0.484$, $p = 0.003$; $r = -0.449$, $p = 0.007$; $r = -0.445$, $p = 0.007$, respectively).

Positive correlations were documented between the SSD, NOSD and the MPAPD (Fig. 2a and 2b) ($r = 0.528$, $p = 0.001$; $r = 0.624$, $p = 0.0001$, respectively).

Table 1 Demographical characteristics of our patients with seasonal allergic rhinitis

Demographical data	Results
Sex	
Female	21 (60%)
Male	14 (40%)
Age in years ± SD (min-max)	30.94 ± 7.2 (19-48)
Occupation	
Unemployed	12 (34%)
Student	8 (22%)
Working	15 (42%)
Duration of symptoms in years ± SD (min-max)	4.69 ± 2.45 (1-12)

DISCUSSION

Basically our research documents, that in patients with seasonal AR, the pulmonary arterial pressure is higher during the symptomatic period than in the non-symptomatic period. We observed that especially nasal obstruction in our patients was closely

Table 2 Symptom scores and echocardiographical findings of our patients with seasonal allergic rhinitis during the symptomatic and non-symptomatic periods

	Symptomatic period	Non-symptomatic period	*P*
Symptom score			
Nasal obstruction	2.41 ± 0.94	0.66 ± 0.94	< 0.01
Rhinorrhea	2.48 ± 0.83	0.31 ± 0.47	< 0.01
Nasal itching	2.31 ± 0.83	0.74 ± 0.44	< 0.01
Sneezing	2.6 ± 0.65	0.65 ± 0.48	< 0.01
Total	10.23 ± 1.63	2.54 ± 1.01	< 0.01
MPAP (mmHg)	18.71 ± 3.8	17.03 ± 3.23	0.05
RVEF (ml)	50.23 ± 3.38	55.63 ± 2.83	< 0.01
LVSD (cm)	2.84 ± 0.44	2.57 ± 0.27	< 0.01
LVEDV (ml)	124 ± 40.22	105.95 ± 29.44	0.04
EF (ml)	62 ± 5.4	64.8 ± 4.25	0.02
AVELOC (cm/sec)	0.66 ± 0.12	0.77 ± 0.14	< 0.01
SV (ml)	76.33 ± 26.67	64.8 ± 19.83	< 0.01
SI	41.54 ± 10.96	36.21 ± 9.95	0.04

MPAP, mean pulmonary arterial pressure; RVEF, right ventricular ejection fraction; LVSD, left ventricular systolic diameter; LVEDV, left ventricular end-diastolic volume; EF, left ventricular ejection fraction; AVELOC, pulmonary arterial late velocity; SV, stroke volume; SI, stroke index.

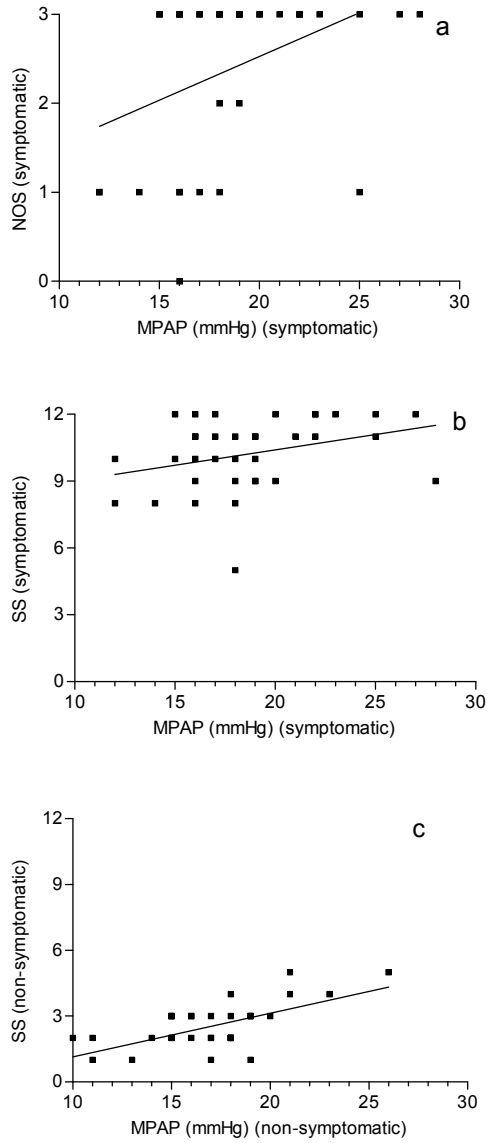

Fig. 1 Correlation between nasal obstruction score (NOS) and mean pulmonary arterial pressure (MPAP) during the symptomatic period (a); correlation between nasal symptom score (SS) and mean pulmonary arterial pressure (MPAP) during the symptomatic period (b); Correlation between nasal symptom score (SS) and mean pulmonary arterial pressure (MPAP) during the non-symptomatic period (c). See text for *p* values.

related to the pulmonary arterial pressure. Previous studies showed that obstructive pathologies in the lower respiratory system can cause PHT.[13,14] How obstructions in the upper airways result in developing PHT is a complex mechanism which is still obscure. A widely believed explanation is that a depolarization of pulmonary arterial organic muscle cells caused by hypoxia and an associated subsequent release of mediators result in pulmonary vasoconstriction.[9-11] However, experiments done on patients with a previous upper airway related illness show that PHT levels vary. A study by Wilkinson *et al.*[15] carried out in children with adenotonsillar hypertrophy showed PHT development in 3.3% of the cases. Similarly, Aji *et al.*[16] and Brown *et al.*[17] reported that hypoxia as a result of hypoventilation brought about by an upper airway obstruction due to tonsillar and adenoid hypertrophy in paediatric cases led to PHT and cor pulmonale development and that the findings were regressive post operation. The above studies showed that airway obstruction and PHT development caused by the upper respiratory system are less common.

In cases of upper airway obstruction due to allergic rhinitis, upper airway resistance elevates to increase the nasal airflow, thus the "upper airway resistance syndrome" develops.[18,19] The fundamental reasons for the upper airway resistance syndrome and nasal blockage in AR are the mucosal oedema and eosinophilic inflammation due to allergic reactions mediated by IgE.[1] In such cases, since it is not possible to provide quality nasal ventilation, respiration occurs through the mouth. However, mouth respiration cannot be well performed especially during sleep, therefore alveolar hypoventilation, hypoxia and hypercapnia develop. There are numerous studies which indicate the development of hypoxia via the nasopulmonary reflex as a result of the nasal blockage.[18-21] In a study by Matsune *et al.*[22] pulse oximetry was used to show the development of hypoxia due to nasal blockage as a result of allergic inflammation in adult patients with AR. In the light of these studies, it could be considered that the nasal obstruction seen in our patients caused hypoxia and through the mechanisms mentioned above evoked PHT.

Some studies used Doppler echocardiography to show the development of PHT due to upper airway obstruction. These studies reported a decrease in RVEF, a dilatation in RV and PA, a failure of the tricuspid and pulmonary valves and an increase in MPAP.[21-23] In a study done by Yuksel *et al.,*[24] 24

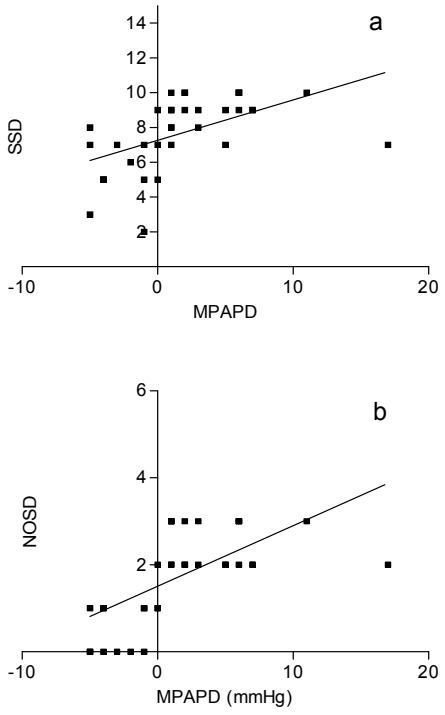

Fig. 2 Correlation between the difference in nasal symptom score (SSD) and the difference in pulmonary arterial pressure (MPAPD) (a); correlation between the difference in nasal obstruction score (NOSD) and MPAPD (b). See text for *p* values.

children diagnosed with AR were assessed by Doppler echocardiography and the MPAP was found to be in high correlation with the symptom scores similar to our study. It was also observed that the pulmonary arterial pressures decreased with a regression in nasal obstruction following topical corticosteroid treatment. Thus, their post-treatment period results correspond to our echocardiographical findings during the non-symptomatic period.

Some studies also verified by echocardiography that the increase in the MPAP was specific for PHT.[19,24] The positive correlations between NOS, SS and MPAP during the symptomatic period and the correlation between SS and MPAP during the non-symptomatic period documented in our study seem to indicate that pulmonary arterial pressure is affected by the symptoms of allergic rhinitis. In addition, correlations between the SSD, NOSD and the MPAPD were observed in our study. All these findings suggest that the severity of the nasal obstruction and nasal symptoms correlate with the pulmonary arterial pressure. Thus, prolonged elevated vascular resistance might bring about permanent PHT and a regression in right cardiac functions over the years.[5]

A study by Pamukcu *et al.*[25] reported LV diastolic dysfunction caused by a RV after-load increase on the LV through the inter-ventricular septum. In our study we have shown a positive correlation between the symptom score and SI and SV parameters which represent the left ventricular functions. In the light of these findings, we can assume that both SI and SV have increased in addition to the elevated pulmonary flow due to symptomatic nasal obstruction and that the LVEDV has also increased by a certain extent as a result of the volume load. This may cause LV diastolic dysfunction in the future.[25,26]

No significant change was determined in E-A parameters, EVELOC and AVELOC when the symptomatic period with its high symptom scores was compared to the non-symptomatic period with low symptom scores, whereas significant changes were monitored in the acceleration time, deceleration time and isovolumetric relaxation time. The presence of a positive correlation between AVELOC and NOS in our study indicates that the LV diastolic early filling velocity increases in relation to the increase of the nasal obstruction. If this phenomenon progressed along with the late velocity suppression, *i.e.* if it had a negative correlation to the EVELOC, it could show a LV restrictive pattern. Such an interpretation of these findings requires further studies though.[25,26]

Further research with a bigger number of AR cases needs to be done in order to determine the cardiac effects of hypoxia and its impact on PHT.

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