

Acoustic rhinometry in nasal provocation test in perennial allergic rhinitis

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Abstract Acoustic rhinometry is one method to evaluate nasal geometry by an acoustic reflection technique. The aim of this study was to investigate the changes in acoustic rhinometry after nasal provocation in patients with exclusively perennial allergic rhinitis. In 19 patients, acoustic rhinometry and active anterior rhinomanometry were performed before and after nasal provocation test. There was a statistically significant nasal flow reduction measured by active anterior rhinomanometry after nasal provocation ($p < 0.05$) and a median symptom score of four points, both indicating a positive response to nasal provocation. On the other hand, there was no statistically significant change in the values of acoustic rhinometry after nasal provocation ($p > 0.05$). In patients with exclusively perennial allergic rhinitis, acoustic rhinometry does not seem to significantly change after nasal provocation. In contrast, active anterior rhinomanometry values decreased significantly after nasal provocation. The presented results indicate that acoustic rhinometry does not seem to be a diagnostic method superior to active anterior rhinomanometry in this context.

Keywords Acoustic rhinometry · Active anterior rhinomanometry · Nasal provocation · Perennial allergic rhinitis

Introduction

Acoustic rhinometry (AR) was first described by Hilberg et al. [11]. It is a quick and non-invasive technique to learn about the geometry of the nasal cavity. Thus, measurements of the relation between the cross-sectional area and the distance into the nasal cavity are possible. It is based on the analysis of sound reflection from the nasal cavity.

In the following years, the interest in AR increased in order to describe and evaluate effects of surgery, of anti-allergic and nasal decongestant drugs, the response to nasal challenge, as well as to study nasal physiology as described by several authors [4, 6, 9, 12, 16, 27]. Nevertheless, the value of AR compared to active anterior rhinomanometry (AAR) is still very much discussed. According to Cole [3], standard operating procedures are indispensable in order to properly evaluate data derived from AR and AAR. AR is supposed to be a non-invasive method, at the same time as sensitive as nasal airflow resistance measurements [24]. AR values are supposed to be less variable than AAR values [22]. In some studies, AR proved to be more sensitive than AAR concerning the diagnosis of allergic and vasomotor rhinitis [17].

According to Roithmann et al. [24], AR is accepted as an alternative objective method for the measurement of nasal mucosal responses especially in the diagnosis of allergies in the past few years. An evaluation of AR after histamine and antigen challenge in non-allergic and allergic guinea pigs showed a significant decrease in volume at 10 and 30 min after challenge [21]. Nevertheless, data dealing with clearly defined collectives of allergic subjects are still missing. This study was

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designed to evaluate changes in AR and AAR parameters before and after NPT in a clearly defined collective of solely perennial allergic subjects [25].

Materials and methods

All experimental procedures were explained in full detail to the study participants, who provided informed consent. The study was performed in accordance with the Declaration of Helsinki/Hong Kong (1964/1989) after receiving approval of the local ethical committee.

Patients

At the Department of Otorhinolaryngology of the University of Ulm (Germany), skin testing and determination of serum-specific IgE in patients with suspected Perennial allergic rhinitis (PAR) were performed. All patients suffered from typical symptoms of house dust mite allergy. Nineteen patients (ten women, nine men) with a median age of 24 years (range 18–48 years) presented positive skin testing for *Dermatophagoides pteronyssinus* (Dpter) and *Dermatophagoides farinae* (Dfar). All 19 patients showed positive tests in serum specific IgE determination either for Dpter and/or Dfar. Additionally, six patients tested positive for *Acarus siro*, three patients for *Lepidoglyphus destructor* and two patients for *Tyrophagus putrescentiae*. The patients did not present with a history of seasonal allergic rhinitis complaints and did not positively react in skin testing for seasonal allergens.

All study participants underwent an otorhinolaryngological examination including anterior rhinoscopy and endoscopy of the nasal cavity. They had no history of sinonasal surgery.

Exclusion criteria were pregnancy, allergic asthma, seasonal allergic rhinitis, considerable septal deviation, serious internal or neurological diseases, age younger than 18 or over 65 years, and patients under continuous medication like steroids, where pharmacotherapy could not be stopped in time. Antiallergic treatment (i.e., treatment with oral or nasal antihistamines, cromolyn sodium, and nasal decongestants) had to be stopped at least 5 days prior to study participation.

Skin testing

The test solutions applied contained 10.000 AU/ml (Allergopharma J. Ganzer, Reinbek, Germany).

Identical saline solution without allergen was used as control. The tests were considered to be positive if the wheal reaction was at least 3 mm in diameter or at least 25% of the wheal area following simultaneous pricking with 1 mg/ml histamine solution. The skin prick test was performed in accordance to the recommendations of the European Academy of Allergology and Clinical Immunology [5].

Determination of serum-specific IgE

Specific IgE of *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* and the other positively skin tested allergens (*Acarus siro*, *Lepidoglyphus destructor*, *Tyrophagus putrescentiae*) was determined using the Pharmacia CAP system (Pharmacia, Freiburg, Germany) (Table 1).

Nasal provocation test (NPT)

NPT was performed using solutions containing extracts of *Dermatophagoides pteronyssinus* (Product-No. 725, concentration: 5.000 BU/ml, Allergopharma J. Ganzer, Reinbek, Germany) and *Dermatophagoides farinae* (Product-No. 708, concentration: 5.000 BU/ml, Allergopharma J. Ganzer, Reinbek, Germany). Identical solutions without allergen were used as control. Both solutions contain 0.4% phenol as preservative. The solutions were sprayed into the less congested nostril (100 µl solution).

In the beginning, a control solution (0.4% phenol without allergen) was sprayed into the less congested nasal cavity, measured by means of active anterior rhinomanometry. Ten minutes after the application of the control solution no reaction was assessed by active anterior rhinomanometry in all patients.

Before 10, and 20 min after NPT clinical symptoms were registered (Table 2), active anterior rhinomanometry and acoustic rhinometry were performed on the challenged side. The values 20 min after NPT had been rejected and the data not shown in the tables as there were no more changes, 20 min after NPT. NPT was considered to be positive if the flow reduction was $\geq 40\%$, or the flow reduction ranging from 20–40% in addition to at least three points in the symptom score, or a symptom score of at least four points, independent of changes in flow in active anterior rhinomanometry. NPT was performed in accordance to the guidelines of the European Academy of Allergy and Clinical Immunology [18].

Table 1 Results of determination of serum-specific IgE and nasal provocation test (NPT)

Subject No.	D pter	D far	Ac siro	Lep dest	Tyr put	Alt alt	Pen not	Eur may	S	I	R	F	Score
1	3	2	0	0	–	–	–	–	2	1	1	21	4
2	3	–	–	–	–	–	–	–	1	2	1	44	4
3	3	3	2	2	–	1	–	–	2	2	0	0	4
4	3	3	2	0	–	–	–	–	2	2	0	26	4
5	3	3	2	2	2	–	–	–	2	2	1	23	5
6	4	4	1	0	–	–	–	–	1	1	0	43	2
7	2	3	0	0	–	–	–	–	2	1	0	42	3
8	3	3	–	2	3	–	–	–	2	1	2	55	5
9	3	4	–	–	–	–	–	–	1	2	1	17	4
10	–	4	–	–	–	–	–	–	2	1	2	24	5
11	2	2	0	0	0	–	–	–	1	2	1	42	4
12	4	4	–	–	–	–	–	–	2	2	1	66	5
13	3	4	1	–	0	–	–	–	1	1	1	36	3
14	3	3	–	–	–	–	–	–	2	1	1	6	4
15	4	5	–	–	–	–	–	–	2	2	1	10	5
16	2	2	–	–	–	–	–	–	2	1	1	13	4
17	4	4	–	–	–	1	1	–	2	0	1	32	3
18	2	2	–	–	–	–	–	1	2	2	0	27	4
19	3	2	1	–	–	–	–	–	2	2	1	22	5

D pter dermatophagoides pteronyssinus, *D far* dermatophagoides farinae, *Ac siro* acarus siro, *Lep dest* lepidoglyphus destructor, *Tyr put* tyrophagus putrescentiae, *Alt alt* alternaria alternata, *Pen not* penicillium notatum, *Eur may* euroglyphus maynei, *S* nasal secretion, *I* irritation, *R* remote symptoms, *F* flow reduction (%)

Flow reduction: reduction <20% = negative, 20–40% = marginal, ≥ 40% = positive

Active anterior rhinomanometry (AAR) and acoustic rhinometry (AR)

Active anterior rhinomanometry (Rhinotest MP 500, Allergopharma J. Ganzer, Reinbek, Germany; trans-nasal reference pressure, 150 Pa) was performed in all 19 patients on the tested side as well as on the non-tested side. At least five measurements from each nostril were taken to calculate the mean values.

Acoustic rhinometry (SRE 2000, RhinoMetrics, Lyngø, Denmark) was also performed in all patients on the tested side as well as on the non-tested side. At least three measurements from each nostril were taken. The mean total volume of the anterior 22 mm (Vol22)

and the mean total volume from 22 to 54 mm (Vol22–54) of the nasal cavity were calculated. Especially the volume from 22 to 54 mm indicates mucosal changes [2, 3, 13].

The mean minimal cross-sectional areas (MCA) were calculated: MCA1 (0–22 mm from the nasal entrance) and MCA2 (22–54 mm from the nasal entrance).

Statistical analysis

The non-parametric Wilcoxon signed rank test was used to compare rhinometrical and rhinomanometrical values before 10, and 20 min after NPT. The null hypothesis (no difference between the parameters before and 10 min after NPT) was to be rejected at the $\alpha = 0.05$ significance level. Statistical analysis was performed using the software Win STAT® (Kalmia Inc., Cambridge, MA, USA).

Results

A complete set of data could be obtained in all patients. There were no individual or technical problems in performing AAR and AR.

The median flow in AAR on the tested side before NPT was 242 cm³/s (range 129–472), after NPT 136

Table 2 Symptom scores for nasal provocation test (NPT) (0–6 points)

Nasal secretion	Irritation	Remote symptoms	Symptom score
No secretion	0–2 sneezes	No remote symptoms	0 points
Little secretion	3–5 sneezes	Lacrimation and/or palatal itching and/or aural itching	1 point
Heavy secretion	> 5 sneezes	Conjunctivitis and/or chemosis and/or urticaria and/or cough and/or dyspnea	2 points

cm³/s (range 16–549). On the non-tested side, the median flow before NPT was 170 cm³/s (range 66–545), after NPT 156 cm³/s (range 16–460). There was a significant flow decrease after NPT on the tested side as well as on the non-tested side ($p < 0.05$). The median bilateral flow decrease was 26% (range 0–66).

The median symptom score was four points (range 2–5).

The results of the AAR and the symptom score proof positive NPT for Dpter and/or Dfar in all patients.

The values of the AR before and after NPT are shown in Table 3.

There was no significant decrease in the MCA1 and MCA2 after NPT on the tested side as well as on the non-tested side ($p > 0.05$). Neither the values of Vol22 nor the values of Vol22–54 showed a significant decrease after NPT as well ($p > 0.05$) (Table 4; Fig. 1). However, the nasal airflow decreased significantly after nasal provocation, both on the tested and the non-tested side of the nose (Table 4; Fig. 2).

Discussion

Acoustic rhinometry (AR) is one practical method to evaluate nasal geometry. In addition to AAR, it seems to be a quick and non-invasive technique to acquire data about the respiratory function and configuration of the nasal airway [10]. It also seems to be a suitable method in the diagnosis of allergies. Acoustic rhinometry was used in nasal provocation testing, both in allergen and histamine provocation, and its value was outlined by several working groups [7, 8, 16, 19–21, 23, 24]. Roithmann et al. [24] consider AR to be an alternative objective method as sensitive as nasal airflow resistance measurements, assessing nasal mucosal response to allergen challenge out of season in patients suffering from ragweed allergic rhinitis. Rasp employed AR in early and late antigen-induced allergic rhinitis in patients suffering from allergic rhinitis. He concluded AR to be a suitable method for measuring local changes after nasal allergen challenge [23].

This study was done to evaluate changes in AR and AAR parameters before and after nasal provocation in subjects suffering from perennial allergic rhinitis only.

In the present study, AAR changed significantly after NPT. Together with considerable symptom scores it was the proof for a positive reaction to NPT, implying that the patients suffered from one kind of house dust mite allergy. On the other hand, AR did not decrease significantly after NPT.

The findings of this study are in contrast to the results of other working groups applying AR in nasal allergen challenge and nasal provocation testing. However, regarding precedent studies, there often seems to be one major problem. Whenever trials of intranasal allergen challenge are carried out, there seems to be a lack of clearly defined collectives of study participants (Table 5). Very frequently the subjects suffer from perennial allergic rhinitis as well as from seasonal allergic rhinitis. It is the mixture of types of allergies, which makes it difficult to assess the meaningfulness of AR. The studies also differ in several other aspects: number of patients (range 8–75), level of allergen/biologic units (range 1.000–100.000), two types of rhinometers, and different analysed acoustic rhinometric parameters (minimal cross-sectional area at the head of the inferior turbinate, total nasal cavity volume, nasal volume from 20–70 mm, volume nasal valve-head of middle turbinate).

Explanations of the finding that AR was not the same sensitive to detect changes after nasal allergen challenge in our study can only be given carefully. One reason for the non-significant decrease in AR after NPT might be the fact that exclusively patients suffering from perennial, non-seasonal allergic rhinitis were considered. Ciprandi et al. [1] demonstrated a minimal persistent inflammation constantly detectable at conjunctival and nasal levels in asymptomatic patients sensitised to mites and continuously exposed to natural allergens. On the other hand, persistent immunologic activation seems to be present in unchallenged nasal mucosa of asymptomatic patients with allergic rhinitis [14]. In the patients of the present study with perennial allergic rhinitis, minimal persistent inflammation might be

Table 3 Median values (range) of acoustic rhinometry before and after nasal provocation in 19 patients with perennial allergic rhinitis

	Vol22 (cm ³)	Vol22–54 (cm ³)	MCA1 (cm ²)	MCA2 (cm ²)
T before NPT	1.74 (1.43–2.64)	4.56 (1.94–4.90)	0.45 (0.41–0.55)	0.41 (0.04–1.10)
T after NPT	1.73 (1.44–1.90)	2.53 (0.08–7.51)	0.37 (0.22–0.60)	0.39 (0.15–1.26)
NT before NPT	1.50 (0.64–2.84)	4.35 (2.15–6.65)	0.39 (0.17–0.69)	0.30 (0.13–0.76)
NT after NPT	1.74 (0.96–2.90)	3.87 (0.46–6.17)	0.39 (0.13–0.76)	0.38 (0.08–1.18)

T tested side, NT non-tested side, NPT nasal provocation test

Table 4 P-values (Wilcoxon-test) of acoustic rhinometry (AR) and active anterior rhinomanometry (AAR) before and after nasal provocation in 19 patients with perennial allergic rhinitis

	AR				AAR
	Vol22 (cm ³)	Vol22–54 (cm ³)	MCA1 (cm ²)	MCA2 (cm ²)	Flow (cm ³ /s)
T before/after NPT	0.59395	0.20757	0.52861	0.35254	0.03815
NT before/after NPT	0.23613	0.24886	0.59395	0.5754	0.0284

T tested side, NT non-tested side, NPT nasal provocation test



Fig. 1 Volume 22–54 (cm³), detected with acoustic rhinometry, on the tested side (T) of the nose before and after nasal provocation (NPT) (box-whisker-plot: *thick line* in the box, median; box, 75%- and 25%-percentile; upper and lower *thin line*, minimum and maximum). There was a non-significant tendency to lower values after nasal provocation in 19 patients with perennial allergic rhinitis

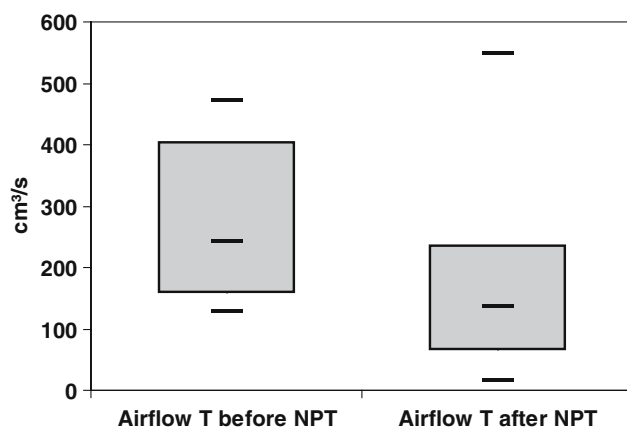


Fig. 2 Nasal airflow (cm³/s), detected with active anterior rhinomanometry, on the tested side (T) of the nose before and after nasal provocation (NPT) (*thick line* in the box, median; box, 75%- and 25%-percentile; upper and lower *thin line*, minimum and maximum). There was a significant decrease ($p < 0.05$) to lower values after nasal provocation in 19 patients with perennial allergic rhinitis

present. Bursts of reaction after allergen challenge might be prevented by simultaneously activated mechanisms of suppression, therefore causing no significant decreases in AR after NPT.

However, the immunological findings of minimal persistent inflammation in perennial allergic rhinitis do not explain that AR was not changed significantly after nasal allergen challenge in the present study because a significant change of nasal airflow was detected with AAR. Thus, the different measurement characteristics of AR and AAR seem to be a more important factor which might influence detection of mucosal changes after nasal allergen challenge. Whereas AR is a static measurement of changes of volumes in a defined intranasal segment, AAR is a functional and dynamic measurement which detects airflow changes of the entire nasal airways [15, 17]. It is imaginable that the total nasal airflow reflecting the functional impairment of the entire nasal airway, measured with AAR, is more adequately representing mucosal reactivity in PAR than the measurement of changes of volumes of defined intranasal segments. We speculate that there is a wide variability how the mucosa within the nasal airways reacts after allergen challenge, and which part of the nose is predominantly reacting and obstructing the nasal airway after nasal allergen exposure.

Acoustic rhinometry is an accepted method applicable to the assessment of nasal surgery, the diagnosis of allergies, as well as to study nasal physiology. It is supposed to be as sensitive and specific to detect significant changes as other methods like active anterior rhinomanometry [7, 8, 17, 19, 20]. In our opinion, AR might not be equal to AAR when it comes to exclusively perennial allergies due to the different levels of mucosa reactivity. In AAR one might also see a pronounced clinical reaction but no significant flow decrease after NPT or vice versa [26]. With AAR being a very well established method within NPT, the presented results indicate that AR does not seem to be a diagnostic method superior to AAR. In order to apply AR more effectively, standardization of its

Table 5 Comparison of acoustic rhinometric findings in patients with allergic rhinitis

	SAR/PAR	No. of patients	Allergen unit	Experimental setup	Main AR findings
Rasp [23]	No information	8	1.000 BU	Rhinoklack, Stimotron, Germany	Significant change of Vol A (nasal valve-head of middle turbinate)
Miyahara et al. [19]	30 SAR or PAR, 45 PAR	75	No information	Rhinoklack, Stimotron, Germany	Significant change of total nasal cavity volume
Ganslmayer et al. [7]	SAR + PAR	30	100.000 AU	Rhinoklack, Stimotron, Germany	29/30 significant change of MCA at head of inferior turbinate
Gotlib et al. [8]	SAR	26	5.000 BU	SRE 2000, Rhinometrics, Denmark	Significant change of CSA-2 = MCA at head of inferior turbinate
Modrzynski et al. [20]	SAR	26	No information	SRE 2000, Rhinometrics, Denmark	Significant change of Vol 20–70
Own results	PAR	19	5.000 BU	SRE 2000, Rhinometrics, Denmark	No significant change of Vol 22–54

AR acoustic rhinometry, SAR seasonal allergic rhinitis, PAR perennial allergic rhinitis, MCA minimal cross-sectional area, CSA cross-sectional area; Vol volume, BU biologic unit, AU allergen unit

performance in NPT has to be achieved and standard values have to be established.

In conclusion, whenever discussing data on acoustic rhinometry in nasal allergen challenge, it is absolutely indispensable to clearly define the examined collectives in order to obtain comparable data.

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