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ORIGINAL ARTICLE

Effect of the nasal cycle on congestive response during bilateral nasal allergen provocation

Tomasz Gotlib[1], Bolesław Samoliński[2], Antoni Grzanka[3]

[1] *Department of Otolaryngology, Medical University of Warsaw, Warsaw, Poland*
[2] *Department of Prevention of Environmental Hazards and Allergology, Medical University of Warsaw, Warsaw, Poland*
[3] *Institute of Electronics Systems, Warsaw University of Technology, Warsaw, Poland*

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Abstract

Background. Bilateral nasal allergen provocation usually produces more pronounced obstruction of one nasal passage. It was found that this could be related to the stage of the nasal cycle before the provocation.
Objective. To discover whether the stage of the nasal cycle is decisive for asymmetry in congestive response observed during bilateral allergen nasal provocation.
Methods. Two bilateral nasal allergen provocations were performed in a group of 26 pollen-sensitive volunteers. Acoustic rhinometry measurements were taken during the nasal cycle, and then after the provocation. A cross-sectional area at the level of the inferior turbinate (CSA-2) was measured. Consecutive challenges were performed in the opposite phase of the nasal cycle: the side which had been wide just before the first challenge, was narrow before the second provocation.
Results. Asymmetry in CSA-2 reduction between the nasal passages was observed in most cases. Significant difference was observed between mean CSA-2 reduction rate (reactivity) of the side that responded with greater congestion, and the opposite side. No significant difference was found in mean CSA-2 reduction rate between the side which was narrow, and the side which was wide before provocation.
Conclusions. Asymmetry of congestive response during bilateral nasal allergen provocation is not dependent on the stage of the nasal cycle preceding the challenge.

Key words

nasal provocation, nasal challenge, acoustic rhinometry, allergic rhinitis

INTRODUCTION

Acoustic rhinometry (AR) and active anterior rhinomanometry (AAR) are most commonly used for objective assessment of nasal response to allergen provocation.

Bilateral nasal provocation is currently preferred to unilateral [1].

Acute bilateral nasal allergen provocation usually produces asymmetric obstruction [2,3,4], which has been linked to the stage of the nasal cycle preceding the challenge [4, 5]. The nasal cycle (NC) is a physiologic phenomenon of spontaneous alteration in nasal mucosa congestion. In the ideal classical nasal cycle described by Kayser in 1895 [5], these alterations are rhythmic, bilaterally reciprocal, and the total nasal resistance and airflow remain unchanged. Prevalence rate of NC in humans varies considerably among studies (0% – 80%). The stricter the criteria of reciprocity and rhythmicity used for classification, the lower the prevalence of the cycle [7]. Recent studies have shown that spontaneous changes in nasal patency are of a less regular pattern [8].

Brooks et al. have shown with the use of active anterior rhinomanometry (AAR) that the side of higher resistance to the airflow before the challenge in approximately 50% of cases responds with greater obstruction, while there is only little or no increase in the resistance on the opposite side [4].

The capability of predicting which side is likely to show greater congestion would be important for the further standardization of the NPT.

Address for correspondence: Tomasz Gotlib, Department of Otolaryngology, Medical University of Warsaw, Warsaw, Poland
e-mail: tgotlib@wum.edu.pl

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The AR is regarded as more sensitive in detecting small changes in congestion of the nasal mucosa compared with AAR [9], and thus seems to be an adequate tool to reevaluate the relationship between the nasal cycle stage and the reactivity of the nasal cavities after allergen provocation. Using AR, Jin et al. found that the side which was narrow before the provocation showed greater congestive response compared to the wide side.

To date, there have been no other reports describing such a phenomenon, although there are several studies on bilateral nasal provocation monitored with the AR [3, 10, 11].

OBJECTIVE

The aim of the presented study was to evaluate whether physiological asymmetry in a cross-sectional area between the sides is decisive for asymmetry in congestive response observed after bilateral allergen nasal provocation.

MATERIALS AND METHOD

Subjects. 26 rhinitis patients sensitive to grass or birch pollens took part in the study. All patients were Caucasians. Their median age was 24 years, range: 16–34 (11 female and 15 males). Diagnosis was based on history and positive skin prick tests (Allergopharma, Reinbek, Germany). None of the patients had any significant nasal deformity (minimum cross-sectional area after decongestion > 0.35 cm^2), nasal polyps, severe asthma or nasal surgery for 6 months prior to the study. Other exclusion criteria were: recent history of respiratory tract infection, intake of steroids for at least 1 month, and antihistamine drugs for at least 2 weeks, or any other drugs in the 3 days prior to challenge, recent or past immunotherapy or pregnancy. The study was approved by the local Ethics committee. All patients gave written consent before participating in The local Ethics committee The local Ethics committee the study.

Study design. Two NPTs were performed in an interval greater than 4 weeks. Before each NPT, spontaneous changes in the patency of the nasal passages were observed.

Consecutive challenges were performed in the opposite phase of the nasal cycle: the side which had been more patent just before the first challenge was congested before the second challenge. The study was conducted out of pollen season. 24 patients were challenged with grass allergen and 2 with birch allergen. Assessment of reaction to the control solution (allergen solvent) was performed during another session.

Allergens. Standardised freeze-dried grass or birch pollen extracts (Allergopharma, Reinbek, Germany) were used. Allergen solutions (5,000 BU/ml) were prepared before provocation. Two puffs (0.05 ml each) of solution at room temperature were applied to each patient's nasal passage with the use of a metered pump spray (total applied dose: 1,000 BU).

Acoustic rhinometry. Measurements were taken with the use of a SRE 2000 rhinometer (Rhinometrics, Lynge, Denmark), with respect to recommendations of Consensus report on Acoustic Rhinometry and rhinomanometry [12]. Transparent anatomical nose-pieces and sealing gel were used.

The measurements were performed every 15 minutes during the nasal cycle observation and every 5 minutes for 30 minutes after allergen application.

Results obtained before the challenge and at 15 minutes and at the maximum congestion after the provocation were further analyzed. Cross-sectional areas at the second valley (CSA-2) were analyzed. Special software enabling identification of CSA-2 was used.

CSA-2 decrease after the provocation was expressed in cm^2 (absolute CSA-2 decrease) and as a percentage of pre-challenge CSA-2 value (Δ = reactivity), according to the formula:

$$\Delta = (\text{CSA-2 after provocation} - \text{CSA-2 before provocation}) / \text{CSA-2 before provocation}$$

The side which reacted with more pronounced congestion was called 'more reactive' in contrast to 'less reactive' side.

The side which was wide before the provocation was called 'wide', in contrast to the 'narrow' side, which was narrow before the provocation.

Recording of nasal symptoms. Symptoms were recorded by the subjects on 100 mm VAS (Visual Analogue Scale). Assessment included: itching, sneezing (three and more sneezes were equal to 100 mm), rhinorrhea, congestion, ocular symptoms, dyspnoea, and one other: itching of pharynx, ear, or cough.

Reaction to control solution. After 20-minutes of acclimatization, the control solution was applied in the same manner as the allergen during the provocation. AR measurements and recording of nasal symptoms were performed before and 15 minutes after application of the control solution.

Statistical evaluation. Students-T test was used with critical p level set at 0.05.

RESULTS

In one of 26 subjects no difference between CSA-2 of the nasal passages greater than 30% was detected during 6 hours of observation. This patient was excluded from further evaluation.

Comparison of reaction to control solution and provocations. After the provocations, all the subjects showed pronounced symptoms, as recorded on VAS (sum of symptoms) compared to reaction to the control solution: 10 mm vs. 206 mm after provocation 1, and 213 mm after provocation 2 ($p<0.001$).

Mean values of reactivity of more reactive and less reactive sides after control solution application were -6% (±12% s.d.) and 5% (± 10% s.d.), respectively. The difference between mean reactivity (Δ) of the more reactive side at 15 minutes after allergen challenge, and after control solution application, was 39% and 40% after provocation 1 and 2, respectively ($p<0.001$).

AR results after allergen challenge. The difference between the mean CSA-2 of the 'wide' and 'narrow' passages before and after the challenges was statistically significant (Tab. 1).

Table 1. Provocation 1 and 2 - comparison of mean CSA-2 before and 15 minutes after challenge, mean CSA-2 decrease (in cm^2) and as Δ (reactivity) for the side that was narrow, and the side which was wide before challenge

Provocation 1 / Nasal passage	CSA-2 before allergen application [cm^2]	CSA-2 15 min. after allergen application [cm^2]	CSA-2 decrease [cm^2]	Reactivity (Δ)
Narrow	0.67 (±0.16 s.d.)	0.44 (±0.18 s.d.)	-0.23 (±0.19 s.d.)	-33% (±0.26% s.d.)
Wide	1.17 (±0.27 s.d.)	0.84 (±0.35 s.d.)	-0.32 (±0.32 s.d.)	-27% (±0.26% s.d.)
Difference between sides – statistical evaluation	p<0.001	p<0.001	n.s	n.s
Provocation 2 / Nasal passage	CSA-2 before allergen application [cm^2]	CSA-2 15 min. after allergen application [cm^2]	CSA-2 decrease [cm^2]	Reactivity (Δ)
Narrow	0.65 (±0.19 s.d.)	0.39 (±0.21 s.d.)	-0.25 (±0.17 s.d.)	-40% (±0.23% s.d.)
Wide	1.15 (±0.31 s.d.)	0.77 (±0.23 s.d.)	-0.38 (±0.29 s.d.)	-31% (±0.19% s.d.)
Difference between sides – statistical evaluation	p<0.001	p<0.001	borderline	n.s

Table 2. Provocation 1 and 2 – comparison of mean CSA-2 decrease (in cm^2) and as Δ (reactivity) for more reactive and less reactive nasal passage at 15 minutes

Provocation 1 / Nasal passage	CSA-2 decrease [cm^2]	Reactivity (Δ)
More reactive	-0.43 (±0.25 s.d.)	-45% (±19% s.d.)
Less reactive	-0.13 (±0.19 s.d.)	-15% (±23% s.d.)
Difference between the sides – statistical evaluation	p<0.001	p<0.001
Provocation 2 / Nasal passage	CSA-2 decrease [cm^2]	Reactivity (Δ)
More reactive	-0.44 (±0.27 s.d.)	-46% (±21% s.d.)
Less reactive	-0.2 (±0.13 s.d.)	-25% (±16% s.d.)
Difference between the sides – statistical evaluation	p<0.001	p<0.001

Mean decrease of CSA-2 (in cm^2) was slightly bigger on the 'wide' side. Conversely, reactivity (Δ) was slightly bigger for the 'narrow' side (Tab. 1). These differences between the 'wide' and 'narrow' sides were not significant during both provocations.

In contrast, the difference between mean reactivity of the more reactive and less reactive side was more pronounced and significant (Tab. 2). The same regularity of congestion response was seen at 15 minutes and at the maximum congestion during both provocations (Fig. 1, 2).

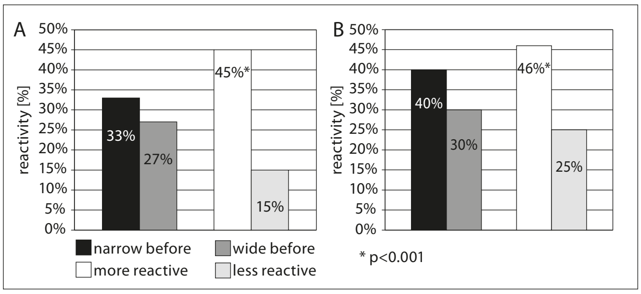

Figure 1. Reactivity of wide and narrow, more reactive and less reactive sides at 15 minutes. Provocation 1 (**A**), and provocation 2 (**B**)

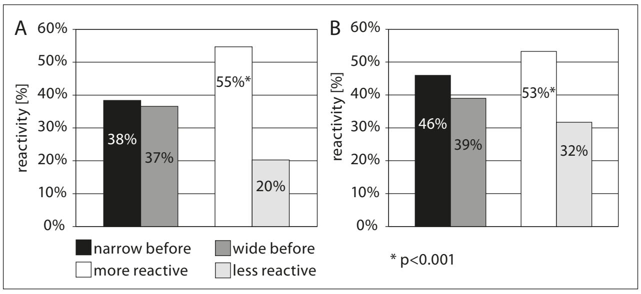

Figure 2. Reactivity of wide and narrow, more reactive and less reactive sides at the maximum congestion. Provocation 1 (**A**), and provocation 2 (**B**)

DISCUSSION

Jin et al. reported significant differences in MCA and volume reduction rate between the 'wide' and 'narrow' passages [5]. There are several potential reasons for discrepancies between the results of the studies. One possible reason is that non-decongested Oriental noses were found to have smaller mean cross-sectional area at 0–6 cm compared to Caucasian ones [12]. Similarly, differences in the nasal resistances were found [14]. In the Jin's Study group, the mean MCA before the provocation was 0.35 cm^2, which is a border-line value for the feeling of nasal obstruction in Caucasians.

Secondly, the patients from Jin's group were allergic to house dust mites, which are very difficult to eliminate from the environment; therefore, minimum persistent inflammation was much more probable in their group than in the presented study.

Finally, in the Jin's study, some patients demonstrated total blockage of at least one nasal passage after the challenge, which was not observed in the presented study group. The occurrence of unilateral nasal blockage could bias the results when the MCA reduction rate was compared; this is because reactivity of the blocked side is always 100%.

In our previous study, retrospective analysis of the consecutive challenges, assessed with different type of acoustic rhinometer (Rhinoklack, Stimotron), in a group of 25 patients was carried out. The results were in accordance with those obtained during the presented study [15].

Wang et al. assessed nasal obstruction during the NPT, using passive anterior rhinomanometry in 18 rhinitic patients, but the early phase assessment was rather limited and the authors focused on late phase reaction. Nevertheless, the influence of the stage of the nasal cycle preceding the NPT on reactivity of the nasal passages was not reported, although the difference in reactivity between the sides was clearly shown [16].

Brooks *at al.* [4] performed bilateral nasal provocation with threshold doses of allergen in a group of 26 Caucasian patients. They found that the side of higher resistance to the airflow before the challenge reacts with a pronounced increase of resistance, while there is no change on the low resistance side (results for average nasal resistances). This pattern of reaction was seen in 14 out of 26 patients. When supra-threshold doses were applied, further fast increase in resistance was observed on the side of higher resistance, and only moderate increase on the low resistance side; therefore, the difference in resistance between the sides rose. Brooks et al. concluded that the two sides of the nose had different potentials for reactivity as a function of the nasal cycle, and that the less resistant side was less reactive.

Apparent discrepancies between results of the presented study and the study by Brooks *et al.* can be explained by the utilization of the two different methods of nasal airway assessment.

Decrease in CSA-2 produces a non-linear rapid increase of resistance to airflow [17]. Thus, equal congestive response results in a greater increase of resistance in the 'narrow' passage (side of higher resistance) compared to the 'wide' passage. This effect is similar to the that observed in viral croup. Thickening of the submucosa of the subglottic region by 1 mm in a neonate leads to profound dyspnoe, while the same thickening in an adult will not result in any breathing disturbances.

Thus, even if congestive response of the sides is comparable, AAR shows a much more pronounced response on the 'high-resistance side'. This phenomenon is the most probable reason why the AR was found to be more sensitive in detecting small mucosal congestion compared with AAR [9]. A detailed comparison of results between the two studies is impossible because, to date, no reliable formula enabling calculation of CSAs to resistance has been found.

In the course of NPT, the spontaneous changes in nasal patency are overridden by type I allergic reaction and are possibly modified by the nasal reflexes. The conjunction of these factors makes the result of the provocation on the nasal patency difficult to predict.

In the opinion of the authors, the 'higher reactivity' of the narrow side (side of higher resistance) observed in studies by Jin and Brooks, in fact, does not reflect increased potential for congestion. It is rather a sequel of the use of certain methods of detection or assessment of congestive response.

CONCLUSIONS

The presented study shows that there is asymmetry of CSA-2 decrease in response to bilateral nasal allergen challenge between the nasal passages. This asymmetry seems to be independent of pre-challenge congestion of nasal mucosa if the threshold or supra-threshold doses of allergens are used in non-congested Caucasian noses. Since relation between the stage of nasal cycle and congestion pattern after the provocation is still a problematic issue, both sides of the nose should be monitored during nasal allergen provocation.

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