Dynamics of early phase congestion after nasal allergen provocation*

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SUMMARY

Background: *It is generally accepted that congestion during the nasal provocation is most pronounced at about 15 minutes after allergen application. However, it may reach its peak at a different time. This can cause inaccurate assessment of the nasal challenge. The aim of this study was to evaluate the dynamics of early phase congestion during nasal allergen provocation (NPT) and its reproducibility.*

Methods: *Two nasal allergen challenges were performed in 26 allergic rhinitis volunteers. Acoustic Rhinometry measurements were recorded before, and then every 5 minutes for 30 minutes after the allergen application. The sum of cross-sectional areas at the level of the head of inferior nasal turbinate (CSA-2) of both nasal passages was analyzed.*

Results: *The mean time to the occurrence of maximum congestion was 20 minutes. The maximum congestion differed significantly from that recorded at 10, 15 and 20 minutes. The observed patterns of congestive response were not consistent, with inter- and intra-individual differences regarding the time to maximum congestion. Percentage change in airway dimension recorded at the maximum congestion was found the least variable.*

Conclusions: *Evaluation of the maximum congestion pattern during the NPT gives more accurate data compared to a single measurement of nasal patency.*

Key words: acoustic rhinometry, allergic rhinitis, nasal provocation, allergen provocation, congestion

INTRODUCTION

Nasal allergen provocation is a valuable tool used for diagnosing and monitoring treatment of allergic rhinitis. Objective assessment of the nasal airways is recommended for evaluation of nasal allergen provocation (1). It is generally accepted that during the nasal allergen provocation (NPT), congestion of nasal mucosa is most pronounced at about 15 minutes after allergen application. However, congestion may reach its peak at a different time. Variability in the time to occurrence of maximum congestion can lead to an underestimation of the response to allergen and result in inaccurate assessment of the challenge. Assessment of nasal patency at maximum congestion has been used to investigate the effect of unilateral nasal provocation (2,3). Bilateral nasal provocation enables us to control for the effect of the nasal cycle and is therefore preferred to unilateral (1,4).

Acoustic rhinometry (AR) is a quick, noninvasive, reproducible method of assessment of nasal cavity geometry considered suitable for monitoring nasal provocation testing (1,5,6). The method enables us to perform repeated measurements as frequently as every 5 minutes.

The aim of this study was to evaluate the dynamics of early phase congestion after nasal allergen provocation and its reproducibility.

MATERIAL AND METHODS

Patients

Twenty-six patients allergic to grass or birch pollen, including 11 women and 15 men, mean age 24 years (range 16 to 34 years), with a history of symptoms during environmental exposure and positive skin prick tests (Allergopharma, Reinbek, Germany) were included in our study. The exclusion criteria were: perennial symptoms, significant nasal deformity, nasal polyposis, immunotherapy (recently or in the past), respiratory tract infection or treatment with antihistamine drugs during the previous two weeks (4 weeks for astemizole), treatment with steroids over the last month or any other drugs the three days prior to NPT. The protocol was approved by the local Ethics Committee. The patients gave informed consent before entering the study.

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Study design

Two provocations were performed at least four weeks apart, in the autumn and winter. The placebo (allergen solvent) challenge was assessed during another session.

Allergens

Standardized grass or birch pollen extracts (Allergopharma, Reinbek, Germany) 5000 BU/ml was used. Two puffs (0.05 ml each) of the solution at room temperature were applied to both nostrils of the subject with the use of a metered pump spray (total applied dose was 1000 BU).

Acoustic rhinometry

AR was carried out with the use of the SRE 2000 rhinometer (Rhinometrics, Lynge, Denmark) according to the guidelines of the Standardization Committee on Acoustic Rhinometry [7]. Transparent anatomical nose adaptors and sealing gel were used. After 20 minutes of acclimatization the baseline measurements were performed every 15 minutes. After the challenge, measurements were taken every 5 minutes for 30 minutes. The sum of cross-sectional areas at the second notch (CSA-2) for both sides was analyzed. Symptom scores were recorded on a VAS scale (100 mm length) for seven symptoms: itching, sneezing, rhinorrhoea, nasal blockage, dyspnoea, ocular symptoms and one additional symptom.

Data analysis

Special software identifying location of the CSA-2 was used. For each patient, the total CSA-2 decrease at 10, 15, 20 minutes and at the maximum congestion observed during a 30-minute period after the challenge were calculated. Decrease in the sum of CSA-2 for both sides of the nose after the provocation was calculated as a change ratio from the initial value. This parameter, defined as "percentage change in airway" (Δ), was calculated according to the formula:

Δ = (CSA-2 after decrease - CSA-2 before decrease) / CSA-2 before decrease x 100%

The variability (V) of assessments was calculated according to the formula:

$V = \Delta 1 - \Delta 2 / \Delta 1 + \Delta 2$

$\Delta 1$ = percentage change in airway at the first provocation,

$\Delta 2$ = percentage change in airway at the second provocation

Statistical evaluation

Student t-test was used.

RESULTS

Compared to the response to the control solution all the challenges were positive as demonstrated by the symptoms (VAS): 10 mm vs. 206 mm after provocation 1 and 213 mm after provocation 2 ($p < 0.001$). Mean total cross-sectional area remained almost completely unchanged following the application of the control solution.

Percentage change in airway (Δ) at 10, 15, 20 minutes and at maximum congestion after allergen provocation are presented in Table 2. The maximum congestion measured as percentage change in airway (Δ) was 38% and 42% during consecutive challenges. The mean Δ at 10, 15 and 20 minutes were 29%, 30%,

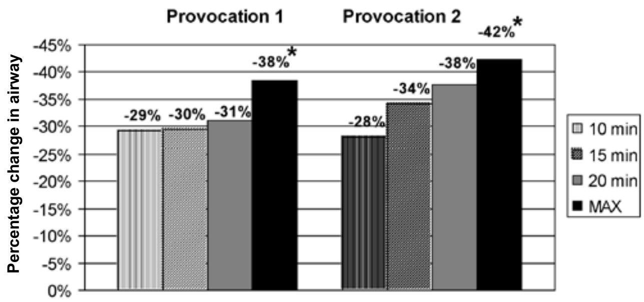

Figure 1. Percentage change in airway (Δ) at 10, 15, 20 minutes and at the maximum congestion after the provocation. Statistical significance: * ($p < 0{,}05$) - compared to near presented values.

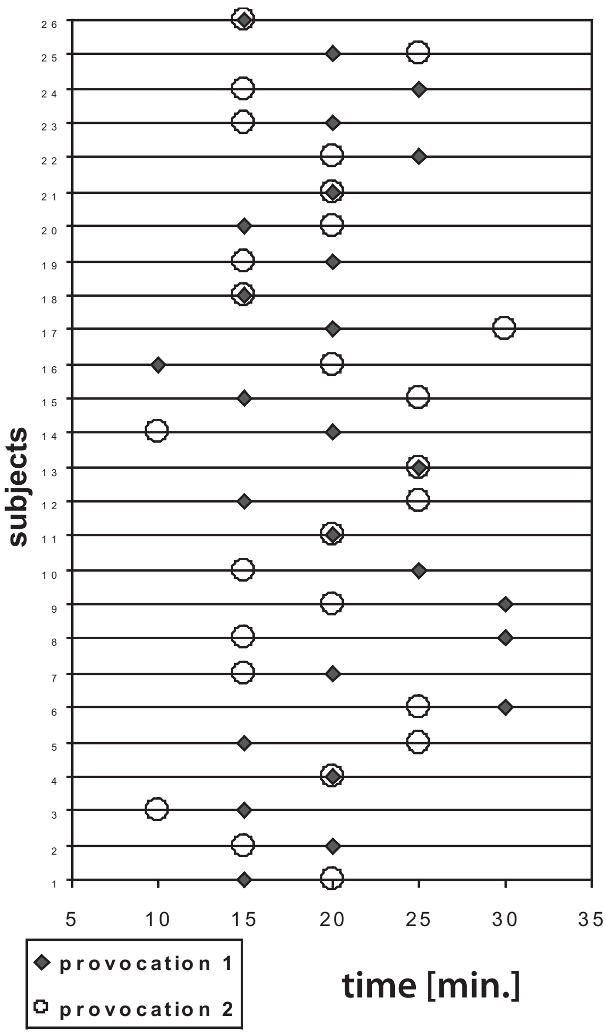

Figure 2. Time of occurrence of maximum congestion after provocation 1 – diamonds, and provocation 2 - circles (longitudinal axis) in individual patients (vertical axis).

31%, during the first provocation and 28%, 34%, 38% during the second provocation respectively (Figure 1). The difference between Δ at the maximum congestion and each at 10, 15 and 20 minutes was statistically significant for both provocations.

The mean time of maximum congestion occurrence was 20 minutes after allergen application for both challenges (range 5-30). Maximum congestion reached peak at 15 minutes in 7 (27%) patients during provocation 1 and in 9 (34%) after provocation 2. The difference in time of occurrence of maximum congestion between the consecutive provocations was 10 minutes or more in 10 cases (38%). The same time of occurrence of maximum congestion was observed in 7 patients (27%)(Figure2).

The lower variability of Δ was observed for the assessment at maximum congestion (Figure 3)

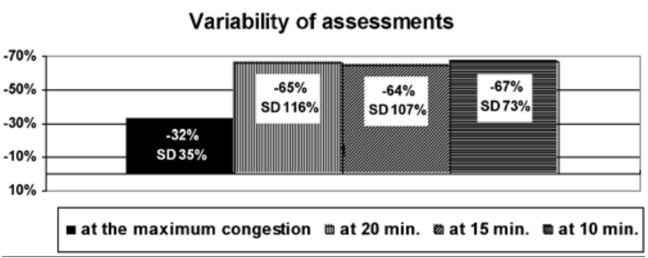

Figure 3. Variability (vertical axis) of assessments at the maximum congestion and at 10, 15 and 20 minutes.

DISCUSSION

Several factors have been proven to influence the congestive response during NPT including a priming effect, sex hormones, environmental factors (temperature, humidity) [8,9]. The difference between mean percentage change in airway (Δ) during the first and second provocation in our study was on the borderline of statistical significance ($p = 0.05$). Higher mean Δ after the second provocation is most probably caused by the priming effect in spite of over four weeks interval between the challenges. The influence of hormones can not be ruled out since we did not evaluate hormonal status of female patients during the challenges.

CSA 2 is not always the only affected area during the allergen challenge. In the present study we analyzed exclusively CSA-2 changes in order to avoid comparing congestive responses that could occur at different depths of the nasal cavity. This could affect further analysis of the results.

To our knowledge there are only few studies evaluating dynamics of early phase congestion response with frequent consecutive measurements after bilateral nasal provocation [10,11]. In these studies the mean-time to maximum congestion was similar to that found in our study group (i.e. 18-20 minutes). In our study group the time to occurrence of maximum congestion did not depend on the value of percentage change in airway (Δ). Higher Δ observed after the second provocation did not influence the mean time to occurrence of maximum congestion. So far there have been no data proving that time to maximum congestion could be dependent on allergen dose. The time to occurrence of maximum congestion is most probably not an constant subject-dependent feature, since it differed in consecutive provocations in the same patient in our study group.

Larivée et al. evaluated the reproducibility of bilateral NPT with histamine and saline phosphate using AR measurements every 5 minutes before and after the provocation. The comparison of the congestive response of the rhinitic subjects revealed that their responses were more dynamic and not steady, compared with those of the normal subjects. In our study group similar inconsistent patterns of congestive response were observed [10]. In an allergen provocation study with similar design, Jin et al. observed marked, statistically significant shortening in period of the nasal cycle after the provocation [11].

All these data suggest the activation of a reflex mechanism and a modification of the nasal cycle besides non-vascular swelling of the tissue during the NPT. There is evidence that unilateral provocation induces contralateral increase of the mediators' concentration, influences the nasal patency, blood flow and secretion [12-14]. This may explain why time of occurrence of maximum congestion is variable.

Inter- and intra-individual differences in congestive response dynamics is the most likely reason for the unsatisfactory sensitivity and specificity of the NPT assessed with a single measurement of the nasal patency and discrepancies between subjective and objective patient evaluation.

It seems that the optimum period of observation to record maximum congestion is 30 minutes after allergen application. Results of previous studies suggest that congestion during the early phase reaction subsides in most subjects 35 to 60 minutes following allergen application [10,11,15]. During the late phase congestion is less pronounced, and observed in only some of patients [15]. In our study group the delayed maximum congestion at 30 minutes was observed in 4 out of 52 provocations only.

Maximum congestion assessment would most probably enable reduction of the allergen dose in NPT protocols with increasing concentrations of allergen.

CONCLUSION

Consecutive recordings of nasal patency over 30 minutes after allergen application allow evaluation of the maximum congestion, which gives more precise data on congestive response to nasal challenge compared to a single measurement.

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