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Nasal mucosa reaction. A model for mucosa! reaction during challenge

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SUMMARY

Rhinological symptoms in aspects of hyperreactivity and allergy are increasing problems. Previous reports on this subject are based on studies of airway obstruction (rhinomanometry), secreted substances during challenge, and symptom scores. To be able to define and evaluate the pathological reactions in nasal hyperreactivity and allergy, it is necessary to find principles to describe and standardize the reactions of the healthy nasal mucosa. The aim of this study was to examine congestion of the nasal mucosa in healthy volunteers. Existing measuring methods, in this aspect, are either indirect or not accurate enough for this purpose. With the development of rhinostereometry, an optical measuring method, it is possible to record nasal mucosa congestion with high accuracy. A nasal challenge test was made in healthy volunteers with gradually raised concentrations of a histamine solution, which was applied to the inferior concha on the right side. Recordings of the mucosa! congestion were made with rhinostereometry. We found that it is possible, with statistical significance, to standardize the reactions of the healthy nasal mucosa: There is no congestion more than 0.4 mm with a histamine concentration of less than 4 mg/ml ($p < 0.05$); congestion of more than 0.4 mm is present at histamine concentrations of 16 mg/ml ($p < 0.05$).

INTRODUCTION

In rhinology, reactions of the nasal mucosa are of great interest. Mucosa! congestion has different causes; the most common are viral infections, allergic reactions, polluted air, pregnancy and hyperreactivity. Objective methods to verify allergy and infections exist since long in pulmonology, and these clinical methods are used to verify bronchial hyperreactivity as well as to estimate the degree of bronchial responsiveness. In rhinology, however, no such methods exist. Previous studies have investigated aspects of airflow obstruction, nasal secretion and secreted substances during challenge. With these methods it has been difficult to reach a sufficiently high accuracy as needed for standardization

procedures, such as reported by Borum (1979). However, the development of rhinostereometry as described by Juto et al. (1984) has made it possible to measure nasal mucosa congestion with a high accuracy. In order to verify and to make an estimate of the degree of nasal hyperreactivity, it is necessary to standardize the reaction of the healthy mucosa. Therefore, rhinostereometry is used in this study with the purpose to standardize the nasal mucosa reactions during histamine challenge in rhinologically healthy volunteers.

MATERIAL AND METHODS

Seven volunteers, 5 women and 2 men with ages ranging from 19 to 33 years, participated in the study. They were all clinically healthy and had no history of allergy or other rhinological disease. The study was performed during the spring of 1989. The nasal mucosa was challenged with histamine diluted in NaCl and 0.5% phenol, with histamine concentrations ranging from 0.1-32 mg/ml. The histamine solution was applied with a syringe to the medial side of the right inferior concha (challenged side). The left inferior concha was unchallenged and served as a control (unchallenged side).

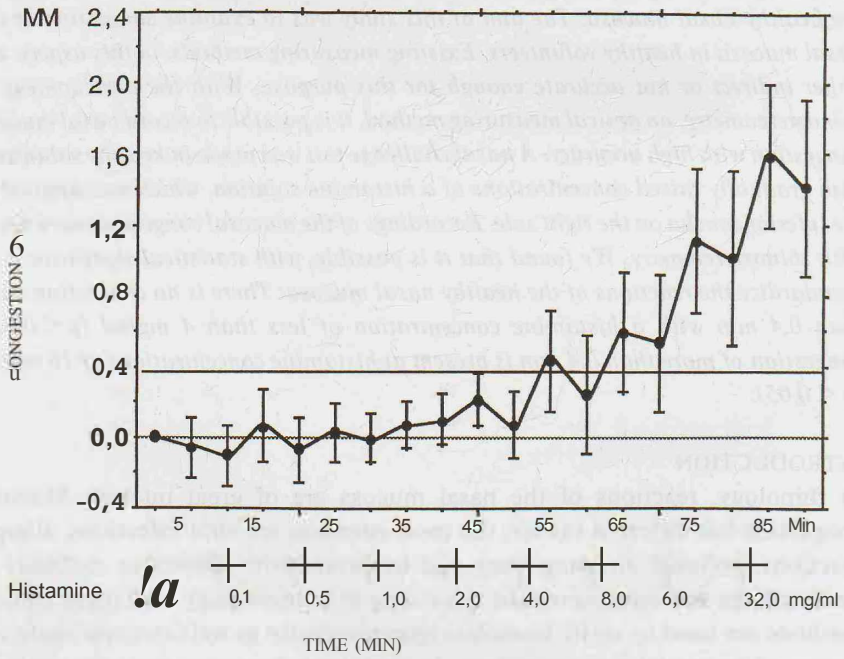

Figure 1. Nasal mucosa congestion on the challenged side after application of histamine in increasing concentrations. The zero-level indicates the mucosal surface position before challenge. Arrows indicate successive applications of histamine solutions with concentrations gradually increased every 10 min. Mean values from 21 recordings with error bars describing 95%-confidence intervals.

To optically measure nasal mucosal reactions, we used rhinostereometry. In the test situation the volunteer was acclimatized for at least 2 hours prior to the challenge. During the last 15 min of the acclimatization period, the position of the mucosal surface of the inferior concha on both sides was recorded every 5 min in order to check whether the mucosal position was stable. The challenge began with 0.14 ml of a histamine-free solution. Recordings of the mucosal surface, on both sides, were made 5 and 10 min after challenge, and then 0.1 mg/ml histamine solution was applied and, again, recordings were made after 5 and 10 min. Challenge and recording procedure were likewise repeated, with gradual raising of the histamine concentrations, up to 32 mg/ml (Figure 1). The test was repeated three times on each volunteer, with at least 24-hour intervals.

RESULTS

All volunteers performed the challenge test up to the highest histamine concentration (32 mg/ml). Analysis of the variance showed that it is statistically valid to regard all 21 recordings as independent, on the challenged as well as the unchallenged side. Therefore, mean values, standard deviations and confidence

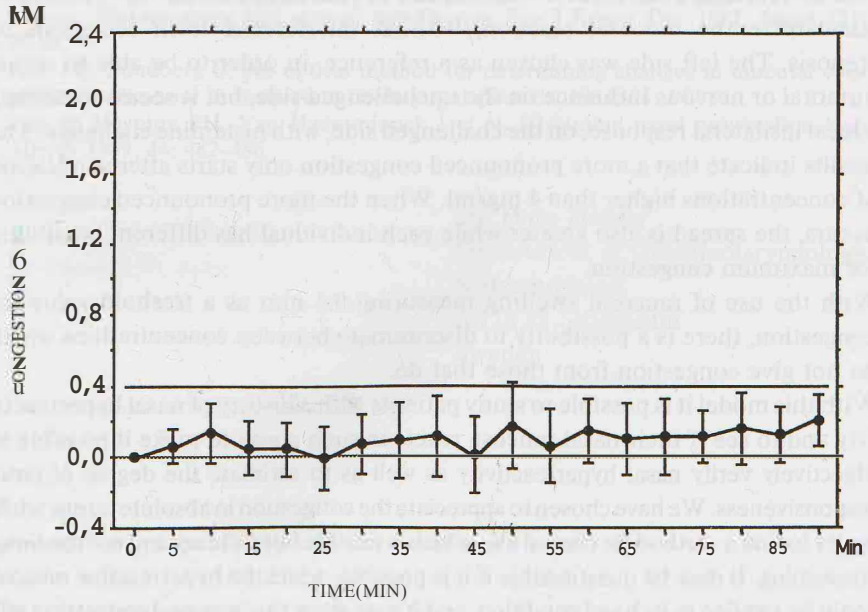

Figure 2. Reaction of the nasal mucosa of the left inferior concha (unchallenged side) during histamine challenge of the right inferior concha (challenged side). Recordings were made 5 and 10 min after challenge. Mean values from 21 recordings with error bars describing 95%-confidence intervals.

intervals (95%) were calculated from the 21 separate test situations, on each side respectively.

On the challenged side, mucosa! congestion following challenge with histamine concentrations of 0.1, 0.5, 1 and 2 mg/ml is relatively constant, with mean values below 0.4 mm ($p < 0.05$). With concentrations above 4 mg/ml the congestion is more pronounced, but mean congestion exceeds 0.4 mm only after histamine concentrations of more than 16 mg/ml were applied ($p < 0.05$; Figure 1). On the unchallenged side there is no corresponding reaction (Figure 2).

DISCUSSION

In this study histamine has been chosen for mucosal challenge because it is a biological substance used in many previous studies. In pulmonology, histamine challenge tests are used in clinical practice to estimate the degree of bronchial responsiveness as reported by Hargreave et al. (1982) and Desjardin et al. (1988). In rhinology, many attempts have been made to find a method to record and estimate the degree of nasal mucosa responsiveness. The method mostly used is rhinomanometry (Ashan et al., 1958), but it has been difficult to find principles of recording for standardization. The recordings are influenced by mucosal secretion and skeletal stenosis as reported by Borum (1979), Broms (1982) and Van de Heyning et al. (1989). With the use ofrhinostereometry it is possible to standardize the mucosa! reaction, without interference from secretions or stenosis. The left side was chosen as a reference, in order to be able to reveal humoral or nervous influence on the unchallenged side, but it seems to be only a local ipsilateral response, on the challenged side, with histamine challenge. The results indicate that a more pronounced congestion only starts after application of concentrations higher than 4 mg/ml. When the more pronounced congestion occurs, the spread is also greater while each individual has different possibility for maximum congestion.

With the use of mucosal swelling measuring 0.4 mm as a treshold value for congestion, there is a possibility to discriminate between concentrations which do not give congestion from those that do.

With this model it is possible to study patients with a history of nasal hyperreactivity and to see if their nasal mucosa reacts in such a way to make it possible to objectively verify nasal hyperreactivity as well as to estimate the degree of nasal responsiveness. We have chosen to appreciate the congestion in absolute terms, while we try to find a method for clinical use, which is reliable but still easy and not too time-consuming. It may be questionable if it is possible, while the hyperreactive mucosa could be swollen in its basal condition, and it may show that mucosal congestion will be better appreciated in terms of percentage variation of thickness. To evaluate the model, we are planning to use the model, with the chosen treshold value, in a study on patients with well-known hyperreactive nasal mucosa.

CONCLUSIONS

From this study, we find that the nasal mucosa in healthy volunteers reacts in a way that makes the reactions possible to standardize. There is no congestion more than 0.4 mm up to a histamine concentration of 2 mg/ml, and there is a congestion more than 0.4 mm with concentrations over 16 mg/ml. We also find that the congestion is ipsilateral.

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REFERENCES

1. Ashan G, Drettner B, Ronge H. A new technique for measuring nasal resistance to breathing, illustrated by the effects of histamine and physical effort. Ann Acad Reg Sci Uppsala 1958; 2: 111.
2. Borum P. Nasal methacholine challenge. A test for the nasal reactivity. J Allergy Clin immunol. 1979; 63: 253-257.
3. Broms P. Rhinomanometry. Acta Otolaryngol. (Stockh) 1982; 94: 361-370.
4. Desjardin A, b e Luca S, et al. Nonspecific bronchial hyperresponsiveness to inhaled histamine and hyperventilation of dry cold air in subjects with respiratory symptoms of uncertain etiology. Am Rev Respir Dis 1988; 137: 1020.
5. Hargreave FE, Ryan G et al. Bronchial responsiveness to histamine or metacholine in asthma: Measurement and clinical significance. Eur J Respir Dis. 1982; Suppl 121: 79-88.
6. Juto J-E, Lundberg C. An optical method for determining changes in mucosa! congestion in the nose in man. Acta Otolaryngol (Stockh) 1984; 94: 149.
7. Van de Heyning PH, Van Haesendonck J et al. Histamine nasal provocation test. Allergy 1989; 44: 482-486.

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