Rhinology, 31, 53-55, 1993

Nasal hyperreactivity. A histamine provocation model*

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SUMMARY

The aim of the study was to see whether it is possible to select non-allergic persons with hyperreactivity, especially in the nose, from healthy individuals with a histamine standardization test. Another aim was to elucidate whether a so-called priming effect could be present in such a non-allergic disorder. Seven patients with a history of perennial rhinitis, expressed as either or both swelling or discharge from the nose and a negative allergic investigation, were examined on three up to seven consecutive occasions. Rhinostereometry was used to register the reaction in the mucous membrane to a solution of histamine in successively increased concentrations. The results showed a statistically significant difference between this group compared with a control group of healthy volunteers. We could not detect any increase in the sensitivity during repeated provocations.

Key words: nasal hyperreactivity, histamine provocation, rhinostereometry

INTRODUCTION

Non-allergic nasal hyperreactivity (NANH) is an increasing problem in ENT outdoor-patient service. Patients describe their symptoms and the diagnosis of NANH is therefore mainly based upon anamnestical data. The symptoms can differ between individuals, with either predominantly congestion or secretion, which divides the patients into two subgroups: "sneezers" and "blockers" (Mygind, 1986). Objective registrations to confirm the diagnosis has hitherto been hard to find; various studies give contradictory results (Malm, 1989). Lung allergologists are, already since a decade, familiar with pulmonary histamine-provocation tests, which appear to be a reliable and useful aid to diagnose and evaluate hyperreactivity.

Recently, a new measuring method was developed with which it is possible to measure changes in nasal mucosal congestion with a high accuracy level (Juto and Lundberg, 1982). With this technique it has been demonstrated that healthy individuals in nasal histamine-provocation tests have a well-reproducable mucosal congestion curve (Hallén and Juto, 1992).

The aim of this study was to see whether it is possible to demonstrate an increased mucosal sensitivity to histamine in NANH patients compared with healthy individuals.

MATERIAL AND METHODS

Seven patients (one male and six female, 16 to 65 years old) participated in the study, which was performed during autumn, 1989. They were consecutively chosen from an ENT outdoor-patient duty. They all had a history of non-allergic perennial rhinitis (NANH), three patients were "blockers" and four "sneezers". They have had daily symptoms for at least one year. Two weeks prior to entering the study medication was stopped and no current infection was tolerated. Anamnestically, they had no allergy which was ruled out with a negative standard skin prick-test ("Phazet"; Pharmacia, Sweden).

Solutions of increasing concentrations of histamine hydrochloride in normal saline containing 0.5% phenol were used. Histamine concentrations ranged from 0.1 to 32 mg/ml. The mucosal positions on the medial side of the anterior part of the concha inferior was recorded with rhinostereometry on both sides. Before the test was initiated the person was allowed to get acquainted to the test situation for 30 min. Next, the mucosal surface position on the medial side of the concha inferior in both nasal cavities was determined repeatedly during 15 min, and in this way a baseline position was established. The provocation was performed unilateral on the anterior aspect of the inferior turbinate, and the other side served as a control. The provocation started with 0.14 ml of the diluent applied within the area of observation and was then followed by application of histamine in increasing concentrations, every 10 min. Recordings of the mucosal surface positions were

* Accepted January 20, 1992

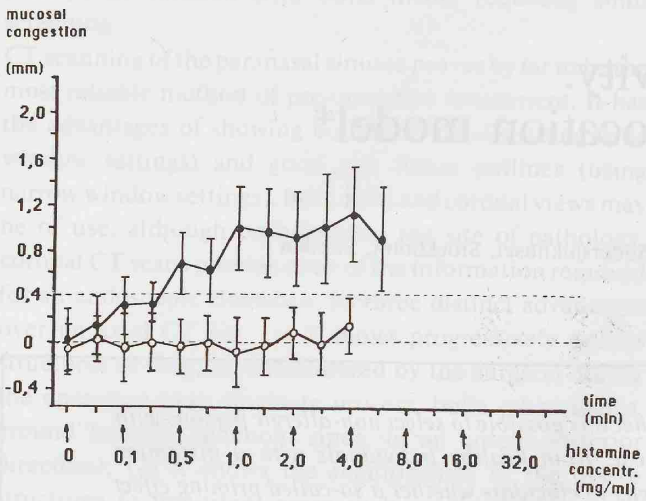

Figure 1. The mean mucosal congestion during repeated nasal provocation with histamine on seven patients with non-allergic nasal hyperreactivity. Closed circles denote the challenged side; open circles denote the unchallenged side, and arrows denote application of histamine in increasing concentrations. Error bars denote 95% confidence interval; dotted line indicates threshold level.

made, on both sides, 5 and 10 min after each dose, directly followed by the next dose of histamine. The test continued in this manner in steps using increasing histamine concentrations until the symptoms became so intense that it was considered dangerous to continue the provocation. Twenty-four to 48 h later a second, and again after 24 h, a third provocation was performed.

RESULTS

All patients were able to participate at three separate events. There were no differences ($p>0.05$) between the mucosal reaction patterns between these occasions concerning the same person. Furthermore, analysis of variance shows that it is legitimate to regard all the provocations as 21 independent observations. This is valid for both sides of the nose separately.

When diluent was applied the mean value of the mucosal congestion of the whole group on the provoked side was increased, although not significantly compared with the mucosal congestion at the start of the provocation. When the test continued the mucosal congestion increased further and on the 0.1-mg/ml provocation level it passed the threshold value of 0.4 mm ($p<0.05$; see Figure 1). This value was established in a previous investigation in healthy volunteers, where this boundary was not exceeded until the 16-mg/ml provocation level (Hallén and Juto, 1992). Most of the patients preferred to interrupt the provocation before the highest concentration was reached, because of the increasing nasal symptoms.

On the non-provoked side there was only an oscillation pattern slightly above the base-line level, well within the threshold area, during the entire provocation procedure (Figure 1).

DISCUSSION

Mucosal physiology is influenced by hormonal factors, and this is well known from clinical practice. For example, nasal mucosal congestion in pregnant women can be profound. In the aforementioned study by Hallén and Juto (1991) nasal mucosal reactivity during histamine provocation in healthy females showed a lean curve with a minimal spread, indicating a minor influence on the mucosal congestion of sex hormones in this group. An epidemiological study on nasal hyperreactivity has shown an equal sex distribution (Jessen and Janzon, 1988).

In the present study five of the hyperreactive patients were women in fertile age. The nasal reactivity of histamine showed a greater variation compared with healthy persons. This is probably primarily connected with the heterogeneous nature of the hyperreactive condition, but it cannot be neglected that hormonal influences can play a part in this.

Histamine was chosen as provocating agent because it is still considered to be the most important mediator in the specific and non-specific response. It acts on both a neuronal and mucosal level, on both vessels and glands, and mimics the biological response better than metacholine (Holzman, 1980; Borum, 1979). Clinically, histamine produces first of all an oedema in the nose, which serves our purpose since rhinostereometry measures changes in mucosal congestion. Metacholine, on the other hand, has a purely secretory response, which makes it less useful in this investigation (Borum, 1979).

Every patient, including the "sneezers", demonstrated a pronounced mucosal congestion already at the 0.1-mg/ml level and had to stop the provocation at 8 mg/ml, due to discomfort. This indicates a high sensitivity for the method. Furthermore, the study did not show any signs of increased sensitivity to histamine in the individual after repeated provocations. This is not surprising as earlier studies have come to the same conclusion (Gronborg et al., 1984).

In conclusion, the aim of the study was to see if it is possible to register an increased sensitivity to histamine in nasal provocation compared with healthy individuals. This was confirmed and makes the method suitable for objective description and further investigations of NANH patients.

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