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Localized aerosol hyperthermia in patients with nasal allergy*

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SUMMARY

A double-blind study was pe1formed to evaluate the efficacy, the safety and the usefalness of localized aerosol hyperthermia (LAH) in 57 patients with nasal allergy. We used two localized aerosol hyperthermia devices, the equipment (AH) with an insujjlated aerosol of 43°C and a placebo device (PH) with aerosol of 32°C. In the evaluation of clinical efficacy, efficacy rates were 46.4% in AH and 3.7% in PH during 2 weeks, respectively, and 53.3% in AH and 7.7% in PH during 4 weeks, respectively. There was a significant difference ($p < 0.01$) between the two treatment groups. The usefalness rates were 63.3% in AH and 7.4% in PH for patients with nasal allergy, showing a statistically significant difference ($p < 0.01$). No patients dropped out of the study due to adverse effects. These results suggest that the LAH is a ve,y useful instrument for the treatment of nasal allergy.

Key words: nasal allergy, aerosols, localized aerosol hyperthermia

INTRODUCTION

Localized aerosol hyperthermia (LAH) was designed and built by Yerushalmi et al. (1982) as the equipment with an insuffiated aerosol of distilled water at 43°C. Some clinical trials indicated that allergic or acute rhinitic symptoms were ameliorated upon evaluation of intranasal temperature. In addition, it has been postulated that fever and local hyperthermia are among the defense mechanisms against viral diseases, a viewpoint now widely accepted. Several fundamental studies investigating mucocilliary activity, blood flow, morphology, and permeability of the nasal mucosa, have been performed since 1984 in Japan (Hashimoto et al., i985; Yano et al., 1986; Ohyama et al., 1988). The purpose of this study was to assess the efficacy and usefulness of the localized hyperthermia device to the upper respiratory tract in the treatment of nasal allergy.

MATERIALS AND METHOD

Subjects

Fifty-seven patients with nasal allergy entered the trial. Thirty patients underwent active treatment (AH), and 27 patients were in the placebo group (PH). There were no significant differences between the active group and the placebo group, regarding age, sex, past history, antigens, onset and severity. The diagnosis of allergic rhinitis was based on clinical criteria, primarily positive skin tests to antigen, eosinophilia in nasal smear, immunological tests (IgE), and medical history, except for slight cases, subjects with progressive specific immunization, and children less than 10 years old. However, any subject that had a remarkable nasal disease such as nasal polyp or sinusitis, and had used antiallergic drugs, anti-histamines, steroid hormones, or globulins was exempted. In each case a full medical history was taken, including information on the duration of the disease, systemic diseases, previous treatments, and severity of present rhinitis symptoms. Physical examination included anterior rhinoscopy with special attention for the colour and swelling of the mucous membranes, type of nasal discharge, and degree of nasal obstruction. The nasal smears were examined for eosinophils and skin tests were performed according to accepted methods, and nasal provocation tests were carried out. Throughout the 4-week study period, daily cards were completed by the patients, recording the severity of nasal symptoms.

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Treatment

We have used the localized aerosol hyperthermia devices modified by Midori Anzen Co. (Tokyo, Japan) in this study. Hot humidified air emerges through two exhaust nozzles and is insuffiated into the nasal passages. The exhaust nozzles are about 2 cm from the nostrils. Temperature reversal by inhalation and exhalation must be avoided. The active hyperthermia device **(AH)** delivers an exhaust aerosol at a temperature of 43°C, and the placebo hyperthermia device **(PH)** at 32°C.

A code system was used so that neither patient nor physician knew who received active treatment and who received the **PH.** After informed consent was obtained, patients selected for the study were treated with either the active or the placebo device by 15-min insuffiations of humidified air at 43°C or 32°C, on a double-blind, randomized basis, according to the order of their admission to the clinic. Both the devices were used for patients with nasal allergy during 4 weeks, 2-3 times per week.

Clinical assessment

Assessments of results were determined at the second week and first month, based on the severity of symptoms from daily cards recorded by the patients and on findings by a local physician. The criteria of each local finding were divided and rated into four categories. Turbinate swelling was rated as: not obvious (3), moderate swelling (2), half of the middle turbinate can be observed (1), or normal (0). The colour of the nasal mucosa was categorized as: pale (3), red (2), slightly red (1), or normal (0). The amount of secretion was rated as: completely filling the nasal cavity (3), moderately (2), slight(1), or not present (0).

The data obtained from the clinical study were analyzed by a paired t-test.

RESULTS

The clinical assessments found in patients treated with **PH** show a deterioration of symptoms from baseline scores, while patients treated with **AH** showed improvement from their previous condition at the second and third clinical visits (Figure 1). This difference between the two treatment groups was significantly in favour of **LAH** for sneezing, nasal secretion, blockage, oedema of turbinates and mucus. The clinical assessment for nasal objective finding of nasal allergy is presented in Figure 2. There were significant differences between both groups with regard to the severity of swelling of the inferior turbinates ($p < 0.01$) and the colour of the nasal mucosa ($p < 0.05$) in the final four weeks, but not in two weeks. Nasal secretions decreased remarkably two and four weeks after using **AH** compared to **PH** ($p < 0.01$). The overall clinical efficacies were 46.4% **in AH** and 3.7% in **PH** at half of the treatment period, and 53.0% in AH and 7.7% in **PH,** at the end of the treatment (Table 1). Two subjects with AH reported slight nasal irritation, and one subject with PH reported increased nasal secretion. At the end of the. treatment, the clinical usefulness was 63.3% in **AH,** and 7.4% in **PH.** There were significant differences between both groups regarding the clinical usefulness for the treatment of nasal allergy ($p < 0.01$).

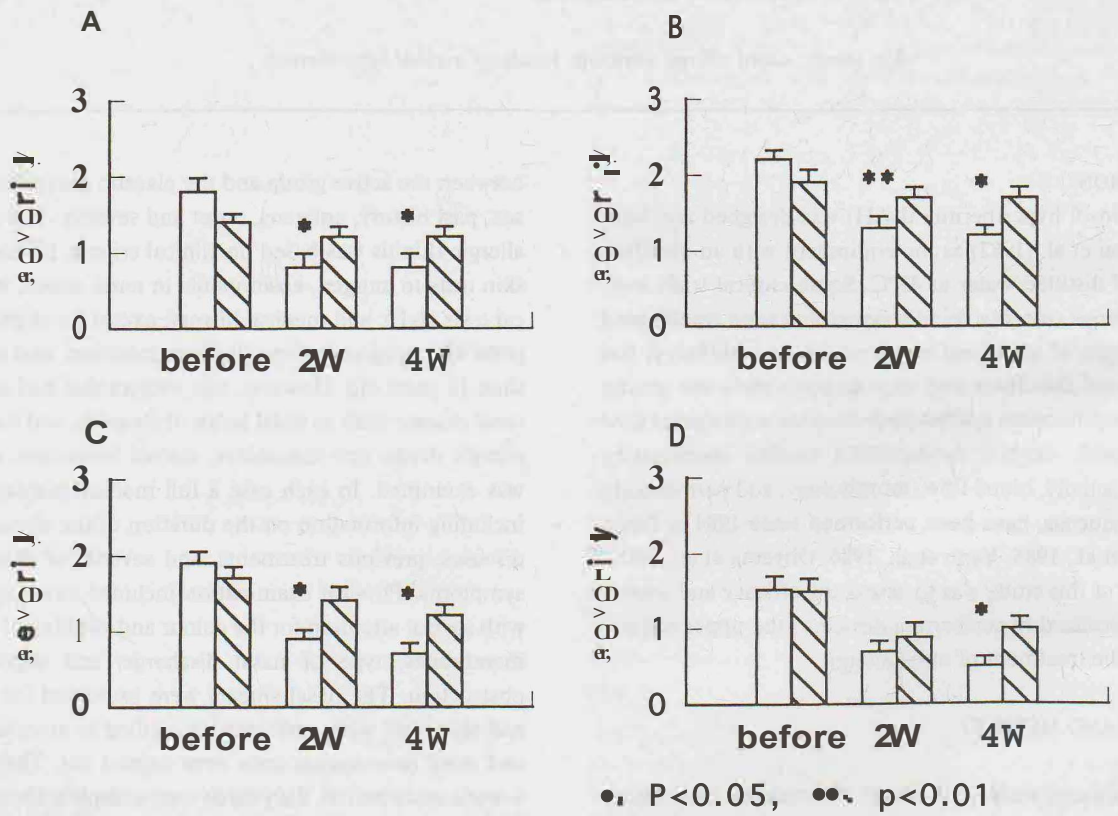

Figure 1. Clinical assessment of localized aerosol hyperthermia for nasal symptoms in patients with nasal allergy (mean± SE). Open bars: group using an active device; filled bars: group with a placebo device. A: sneezing; B: nasal secretion; C: nasal obstruction; D: disturbance of daily life.

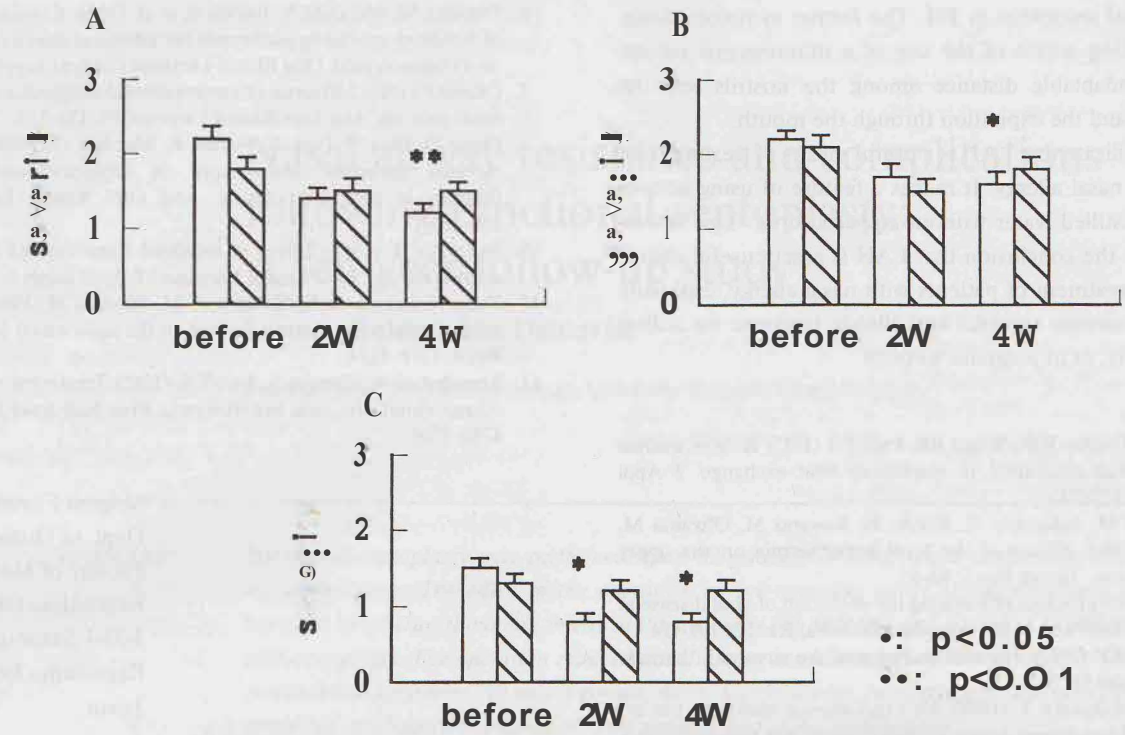

Figure 2. Clinical assessment of localized aerosol hyperthermia for the objective findings in patients with nasal allergy (mean±SE). Open bars: group using an active device; filled bars: group with a placebo device. A: swelling of turbinate; B: colour of mucosa; C: amount of secretions.

Table 1. Clinical efficacy of localized aerosol hyperthermia in patients with nasal allergy.

	2 weeks	4 weeks
hyperthermia	46.4%	53.0%
placebo	3.7%	7.7%

DISCUSSION

Some clinical trials in Europe have indicated that LAH would improve the symptoms of nasal allergy or acute-rhinitis-associated virus infections (Yerushalmi et al., 1982; Ophir et al., 1988). Increase of temperature is the consequence of a more specific response to the infected organism. The thermal inactivation of viral particles in a few hours at temperatures ranging from 37-41 °C is negligible. Temperature markedly affects the viral development (Lwoff, 1959). On the other hand, it has been shown that the anaphylactic release of histamine from guinea pig lung, rat mesentery, and human leukocytes is abolished by pre-heating the tissue or cells at 45 °C. In addition, we have reported that a reduced blood flow following the allergen provocation test was found after receiving local hyperthermia therapy for eight days. This phenomenon was presented in some patients with nasal allergy who had marked decrease of some clinical symptoms as compared with that of the initial time (Yano et al., 1986). The results indicated that LAH suppressed the release of chemical mediators from mast cells and basophils, and was effective in the allergic symptoms as the improvement of the failure of local circulation and oedema on nasal mucosa. Due to cooling produced by the air flow, the temperature of the nasal turbinates varies between 32-35 °C (McFadden, 1986). A previous study by Hashimoto et al. (1985) indicated that the temperature in the nasal airway up to the nasopharynx remained at above 43 °C, and the mean temperature on the surface of the nasal mucosa ranged from 37-38 °C during the LAH. This is why we were planning to study local hyperthermia for nasal diseases.

Yerushalmi et al. (1982) reported that 75% and 68% of patients with nasal allergy were free of symptoms one week and one month, respectively, after the treatment which consisted of one series of three 30-min insuffiations of humidified air at 43 °C with 2-h intervals. With regard to the improvement of nasal blood flow and the reduction of the sensitivity of the nasal mucosa, however, it is very important to investigate the continuity of the effects after treatment. There was a significant difference between the clinical effects of AH and PH in cases of nasal allergy. Our results agree with those obtained in Europe (Ophir et al., 1988). As there was no significant difference between the effect of LAH after two weeks, nor after four weeks, in patients with nasal allergy, its effect was obtained in an early stage after treatment.

If the homoeostasis of the nasal mucosa, the mucociliary activity or both the perfusion and permeability are disturbed by heat-induced changes, then LAH should be desirable in no case. The mucociliary activity detected by the photo-electrical method in guinea pigs, however, was not disturbed by the hyperthermic load at 43 °C *in vivo* (Hashimoto et al., 1985). Odaira and Takasaka (1988) have reported that the humidified hot-air insuffiator did not enhance the permeability of the nasal mucosa nor did it morphologically change the cell membranes in guinea pig nasal mucosa. In the present study, non-significant short-duration side effects during the treatment were noted: two patients with nasal irritation in AH, and a patient with

increased nasal secretions in PH. The former symptom disappeared by taking notice of the use of a rhinothermic device, such as an adaptable distance among the nostrils and the nozzles of it, and the expiration through the mouth.

The results indicate that LAH is a useful means of treatment for patients with nasal allergy. It makes a feature of using aerosol particles of distilled water without a special drug. This assessment leads to the conclusion that LAH is a very useful instrument in the treatment of patients with nasal allergy, especially in cases with allergic sinusitis and allergic response for a drug constitutionally, or in pregnant women.

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