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Efficacy of systemic corticosteroid treatment for anosmia with nasal and paranasal sinus disease*

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SUMMARY

Systemic administration of corticosteroids was attempted in the treatment of olfactory loss resistant to topical corticosteroid treatment in patients with nasal and paranasal disease and post-upper respiratory infection. Significant efficacy was achieved with a short course of high-dose oral corticosteroids in patients with non-allergic sinus disease. On the other hand, anosmia induced by upper respiratory infection failed to respond to systemic corticosteroid treatment, suggesting permanent damage to the olfactory receptor cell. The underlying mechanism of effectiveness observed in patients with sinus disease may be explained by improvement of the mucosal thickening of the olfactory fissure, leading to the access of an odorant to the olfactory neuroepithelium.

Key words: non-allergic sinus disease, anosmia, post-upper respiratory tract infection, corticosteroid treatment

INTRODUCTION

Major aetiological categories of olfactory loss are nasal and paranasal sinus disease, and upper viral respiratory disease (Zusho et al., 1981; Scott, 1989a; Deems et al., 1991). Although many options in the treatment of nasal and paranasal sinus disease can be considered, anosmia as a chief complaint in patients with nasal and paranasal disease may be decided to be first amenable to medical treatment. A few studies have demonstrated the effect of oral corticosteroid treatment for restoring olfactory function in nasal and paranasal sinus disease (Hotchkiss, 1956; Fein et al., 1966; Jefek et al., 1987). The action of topical corticosteroids upon olfactory dysfunction has also been reported in nasal polyps with allergic rhinitis (Brown et al., 1977; Tarlo et al., 1977; Neuman and Toshner, 1978; Scott et al., 1988). Topical application of corticosteroids to the nasal cavity is the first choice in treating olfactory dysfunction associated with nasal and paranasal disease because of minimal adverse effects. Systemic corticosteroids are administered to patients insensitive to topical application. On the other hand, it is known that restoring olfactory dysfunction following upper respiratory viral infection is difficult to achieve (Leopold et al., 1991), presumably due to permanent damage to the olfactory neuroepithelium (Jenkin et al., 1975; Deems et al., 1991).

In the present study, we have assessed the effect of systemic application of corticosteroids upon olfactory dysfunction in patients with non-allergic sinus disease and post-upper respiratory infection (post-URI), who were resistant to intranasal topical application of corticosteroids.

METHODS

Patients

Twelve patients were diagnosed as having chronic sinusitis by means of intranasal endoscopy and radiological imaging techniques (plain X-rays and/or CT scanning). Pathological lesions involved the ethmoidal sinuses in all patients. Maxillary sinus lesions were observed in four patients. There were five males and seven females, aged 19-62 (average: 44.7 years).

Olfactory loss after upper respiratory infection was seen in nine patients. These patients, four males and five females, aged 41-64 (average: 53.7 years). Patients were referred to our clinic 1-15 months (average 4.2 months) following an upper respiratory illness. Nasal endoscopy and radiological imaging techniques showed no evidence for the presence of nasal and paranasal sinus disease.

Olfactory testing

Olfactory acuity tests were performed using a T&T olfactometer (Zusho et al., 1981; Ikeda et al., 1988). The subjects were asked to smell at a strip of paper soaked with one of the five standard odorants, i.e. ß-phenyl ethylalcohol (odorant A), cyclotene

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(odorant B), isovaleric acid (odorant C), γ-undecalactone (odorant D), and scatole (odorant E). The odorants were diluted and there were eight degrees of concentration, each of which differed by a magnitude of 10. The test was successively performed from odorant A to E without olfactory fatigue. The minimum concentration at which an odorant was sensed was termed the "detection threshold". The point at which the minimum concentration of an odorant could be qualitatively judged was termed the "recognition threshold". Results were compiled in the olfactogram, in which grades -2 and 5 (ordinates) show the minimum and maximum concentrations of each odorant, respectively, except for odorant B whose maximum is 4. The detection threshold was located around grade 0, the recognition threshold around 1.

Treatment protocol

The initial treatment consisted of a topical corticosteroid, either betamethasone (n=5) or beclomethasone dipropionate (n=16) applied to the nose. A few drops of 0.1% betamethasone were applied to the superior part of the nasal cavity in a head-down position, twice a day. Beclomethasone dipropionate was applied as an aerosol in a dose of 400 mg/day. The patients shown here were not responding to topical corticosteroids.

The next option in treatment was a short course (10–14 days) of oral prednisolone starting at 40–60 mg per day with a quick taper. Throughout the corticosteroid treatment, no patients complained of adverse effects.

RESULTS

Patient 1

This 31-year-old woman developed olfactory loss in 1988 and visited our clinic on November 30, 1992. She complained of nasal discharge and postnasal drip without nasal obstruction. Nasal smears demonstrated several neutrophils per high-power field, but they did not include eosinophils. Total IgE levels and specific IgE-antibody levels, as measured by a radio-allergosorbent test ruled out allergic disease. Coronal CT views revealed evidence of bilateral partial opacification of the ethmoids and olfactory clefts.

Olfactory tests using the T&T olfactometer showed a high elevation of both detection and discrimination thresholds for odorants A and B, and no sense of smell for odorants C, D and E (Figure 1). The scores of the detection and recognition thresholds were 5.2 and 5.4, respectively.

Topical application of beclomethasone dipropionate did not result in an improvement of the patient's olfaction. The scores of the detection and recognition thresholds after 2 months on topical corticosteroid were 5.0 and 5.6, respectively. Oral administration of prednisolone (at an initial dose of 60 mg per day, tapered during the next 12 days) restored her sense of smell. The average score for detection and recognition thresholds were 0 and 0.2, respectively (Figure 2). CT scans of the nose showed that the opacification of the ethmoidal sinus had disappeared as well as improvement of olfactory cleft patency. Olfactory acuity remained normal following corticosteroid discontinuation, also after a follow-up of one year.

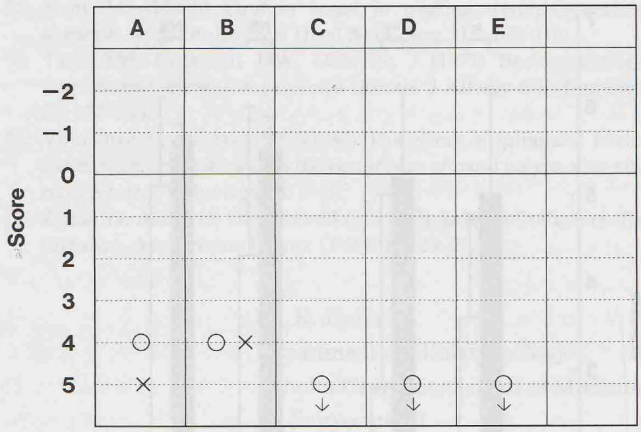

Figure 1. Olfactogram of patient 1 before treatment.

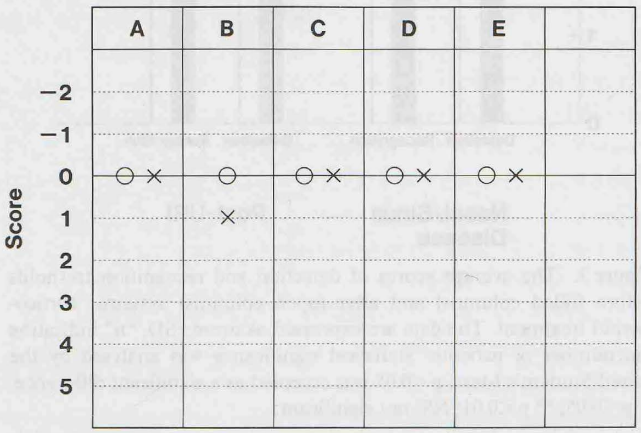

Figure 2. Olfactogram of patient 1 after systemic corticosteroid treatment.

Patient 2

This 56-year-old woman presented symptoms of an influenza-like infection, fever, malaise, and anorexia followed by upper respiratory illness in March, 1993. She began to feel a decrease in smell and nasal obstruction. A few weeks after complete recovery of the upper respiratory illness, she noted a development of anosmia. Three months later she was referred to our clinic. Endonasal fiberscopic and CT findings provided no evidence for nasal or paranasal sinus disease, nor olfactory cleft obstruction. All odorants tested were beyond detection levels. Intranasal inhalation of beclomethasone dipropionate (400 μg daily) or systemic administration of prednisolone (60 mg per day at an initial dose, tapered over a period of 12 days) failed to improve the sense of smell.

Figure 3 displays the function scores of detection and recognition thresholds for 12 patients with nasal and sinus disease and nine patients with post-URI before and after oral corticosteroid administration. Significant improvement of the scores was seen in both detection (1.4 ± 1.7; $n=12$, $p<0.05$) and recognition thresholds (2.4 ± 2.0; $n=12$, $p<0.01$) with nasal and paranasal sinus disease. In eight patients improved olfactory function lasted for a long-term follow-up of more than six months. Olfactory function was deteriorated after corticosteroid discontinuation in two patients: one required long-term corticosteroid treatment,

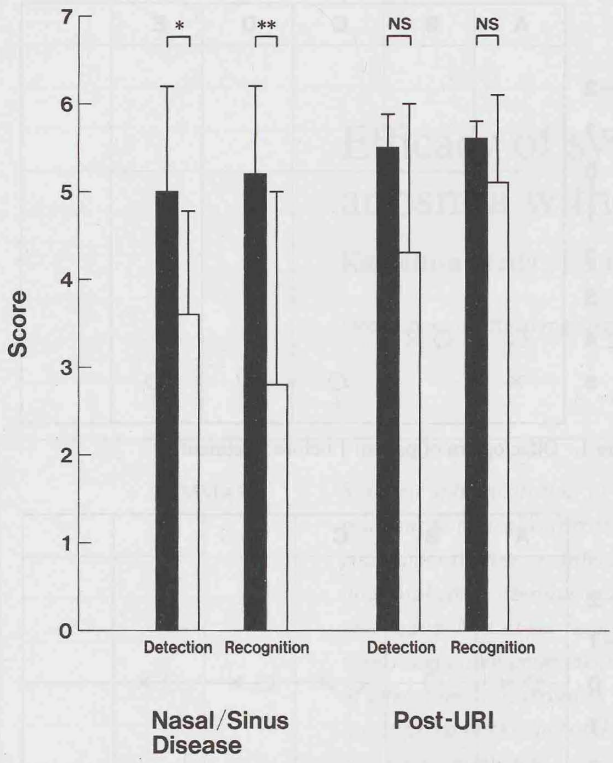

Figure 3. The average scores of detection and recognition tresholds before (filled columns) and after (open columns) systemic corticosteroid treatment. The data are expressed as mean±SD, "n" indicating the number of patients. Statistical significanse was analysed by the paired Student's t-test; $p < 0.05$ was accepted as a significant difference. *: $p < 0.05$; ** $p < 0.01$; NS: not significant.

orally and topically, and the other underwent ethmoidectomy followed by topical corticosteroids resulting in improvement of olfactory acuity. Two patients did not show satisfactory improvement, at all.

Although three patients with post-URI showed a moderate improvement in both thresholds (scores >2.0), there was no significant improvement in scores (detection threshold: 1.2±1.8; recognition threshold: 0.5±1.0) following oral corticosteroids.

DISCUSSION

The present study shows that systemic administration of corticosteroids improved olfactory acuity in patients with non-allergic sinus disease resistant to topical nasal application of corticosteroid, but not in patients with post-URI. Mygind et al. (1978) have proposed that the therapeutical effects of corticosteroids on olfactory loss were due to an anti-inflammatory action reducing tissue oedema and vasodilation. Furthermore, it has been speculated that corticosteroids have a direct effect on the olfactory epithelium (Jefek et al., 1987).

Ineffectiveness of topical corticosteroid treatment can be explained by the fact that nasal polyps and obstructive lesions in the nasal cavity may interfere with the accessibility of corticosteroids to the olfactory tissue. On the other hand, systemic application can reach the swollen nasal mucous membrane surrounding the olfactory fissure via a haematogenous route, hence the odorant can reach the olfactory neuroepithelium. In two patients the treatment was ineffective regardless of a temporary improvement with oral corticosteroid treatment. Olfactory function in one patient was maintained by low-dose oral corticosteroids combined with topical therapy; this case can be called steroid-dependent anosmia, as was advocated by Jefek et al. (1987). The other patient required surgical treatment for improvement of olfactory function with topical corticosteroid therapy. Surgical removal of ethmoidal lesions and polyps may enhance the transport of an odorant to the olfactory epithelium, and topical corticosteroids are likely to present new formation of polyps and swollen mucosa (Mygind et al., 1978; Virolainen and Puhakka, 1980; Karlsson and Rundcrantz, 1980). When patients with non-allergic chronic sinusitis chiefly complain of anosmia, we recommend the following therapeutical approach: (1) the first option is topical corticosteroid therapy, because it has minimal side effects; (2) the second option is a short-term course of systemic corticosteroid therapy; and (3) the last option is the combined therapy of corticosteroids following surgery. However, we should pay much attention to adverse effects of long-term administration of corticosteroid therapy (Scott, 1989b).

In contrast to anosmia induced by sinus disease, systemic application of corticosteroids has failed to improve the olfactory loss in patients with post-URI. In three patients olfactory function has improved following corticosteroid therapy. Experimentally induced damage of the olfactory neuroepithelium in mice has been demonstrated to improve after immediate administration of topical corticosteroids (Kimura et al., 1989). This finding may indicate that acute damage to the olfactory neuroepithelium can be reversed by corticosteroids. Therefore, the patients with improved smell function presented here may be in the reversible stage.

In conclusion, systemic administration of corticosteroids in patients with non-allergic sinus disease resulted in appropriate restoration of olfactory acuity that is resistant to topical corticosteroid treatment.

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