

The treatment of hyposmia with intranasal steroids

DAVID G. GOLDING-WOOD, MATS HOLMSTROM, YVONNE DARBY, GLENIS K. SCADDING,
VALERIE J. LUND

Abstract

Hyposmia is a neglected symptom in patients with rhinitis. We studied 25 patients presenting with perennial rhinitis. Fifteen patients expressed hyposmia as a significant symptom. University of Pennsylvania smell identification test (UPSIT) and visual analogue scales (VAS) were used to score the symptoms of hyposmia, nasal obstruction and nasal discharge before and after six weeks treatment with betamethasone sodium phosphate drops. Those patients with initial symptoms of hyposmia significantly improved their UPSIT scores ($p = 0.00009$) and their VAS scores for hyposmia ($p = 0.00133$). Despite a significant decrease in the sensation of nasal obstruction, the non-hyposmics showed no increase in UPSIT scores after betamethasone therapy. There was no clear correlation between UPSIT results and other symptom scores. The judicious use of betamethasone drops in the treatment of rhinogenic hyposmia can be recommended.

Key words: Hyposmia; Betamethasone; Rhinitis

Introduction

Perennial rhinitis is a common condition for which the symptoms most frequently voiced are nasal obstruction, and discharge. The impairment of the sense of smell may significantly raise the morbidity from rhinitis, yet it is rarely mentioned by the patient and is often overlooked by the clinician. The most prevalent cause for the loss of smell is rhinological in nature. Olfactory disturbance may reflect the extent of mucosal disease within the nasal cavity particularly within the upper part of the nose. It has therefore been suggested that the success of any treatment for rhinitis could be gauged by improvements in the sense of smell (Moore-Gillon, 1989).

Once infective causes are excluded then corticosteroids, presumably as a result of their anti-inflammatory properties, appear to improve the sense of smell in some hyposmic and anosmic patients with sinonasal disease. There is little information regarding the efficacy of oral corticosteroids in this regard, because they are seldom prescribed purely for improving smell function in view of their adverse systemic effects. Severe nasal symptoms often justify the short term use of systemic steroid therapy. High-dose corticosteroid therapy has been shown to restore the ability to smell in patients with obstructing nasal polyposis, proportional to the amount of polyp shrinkage. Such treatment may temporarily alleviate symptoms that will recur on reduction or withdrawal of steroid treatment, hence the term 'steroid-dependent anosmia' (Jafek *et al.*, 1987).

Symptomatic benefits from steroid therapy may be enhanced by combination with surgery (Fein *et al.*, 1966). The value of steroid therapy in the differential diagnosis of olfaction is apparent in distinguishing sinonasal disease from central causes.

Topical steroid therapy has a dominant position in the treatment of rhinitis. Although the sense of smell remains 'the Cinderella of the senses' it is still surprising that the effect of topical steroid treatment of the nose has rarely been systematically studied in terms of olfactory function. We have investigated the effect of intranasal betamethasone taken in the head down and forward position, among a study group of 25 patients presenting with perennial rhinitis, with particular reference to olfaction.

Materials and methods

A consecutive group of 30 adult patients, between the ages of 16 and 65, with perennial rhinitis referred to the Rhinitis clinic at our hospital, who had not been previously treated with topical nasal steroids, were offered entry into the study. Full informed consent was given by all participants. Each patient was subjected to a full history, examination and investigation by sinus X-rays and skin prick tests. Patients with either abnormal sinus X-rays (none), nasal polyps (two) or severe septal deformity (three) were excluded from the study. Two study groups were identified from their history in response to the question 'Is your sense of smell impaired?' Patients

were grouped as hyposmic and non-hyposmic accordingly.

The sense of smell was assessed by University of Pennsylvania smell identification test (UPSIT) (Doty, 1984) with 40 microencapsulated odours. After scratching and sniffing an impregnated patch, the test subject must make a forced choice from one of four options, rendering a maximum score of 40. A score between 34 and 40 is regarded as normal, 20–34 as hyposmic, less than 19 as anosmic. Since a score of 10 will be produced by random choice, scores of 0–2 may be evidence of malingering. Subjective symptom scores of hyposmia, nasal obstruction and nasal discharge were also recorded by separate visual analogue scales (VAS). All patients were asked to indicate the severity of their symptoms by intersecting a 10 cm horizontal line. The indicated position was measured, where 0 is the best possible response and 10 the worst imaginable response for each symptom.

Each patient was invited to use three drops of betamethasone sodium phosphate three times daily to each nares in the head down and forward position for six weeks. At the completion of six weeks continuous treatment each patient again performed an UPSIT test and indicated their symptom scores on VAS.

Owing to the proven consistency of the UPSIT test in terms of test/retest reliability, a control group for placebo effect was felt unnecessary. Given the possible side effects of betamethasone nose drops namely nasal soreness, epistaxis and anosmia, it was decided to choose a control group for whom the use of betamethasone nose drops could be justified.

Statistical analysis was performed by paired *t*-test to examine differences in UPSIT and symptom scores before and after treatment. Analysis by Spearman rank correlation coefficient was performed to determine any correlation between UPSIT and other symptom scores before and after treatment.

Results

A total of 25 patients, 11 men and 14 women were studied. Their ages ranged from 16 to 64 years, median 41 years. There were no patients with abnormal sinus X-rays and 22 patients had positive skin tests. There were 15 hyposmic patients (group I) with ages ranging from 22–60 years, median 50 years and 10 non-hyposmic patients (group II) with ages ranging from 16–64 years, median 36 years. There was no significant difference in age ($p = 0.181$; *t*-test), atopy or smoking habits between the two groups.

The individual results of the UPSIT and symptom scores are shown in Table I and illustrated in Figures 1 and 2. Interestingly, one patient in the hyposmic group produced a pre-treatment UPSIT score of 37 and four patients without symptoms of hyposmia scored 31 or less on UPSIT. Analysis with paired *t*-test showed that those patients with symptomatic hyposmia significantly improved their UPSIT ($p = 0.00009$) and VAS for hyposmia ($p = 0.00133$) and nasal obstruction ($p = 0.0066$) after treatment with betamethasone drops. There was no convincing improvement in either olfaction score for those without initial symptomatic hyposmia, whereas the subjective sensation of blockage did decrease ($p = 0.00334$).

The UPSIT and VAS scores for both the hyposmic and non-hyposmic group, separately and combined were contrasted in pairs and subject to Spearman rank correlation analysis. Comparison of the UPSIT scores before and after treatment for all patients gave a correlation coefficient of 0.75. Comparison of the UPSIT scores and the VAS scores for hyposmia, for all patients, shows correlation coefficients of -0.52 and -0.58 before and after treatment respectively.

Discussion

Topical steroid therapy is effective in the treatment of seasonal and perennial rhinitis and for the

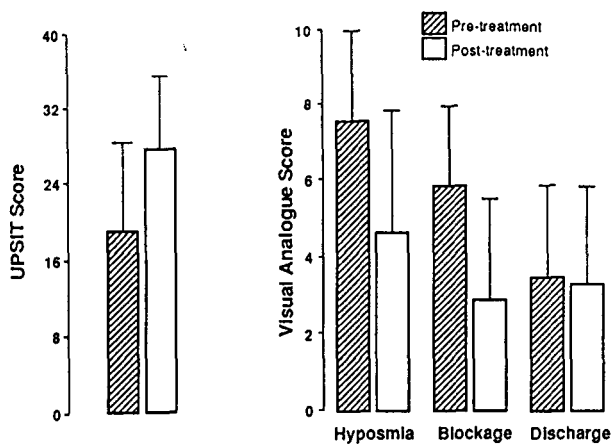


FIG. 1

Group I UPSIT and Visual analogue scores Rhinitis with hyposmia: Before and after treatment with topical nasal betamethasone. (Mean with standard deviation)

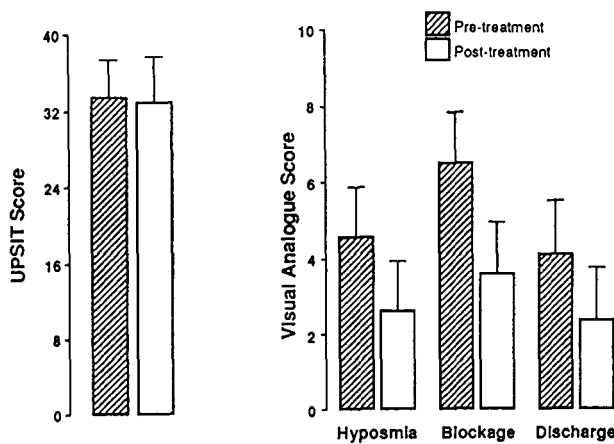


FIG. 2

Group II UPSIT and Visual analogue scores Rhinitis without hyposmia: Before and after treatment with topical nasal betamethasone. (Mean with standard deviation)

TABLE I
UPSIT AND VISUAL ANALOGUE SYMPTOM SCORES: PRE- AND POST-TOPICAL NASAL BETAMETHASONE

No.	Age	Sex	UPSIT Scores		Visual analogue symptom scores					
			Pre -	Post -	Hyposmia		Nasal obstruction		Nasal discharge	
					Pre -	Post -	Pre -	Post -	Pre -	Post -
Group I										
1	60	M	19	26	8	8.4	4.8	6.8	2.2	1.4
2	47	M	28	32	1.4	1.4	5.4	0.8	5.4	0.8
3	43	F	32	37	5.6	2.5	6	2.9	2.5	6.2
4	55	M	10	30	9.8	2.3	2.8	2.3	0.2	0.2
5	25	F	16	21	9	10	6	0	6	8
6	42	F	7	14	10	8.6	8.9	1.9	0	1.9
7	36	F	10	35	8.4	6.8	7.6	5.8	2	3.4
8	42	F	19	32	9.5	3	8.5	2	5	3
9	28	F	22	31	8	2	4	2	6	3
10	50	M	7	15	4.5	1.2	3	5.9	0.5	4.8
11	59	F	15	17	9	9.6	5.2	0	5	5.6
12	55	F	10	22	9.9	2.4	9	0	2.1	0
13	39	M	26	31	8	5.2	6.5	5.5	6	3.2
14	22	F	37	39	8	1.2	7.1	0.3	7	1.2
15	52	M	26	30	4.8	4.8	2.6	7.2	2.5	7
Mean			18.93	27.47	7.59	4.63	5.83	2.89	3.49	3.31
Standard deviation			9.4	7.93	2.46	3.24	2.15	2.64	2.38	2.52
Paired <i>t</i> -test (<i>p</i>) value			0.00009		0.00133		0.0066		0.415	
Group II										
20	64	M	37	36	8.2	2.2	4.7	0.5	4.7	0.5
21	34	M	35	38	7	1.4	8	5.5	8	5.9
22	23	F	37	34	6.9	0	7.8	5	0	0
23	34	M	27	26	5	6.2	4.3	5.4	2	1
24	36	F	37	39	1	0	4	1	6	1
25	16	M	31	30	8.5	5.5	8.9	3.8	6.5	4
26	50	M	35	32	0	1.8	9.4	5.5	0	1.6
27	38	F	30	26	0.7	4.3	7.3	0.3	0.5	0.5
28	42	F	28	29	7	2	7	4	7	6
29	32	F	37	38	1	2.5	3.2	4.8	6	3
Mean			33.4	32.8	4.53	2.59	6.46	3.58	4.07	2.35
Standard deviation			4.01	4.94	3.45	2.19	2.22	2.14	3.13	2.25
Paired <i>t</i> -test (<i>p</i>) value			0.217		0.072		0.00334		0.0128	

postsurgical recurrence of nasal polyps (Mackay, 1989). While the detrimental effects of parenteral steroid therapy are widely recognized, there are no detrimental changes in the nasal mucosa or adverse systemic effects from topical nasal steroid application, supporting the safety of long-term use (Holopainen *et al.*, 1982). There is no evidence to support any vasoconstrictor action or alteration in mucociliary transport within the nose from the use of topical nasal steroids (budesonide) (Lindqvist *et al.*, 1989). It is interesting that betamethasone is ciliotoxic *in vitro* yet has no adverse effect *in vivo* (Stanley *et al.*, 1985).

While the distribution of aerosol within the nose has been shown to be limited (Mygind and Vesterhauge, 1978), it is likely that nose drops will achieve a greater distribution to the affected mucosa, especially when the head down and forward position is used (Chalton *et al.*, 1985). The recommended bilateral dosage of betamethasone sodium phosphate three drops three times daily is estimated as equivalent to 3.36 mg of prednisolone (Mackay, 1989). Uncertainty remains as to the mode of action of such a dose, whether this is purely topical or whether there is a systemic effect. While no adverse systemic effects have been shown at these recommended doses, the excessive use of topical steroids may result in adrenal suppression (Flynn *et al.*, 1992) or even Cushing's syndrome (Stevens, 1988).

Among studies for patients with the treatment of rhinitic symptoms with topical steroids there are incidental findings regarding hyposmia. Small numbers of patients with perennial rhinitis treated with beclomethasone dipropionate (BDP), recover their sense of smell after absences of several years (Brown *et al.*, 1977). Similarly, the treatment of olfactory disturbance with corticosteroid nosedrops is reportedly successful in over 68 per cent of 1376 patients (Fukushima, 1978) and 70 per cent of 1400 patients with hyposmia from sinonasal disease (Zusho *et al.*, 1981). Limited details regarding the assessment of olfaction are provided in all these reports which seem to relate to the patients' subjective judgement. These studies point to a limited effectiveness for steroid aerosols, which led us to the use of steroid drops for this study.

The apparent difference in efficacy between topical and oral steroids is not readily understood. Several weeks of treatment are required before one can dismiss topical agents as being ineffective. The limited effectiveness of topical steroids may result from substantial mucosal swelling in the upper nasal cavity that impedes the delivery of topical steroids. The success rate with topical steroids might be improved by a preliminary short course of oral steroids (Brown *et al.*, 1977). Even with an adequate course of treatment, the restoration of normal olfaction cannot be predicted.

While the only objective measure of olfactory capability is cortical olfactometry, the UPSIT test has proven both reliable and reproducible as a simple clinical test of olfaction. In our study there was a convincing improvement in olfactory capability in those with impaired perception of smell when assessed by UPSIT scores. The UPSIT test is shown to have excellent short ($r = 0.95$) and long-term ($r = 0.92$) test/retest reliability, as such the effectiveness and reproducibility of the UPSIT test in clinical use is proven (Doty, 1985). These facts help support the universal improvement in olfaction, as measured by UPSIT, among our study group as a true observation.

Visual analogue scales have proved a useful technique for the measurement of subjective experience. They are described as being particularly suitable for the measurement of change and the observation of its significance (Zealley and Aitken, 1969). They appear more useful for within subject comparisons than those between subjects and therefore of limited statistical value as a comparative index (Nicolson, 1978). The applications, advantages and limitations of visual analogue scales are effectively reviewed by McCormack *et al.* (1988).

Unfortunately there is no convincing correlation between nasal symptoms among individuals to allow group comparisons for their VAS scores. All of our patients with initial hyposmia showed improvement of their UPSIT scores after steroid treatment whereas five of these patients indicated worse symptom scores when measured by visual analogue scales. The limited correlation between any of the symptom groups may reflect the inherent difficulties of comparison of VAS scores between individuals or the small number of subjects in our study.

A cautionary note must be sounded about the use of betamethasone especially when combined with neomycin. The use of either preparation may rarely produce anosmia, which might be attributable to the preservative in the preparation (Whittet *et al.*, 1991).

Chemosensory dysfunctions are nagging problems that can reduce the enjoyment and quality of life. They are of considerable importance to those who have them. While we would not claim universal benefit from topical steroid therapy for impaired olfaction, hyposmia is an important symptom in perennial rhinitis which may be substantially improved with appropriate topical steroid therapy.

Acknowledgements

We wish to thank Jill Richardson-Jones for the illustrations and Dr T. Nakashima for his translation of the Japanese references.

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Address for correspondence:
Mr D. G. Golding-Wood, F.R.C.S.,
The Department of ENT and Head and Neck Surgery,
Farnborough Hospital,
Farnborough Common,
Orpington,
Kent, BR6 8ND.