

Evaluation of Flunisolide Nasal Solution in the Symptomatic Treatment of Perennial Rhinitis

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The effectiveness of a topical steroid, flunisolide, was evaluated in patients with perennial rhinitis. Thirty-four patients went through a double-blind cross-over study, comparing flunisolide 200 µg per day with placebo. The symptoms were assessed over two treatment periods each of 4 weeks, with a 2 weeks' washout period in between. There was a statistically significant difference in favour of flunisolide. About half of the patients complained of mild initial irritation from both active drug and placebo.

Keywords: flunisolide; nasal spray; perennial rhinitis.

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The treatment of perennial rhinitis with antihistamines and decongestants is often unsatisfactory. The antihistamines often cause side effects such as sedation and/or dryness of the mouth and other mucous membranes, troublesome enough to warrant withdrawing the drug. Long-term use of decongestant nose drops are not recommended because of the danger of secondary hyperaemia and tachyphylaxis. Corticosteroids have long been known to be highly effective in allergic rhinitis. The severe side effects of injectable and oral corticosteroids preclude widespread use, however. When used topically, the corticosteroids can achieve the same therapeutic effect with smaller doses, and therefore less risk for untoward systemic effects. There are, however, some reports concerning side effects of dexamethasone nasal spray (2, 9). Topical treatment using different corticosteroids has been performed for several years. The effect is usually very good (1, 6, 7, 9, 10). Besides the systemic side effects, irritation in the nasal mucosa is reported (12). The purpose of this investigation has been to assess the efficacy and clinical tolerance of flunisolide nasal spray in perennial rhinitis as it occurs in a Norwegian setting.

MATERIAL AND METHODS

Thirty-four patients of either sex suffering from perennial rhinitis were included in the trial (Table 1). Patients who were pregnant, who were suffering from nasal obstruction due to nasal polyps, or who were taking corticosteroids by oral or systemic routes were excluded from the trial. Before entrance to the study, the patients went through a routine ENT-examination.

The trial was designed as a double-blind cross-over study comparing flunisolide with placebo treatment. The patients were randomly allocated to two groups. Prior to treatment there was a 2 weeks' baseline period. During a first period of 4 weeks, one group received flunisolide and the other group received placebo. After a 2-week washout period, the groups were switched and the patients were given the alternate nasal spray for another 4-week test period.

The active agent contained an aqueous solution of 0.025% flunisolide with 20% propylene glycol and 15% polyethylene glycol. The placebo consisted of the vehicle alone in an identical bottle. The trial medication was delivered to the

Table 1
Patient characteristics

Variable		
Age (years)	mean	32.5
	range	16-76
Sex	male	14
	female	20
Duration of disease in years	mean	5.9
	range	1-20
Symptom severity	severe	9
	moderate	24
	slight	1
	house dust/mite	7
Prick test positive to	animals	2
	feather	1
	Cladosporium	1
	tree pollen	2
Allergic disease in close family		9
Negative test, as well as family history		12

nasal membranes as a coarse droplet spray by a metered pump spray device. When primed this device delivers approximately 25 µg of flunisolide per activation. The patients were instructed to administer two sprays into each nostril twice a day during the two test periods. This was equivalent to a dose of 200 µg flunisolide each day.

During the entire trial the patients recorded in a diary card the daily overall severity of their nasal symptoms, graded as: questionable = 0,

slight = 1, moderate = 2, or severe = 3. The patients were examined on admission, and at the end of each 4-week treatment period. The severity of sneezing, running nose, nose blowing and postnasal drip was elicited by direct questioning, and recorded as: none = 0, minor = 1, slight = 2, moderate = 3, or severe = 4. The condition of the nasal mucosa as well as the type and quantity of nasal secretions were noted at each visit.

Variables measured on an interval or ratio scale, such as duration of disease, were analysed by the Student's *t*-test, whereas variables measured on an ordinal scale, such as symptom scores were analysed by Wilcoxon matched-pairs signed-rank test, being arranged according to a nominal scale, by the McNemar test for the significance of changes. Two-tailed tests were used, and 5% significance limit was chosen as suitable for the purpose of the trial.

RESULTS

The results of the trial are presented in Tables 2-7. There were no adverse changes seen in the nasal mucosa during the trial. There was a significant reduction in the occurrence of swelling and redness of the nasal mucosa during treatment with flunisolide (Tables 4, 5). The judgement of the patients was in favour of flunisolide (Table 6).

The side effects registered were mainly nasal irritation of a mild degree, and of short duration. Three patients found it to be very troublesome, one in the flunisolide period, and two in the placebo period.

Table 2
Mean total symptom scores per treatment period. Mean + SD

Symptom	Observation period and score			Probability		
	Baseline	Flunisolide	Placebo	F-B	F-P	P-B
Sneezing	0.9 ± 1.0	0.5 ± 0.7	0.9 ± 1.0	0.04	0.08	0.94
Stuffiness	1.5 ± 1.1	0.8 ± 1.0	1.4 ± 1.0	0.04	0.04	0.86
Runny nose	1.4 ± 1.0	0.6 ± 0.8	1.2 ± 0.9	0.008	0.02	0.64
Nose blowing	0.6 ± 1.0	0.7 ± 0.8	1.3 ± 0.9	0.0002	0.01	0.46
Postnasal drip	0.6 ± 1.0	0.3 ± 0.6	0.8 ± 1.0	0.16	0.06	0.56

Score: 0 = none, 1 = minor, 2 = slight, 3 = moderate, 4 = severe.

Table 3
Appearance of nasal secretions

Quality	Observation period		
	Baseline	Flunisolide	Placebo
None	5	21	5
Clear watery	26	10	24
Opalescent	3	2	4
Gross purulent	0	1	1

$P = 0.012$ (F-B); 0.016 (F-P); 0.66 (P-B).

Table 4
Swelling of nasal mucosa

Condition	Observation period		
	Baseline	Flunisolide	Placebo
Normal	1	7	3
Oedematous	17	11	15

$P = 0.04$ (F-B); 0.28 (F-P); 0.6 (P-B).

Table 5
Rubor of nasal mucosa

Aspect	Observation period		
	Baseline	Flunisolide	Placebo
Normal	11	6	9
Red	7	12	9

$P = 0.08$ (F-B); 0.24 (F-P); 0.6 (P-B).

Table 6
Patients' evaluation of effect of nasal spray

Symptom control	Treatment	
	Flunisolide	Placebo
Worsening	2	3
No benefit	10	19
Minor control	5	4
Substantial control	12	7
Total control	5	1

$P = 0.02$.

The patient with "total control" of symptoms using placebo had during the placebo period been elsewhere, with no symptoms before the period began, and in fact preferred the flunisolide period.

Table 7
Summary of side effects

Side effects	Flunisolide	Placebo
Nasal irritation	13	16
Nose bleed	5	1
Nasal dryness	1	1
Increased sneezing	0	1
Sore/dry throat	1	1
Others	2	4

Others include: headache, nausea, tiredness, skin rash, loss of smell and taste.

Table 8
Evaluation of effect in accordance with type of rhinitis

Type	Total No.	Effect No.	Degree of effect		
			Total	Substantial	Minor
Allergic	22	14	4	8	2
Vasomotor	12	6	0	3	3

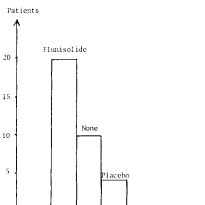


Fig. 1. Preference at end of study.
 $P = 0.001$.

DISCUSSION

Flunisolide is a synthetic fluorinated adrenocortical steroid with potent antiinflammatory activity. It has been found active in patients with perennial rhinitis (3).

In this trial it was found to be significantly more effective than placebo when administered in a nasal spray at a dose of 100 µg twice a day to patients suffering from perennial rhinitis.

The nasal irritation observed in a relatively high number of patients, is probably due to the vehicle. However, most of the patients thought it to be negligible, and none of them stopped the treatment because of the irritation.

There was a relatively high number of nose bleeds, mainly in the flunisolide group. This is reported by some (4, 5, 7) while others did not find it (1, 10). The bleeding was, however, mild, and in no cases did the treatment have to be stopped.

Some authors (1, 4, 6, 8) report slightly more favourable response rates to nasal corticosteroids in patients with higher indicators of allergic state. This trial also seems to support this (Table 8); however, the figures are too small to permit statistical analysis. The conclusion is that flunisolide is effective in patients with allergic perennial rhinitis as well as vasomotor rhinitis.

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