Flunisolide nasal spray in the treatment of perennial rhinitis

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Summary
Twenty patients with perennial rhinitis took part in a double-blind, randomized, cross-over comparison of flunisolide nasal spray (Syntaris; Syntex) and placebo (its vehicle). The sprays were used twice daily for 4 weeks and a total daily dose of 200 μg flunisolide was used. Flunisolide was superior to the placebo in relieving sneezing, runny nose and nose-blowing ($P < 0.05$). Patient and doctor treatment preferences were significantly in favour of the active spray. Side-effects were mainly confined to nasal irritation and occurred equally in both treatment groups.

Flunisolide nasal spray (Syntaris; Syntex) has been shown to be an effective treatment for perennial rhinitis in the UK and the USA. It has been found to be superior to placebo and as effective as beclomethasone dipropionate. Flunisolide nasal spray is also effective in seasonal allergic rhinitis and has been shown to be superior to sodium cromoglycate. Flunisolide has proved both safe and effective in long-term use. However, it cannot be assumed that the response to flunisolide will be the same world-wide, since exposure to allergens may differ. This trial was set up to study the effect of flunisolide nasal spray on perennial rhinitis in South African patients.

Patients and methods
The study was a double-blind, cross-over comparison of flunisolide nasal spray and placebo (its vehicle). Twenty patients (7 men and 13 women) with perennial rhinitis of at least 2 years' duration were randomly allocated to the two treatment groups. Their ages ranged from 14 to 51 years (mean 28 years). Patients with bronchial asthma were permitted to enter the trial provided their condition had reached a stable state. Nasal sprays of corticosteroids or sodium cromoglycate were discontinued 1 week before the start of the trial. Each preparation was administered for 4 weeks. The dose of flunisolide was two 0.1 ml puffs of a 0.025% solution into each nostril twice daily (total daily dose 200 μg), delivered by a metered pump. The placebo was administered in an identical manner.

Patients were assessed at the admission visit and at the end of each treatment period (0, 4 and 8 weeks). Assessments were made of the incidence and degree of sneezing, stuffiness, nose-blowing, postnasal drip and epistaxis (none, mild, moderate or severe), and patients were asked whether their symptoms interfered with daily routine and sleep. An examination of the nasal mucosa and secretions was carried out.

After each treatment the physician assessed the degree to which symptoms had been controlled and at the end of the study doctor and patient indicated which spray, if either, had been the most effective.

Side-effects were elicited at each follow-up visit by an indirect question: 'Is this inhaler suitng you?'.

Results
Of the 20 patients 11 received flunisolide and then placebo sprays (group I) and 9 received placebo and then flunisolide sprays (group II).

All patients had perennial rhinitis, the mean duration of which was 11.5 years in group I and 19.9 years in group II ($P = 0.028$, Mann-Whitney U test). Symptoms were graded overall as moderate or severe in all but 1 patient. Skin tests produced a positive reaction in 18 out of 19 patients and 14 patients had a family history of allergy. Eight patients also suffered from bronchial asthma.

Symptoms
The mean changes in symptom scores are shown in Table I. The scores for sneezing, runny nose and stuffiness were significantly reduced from admission values by flunisolide in both groups, and for runny nose and sneezing the changes produced by flunisolide were significantly greater than those on placebo ($P < 0.05$, Mann-Whitney U test).

The difference between flunisolide and placebo as regards their effect on nose-blowing was also significant, and both sprays significantly reduced the effect of symptoms on daily routine and sleep. Overall relief of symptoms was graded good or total by 14 patients on flunisolide treatment compared with 9 on placebo. Six patients on placebo reported no benefit at all from the spray, while all patients using the active spray reported some benefit. A direct comparison of the sprays at the end of the study (Table II) showed a significant preference by both doctor and patients for the flunisolide spray.

Examination of the nasal mucosa showed no significant changes, but there was a trend for nasal secretions to return to normal with both preparations.

Side-effects and withdrawals
There was no difference in the incidence of side-effects between the flunisolide and placebo sprays: 14 patients using the active spray and 13 using the placebo reported nasal irritation. Other side-effects were few. One patient withdrew from the study while using the active spray because of absence of symptoms and nasal irritation.

Discussion
The results of this study show a clear difference between the flunisolide and placebo sprays. However, the number of patients
TABLE I. CHANGES IN SYMPTOM SCORES (MEAN ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Group I (N = 11)</th>
<th>Group II (N = 9)</th>
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<tbody>
<tr>
<td></td>
<td>Flunisolide (4 weeks)</td>
<td>Placebo (8 weeks)</td>
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<tr>
<td>Sneezing</td>
<td>2.18 ± 1.17</td>
<td>-1.45 ± 1.13**</td>
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<tr>
<td>Stiffness</td>
<td>2.73 ± 0.47</td>
<td>-1.36 ± 0.92**</td>
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<tr>
<td>Runny nose</td>
<td>2.45 ± 0.82</td>
<td>-1.91 ± 1.30**</td>
</tr>
<tr>
<td>Nose-blowing</td>
<td>2.27 ± 0.90</td>
<td>-1.27 ± 1.35*</td>
</tr>
<tr>
<td>Postnasal drip</td>
<td>2.00 ± 1.26</td>
<td>-1.60 ± 1.07**</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>0.20 ± 0.42</td>
<td>0.00 ± 0.67</td>
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Scores: 0 = none, 1 = mild, 2 = moderate, 3 = severe.
Change from admission — Wilcoxon signed rank test:
*P < 0.05
**P < 0.01
†Pooled test of flunisolide v. placebo — Mann-Whitney U test.
‡Baseline significantly different.

TABLE II. TREATMENT PREFERENCE†

<table>
<thead>
<tr>
<th></th>
<th>Flunisolide</th>
<th>Neither</th>
<th>Placebo</th>
<th>Physician</th>
<th>Patients</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>14</td>
<td>2</td>
<td>1</td>
<td>14</td>
<td>2</td>
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<tr>
<td>P value</td>
<td>0.001</td>
<td>0.013</td>
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"The physician made no choice in 3 cases and 1 patient did not complete the trial.

was small, and a larger series of patients should be investigated under South African conditions, which would permit a more significant statistical analysis.

Treatment with placebo produced significant beneficial effects on the symptoms of sneezing, stuffiness and runny nose in the group using the placebo after the active spray; some of the benefit of the 4 weeks' treatment with flunisolide may have persisted into the placebo period. However, overall flunisolide spray was significantly better than the placebo spray in relieving sneezing, runny nose and nose-blowing. The difference between the active and placebo sprays in relieving stuffiness was not significant, mainly because of the considerable placebo effect in the group using placebo after the active spray. Side-effects, mostly confined to nasal irritation, were reported frequently and equally with active and vehicle sprays.

In conclusion, this South African study confirms the finding in other parts of the world that flunisolide is an effective treatment for perennial rhinitis.

REFERENCES