THE JOURNAL OF INTERNATIONAL MEDICAL RESEARCH

VOLUME 14 No 1 1986

International Editorial Board

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All editorial correspondence should be addressed to Dr J Eric Murphy, Editor-in Chief, The Journal of International Medical Research, Editorial Office, 435/437 Wellingborough Road, Northampton NN1 4EZ, England.

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0300-0605/86 $2·00

J Int Med Res (1986) **14,** 35

Treatment of Seasonal Allergic Rhinitis with Flunisolide and Terfenadine

C I Backhouse, MB, BChir, DObst, RCOG, V P Finnamore, BM, BCh, DRCOG and C W Gosden, MB, BS, *The Surgery, Kingston Avenue, East Horsley, Surrey, KT24 6QT, England*

A study of ninety-nine hay fever sufferers was conducted to compare the effect of treatment with flunisolide nasal spray plus terfenadine tablets with that of terfenadine alone. The study was carried out over an 11-week period, which covered the pollen season between May and August. All patients received 60 mg terfenadine twice daily and one group, of forty-nine patients, also received 50 mcg flunisolide to each nostril twice daily.

Clinical assessments of nasal and ocular symptoms were made at admission and following 3, 7 and 11 weeks' treatment. An over-all evaluation of treatment effect was performed at each follow-up visit and nasal examination was carried out. Patients also completed diary cards daily.

Both treatments were effective in reducing symptom severity, in comparison with previous seasons, but the combination treatment gave consistently better symptom relief. Statistically significant differences were detected in favour of the combined treatments group for nasal symptoms. Eye symptoms were found to be relieved to a comparable degree by both treatments. Results from daily patient self-assessments were consistent with these findings.

The over-all evaluations by both patients and doctors were significantly in favour of flunisolide plus terfenadine.

In conclusion, treatment of hay fever with flunisolide in addition to terfenadine was significantly more effective than treatment with the antihistamine alone.

Introduction

Antihistamine compounds and mast cell inhibitors, such as sodium cromoglycate, are long-established treatments for seasonal allergic rhinitis. Topical steroid preparations have since been introduced and flunisolide is one such compound, being a potent corticosteroid. Its efficacy in the treatment of hay fever in general practice has been shown (Backhouse 1979). Superior efficacy to sodium cromoglycate has been demonstrated (Brown, Engler & English 1981) as has comparable efficacy with beclomethasone dipropionate (Langrick 1984).

Very few direct comparisons have been made between topical corticosteroids and antihistamines, and indeed these two forms of treatment are often prescribed together, possibly because of their different modes of action.

There is little information available on the combined use of topical and systemic

treatments in the control of hay fever symptoms and so it was of interest to compare the effect of terfenadine alone with that of flunisolide and terfenadine. Terfenadine has been chosen because of its reported lack of sedative effect (Backhouse *et al* 1982), this being the major drawback to antihistamine therapy.

The aim of the study was to compare the efficacy of flunisolide plus terfenadine with that of terfenadine alone in relieving symptoms of hay fever. The incidences of side-effects in the two treatment groups were also compared.

Patients and Methods

The study was of single-blind, parallel design with ninety-nine patients being randomly allocated to receive either terfenadine alone (T) or terfenadine plus flunisolide (T + F). The dosages were 60 mg terfenadine twice daily and two 25 mcg sprays flunisolide to each nostril twice daily. Treatment was started before the onset of the pollen season and continued for 11 weeks.

Patients gave verbal informed consent to enter the study and ethical approval was obtained. The study conformed with the Declaration of Helsinki.

Patients were aged thirteen to sixty-five years and had at least a 2-year history of moderate to severe seasonal allergic rhinitis. Patients were excluded from the study if they were pregnant or lactating, if they had a respiratory tract infection or nasal abnormalities causing obstruction. Also excluded were those who had received systemic steroid therapy within the previous 3 months or any anti-allergic treatment within the previous 2 weeks.

Patient history was taken at admission and the usual severity of hay fever symptoms, in previous years, was established. At subsequent assessments, after 3, 7 and 11 weeks, the severity of individual symptoms was recorded and an examination of the nasal mucosa was made. Sneezing and nose blowing were rated as never/seldom (=1), infrequent (=2), frequent (=3) or very frequent (=4). Runny nose, stuffy nose and ocular symptoms were rated as none (=1), mild (=2), moderate (=3) or severe (=4). At each visit an over-all assessment was made, rating the effect of treatment as excellent, good, poor, none or symptoms worse.

In addition to the assessment visits, patients completed a daily record of the severity of sneezing, runny nose, blocked nose and eye symptoms.

Non-parametric statistical tests were used to analyze the data. Within-group comparisons were made of assessment data with both admission and usual severity scores. Between-group differences were examined for each assessment as well as the changes from admission and from usual severity. Symptom scores from diary card data were also compared.

Results

Forty-nine patients were allocated to the T + F group and fifty to the T group and the groups were well balanced in terms of age, sex, diagnosis and disease history (see Table 1). Patients had, in previous seasons, been treated with a variety of topical and systemic anti-allergic treatments.

Seventy-five patients remained in the study for the full 11 weeks. Seventeen patients withdrew from the T group; reasons for this were poor symptom control (10), headaches (1), pregnancy (1), glandular fever (1), lack of symptoms (2), personal reasons (1), lost to follow-up (1). Five patients from the T + F group withdrew because of poor symptom control (2), personal reasons (2) and leaving the country (1). There was a significant difference between the groups with respect to the total numbers of patients withdrawing ($p < 0.005$) and this was largely accounted for by the patients who withdrew because of inadequate symptom control. Twenty per cent of patients withdrew, for this reason, from the terfenadine group and 4% from the T + F group ($p = 0.015$).

Local pollen counts, recorded for a 6-week period during June and July, indicated that substantial amounts of pollen were released during this time. This period coincided with weeks 3 to 9 of the study. Pollen counts are shown in Figures 1–4.

Table 2 shows the mean symptom scores at each assessment and the significances of the differences between the treatment groups, both on direct comparison and when change from admission and usual severity are considered.

Table 1

Admission characteristics

	Treatment Group	
	T	*T + F*
n	50	49
Males	23	28
Females	27	21
Mean age ± s.d. (years)	35·0 ± 11·0	35·0 ± 14·3
Mean duration of disease ± s.d. (years)	17·0 ± 9·7	18·5 ± 11·9
Seasonal rhinitis	41	40
Seasonal/perennial rhinitis	9	9
Skin test – positive	15	18
– not known	35	31
Asthma	10	11
Dermatitis	5	8
No other known allergy	35	31
Usual symptom severity Mean score ± s.d.		
– sneezing	3·1 ± 0·7	3·1 ± 0·7
– nose blowing	3·2 ± 0·6	3·2 ± 0·6
– runny nose	2·9 ± 0·8	3·1 ± 0·6
– stuffy nose	2·6 ± 0·9	2·9 ± 1·0
– eye symptoms	3·2 ± 0·7	3·4 ± 0·7

All symptoms were at their most severe at week 7, when the pollen level was high. Symptoms were less severe on all occasions in patients in the T + F group and these differences were statistically significant for all nasal symptoms, except for runny nose and stuffy nose at week 11. Differences between the groups with respect to changes from usual severity were significant in most instances, indicating that the combined treatment was more effective than terfenadine alone in reducing the degree of allergic reaction normally experienced.

The over-all response to treatment, as assessed by both the doctor and the patient was statistically significantly greater in the T + F group at all three follow-ups. At week 7, a good or excellent response was achieved by 96% patients in the T + F group as compared to 62% in the T group ($p = 0{\cdot}001$).

Figures 1-4 show the daily severities of symptoms as assessed by the patients. Symptoms were consistently worse for patients in the T group and the difference between the groups was greatest between days 20 to 50, (i.e. when the pollen levels rose). There was less worsening of symptoms compared to baseline with regard to all symptoms for the T + F group, although this effect was more pronounced for nasal symptoms.

Similar numbers of side-effects were reported in each treatment group. The most commonly reported reaction in the T + F group was nasal irritation (ten patients), while drowsiness was most frequently reported in the T group (nine patients). Nausea was also reported five times in the latter group. Other side-effects in both groups were those that could be expected with antihistamine therapy. Details of side-effects are given in Table 3.

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