ORIGINAL RESEARCH ARTICLE

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Evaluation of Fluticasone Propionate Aqueous Nasal Spray Taken Alone and in Combination with Cetirizine in the Prophylactic Treatment of Seasonal Allergic Rhinitis

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Summary

This was a multicentre, double-blind study in 454 patients to compare the effectiveness and tolerability of fluticasone propionate nasal spray (FPANS) 200μg used once daily for 8 weeks on its own or in combination with oral cetirizine 10mg once daily in the treatment of seasonal allergic rhinitis. The results showed no significant difference between treatments in any of the symptoms or in the proportion of symptom-free days. Watery eyes were recorded as being the most troublesome symptom in the previous hayfever season, whilst during the study patients were, on average, free of eye symptoms for 56% of the time. Additionally, no difference was detected between the two groups with regard to the use of rescue medication. More than 75% of patients concluded at the end of the study that their symptoms had been adequately controlled and, similarly, investigators rated both treatments as being successful for the majority of patients. Overall, this study suggests that there is no significant difference in efficacy between FPANS 200μg, taken once daily in the morning, and FPANS 200μg once daily in combination with oral cetirizine 10mg, in the prophylactic treatment of seasonal allergic rhinitis.

Seasonal allergic rhinitis (SAR), defined as a noninfectious inflammatory reaction of the nasal mucosa to allergens such as pollen from grasses and trees, clinically presents with symptoms ranging from uncomfortable nasal congestion, chronic or recurrent sneezing and rhinorrhoea, to headache and cough. Additionally, some patients complain of nasal itching, eye irritation, and wheeziness (seasonal allergic asthma).[1,2] The pathogenesis of seasonal allergic rhinitis is believed to involve immediate type 1 allergic reactions with diagnosis confirmed by the 'skin prick test' if necessary.

The prevalence of the condition in the UK population ranges from 10 to 15%, with the incidence apparently increasing, possibly due to pollution.[3] The hayfever season in the UK starts in about March (tree pollination), continues through June and July (grass pollination), and ends in August after weed pollination, although some sensitivity to mould spores can occur in August or September.[3]

There are several approaches to the treatment of seasonal allergic rhinitis, including avoidance of the appropriate allergy, topical nasal sprays or eye drops, and systemic therapies.[4] For the past 20 years, topical corticosteroids have been used successfully in the treatment of allergic rhinitis. These drugs have vasoconstrictor and anti-inflammatory properties that alleviate the symptoms of rhinitis. Fluticasone propionate nasal spray (FPANS) is a recent addition to the currently available topical corticosteroids, which, at a once-daily dose of 200µg, has been shown to be highly effective in the treatment of allergic rhinitis[5] and equivalent in efficacy to that of other comparator topical corticosteroids (intranasal beclomethasone dipropionate 168µg twice daily[6,7] and flunisolide 100µg twice daily[8]). Furthermore, FPANS possesses 2 distinct advantages over other topically active corticosteroids: (a) being effective as a once-daily dosage, the drug may act as an aid to patient compliance,[9] and (b) it has extremely low oral bioavailability[10] and therefore a low potential to produce unwanted systemic side effects. This lack of systemic activity has been demonstrated in healthy volunteers taking either high oral doses of fluticasone propionate[10,11] or high intranasal doses[10] over a period of several days.

Systemic antihistamines have also been used as a treatment for SAR, with the original histamine H_1-receptor antagonists now being replaced by second generation nonsedative drugs in this class.[4] Cetirizine dihydrochloride is an antihistamine in this group that has been shown to be effective in controlling the symptoms of hayfever at a once-daily dosage of 10mg.[12] Furthermore, it has been shown to produce a significant improvement in eye irritation and watering.[12] While intranasal corticosteroid therapy is highly effective in reducing the nasal symptoms associated with seasonal allergic rhinitis, it may be less effective in controlling eye symptoms.[13] In a recent study in which loratidine and beclomethasone dipropionate were used in combination, there was some evidence that overall control of symptoms improved.[14]

This study aimed to evaluate the efficacy and safety of FPANS 200µg once daily, taken alone and in combination with one tablet of cetirizine dihydrochloride 10mg, in the treatment of seasonal allergic rhinitis.

Patients and Methods

Patients

Patients eligible to take part in this study were males or females aged over 12 years who had required treatment for the symptoms of hayfever during the month of June in the 2 previous years. Patients must have had at least two of the following symptoms, one of which should have been a nasal symptom: sneezing, nasal itching, runny nose, nasal congestion, eye watering/irritation and headache. Patients were to remain in their usual environment throughout the study.

Patients not eligible were those who had received a prescription medicine for the treatment of an upper or lower respiratory tract infection within the previous 2 weeks, or had received treatment for allergic rhinitis within the last week. Any patients who had received intranasal corticosteroids or oral corticosteroids within the previous 4 weeks were also excluded, as were those who had received ketotifen or sodium cromoglycate in the same time period. Patients taking astemizole within the previous 6 weeks, depot corticosteroids within 8 weeks, or receiving desensitisation injections to grass pollen in the previous 6 months were also excluded.

Additional exclusion criteria included: nasal surgery in the previous 2 months, nasal infections or significant nasal pathology (polyps, septal deviation, hypertrophy of turbinates), chronic infective rhinosinusitis, serious concomitant disease, treat-

Table I. Patient characteristics (total study population)

	No. of patients (%)	
	FPANS alone	FPANS plus cetirizine
Total no. of patients	**227**	**227**
Males	95 (42)	99 (44)
Females	132 (58)	128 (56)
Mean age (years) [range]	31 [12-80]	30 [12-66]
Duration of seasonal allergic rhinitis		
<10y	104 (46)	109 (48)
>10y	123 (54)	118 (52)
Severity of seasonal allergic rhinitis		
Mild	21 (9)	12 (5)
Moderate	160 (70)	162 (71)
Severe	46 (20)	53 (23)
Hayfever symptoms of previous year		
Headache	81 (36)	98 (43)
Sneezing	216 (95)	216 (95)
Watering eyes	207 (91)	201 (89)
Most troublesome symptom last year		
Watering eyes	108 (48)	126 (56)
Most widely used medications		
Antihistamines (49% of all medications)	169 (74)	176 (78)
Corticosteroids (29% of all medications)	108 (48)	97 (43)

Abbreviations: FPANS = fluticasone propionate aqueous nasal spray 200µg once daily in the morning; FPANS plus cetirizine = fluticasone propionate aqueous nasal spray 200µg once daily in the morning plus one tablet of cetirizine 10mg.

ment with concomitant medication likely to interfere with the efficacy of the study medication, recurrent conjunctivitis, the wearing of soft contact lenses, and pregnancy or lactation. Women of childbearing potential were only included if the investigator considered that they were taking adequate contraceptive precautions.

Finally, patients with asthma were eligible for entry into the study provided that they were unlikely to require a change in medication over the 8-week study period.

All patients were required to give their written informed consent before participating in the study, with those under the age of 16 years providing the consent of a parent or legal guardian. The study was approved by one local Ethics Committee on behalf of all participating centres.

Design

This was a double-blind, multicentre, parallel group study carried out amongst general practice patients in the UK. Eligible patients were randomly assigned to one of two treatment groups; either FPANS 200µg once daily (2 actuations per nostril) in the morning plus 1 placebo tablet, or FPANS 200µg once daily in the morning plus one cetirizine 10mg tablet. Medication was taken for 8 weeks starting on 14 May, 1990, to ensure that treatment was commenced before the beginning of the expected hayfever season in the UK. Patients were also provided with eye drops containing a mixture of antazoline and xylometazoline (Otrivine-Antistin®, Ciba Vision) to be used if eye symptoms became troublesome.

Table II. Mean symptom scores[a] for the total population

	FPANS alone	FPANS plus cetirizine	95% Confidence interval
Total no. of patients	**227**	**227**	
Nasal symptoms			
Mean	1.5	1.5	–0.3 to 0.3
SD	1.4	1.6	
Range	0.0 to 7.1	0.0 to 8.4	
(Missing)	(30)	(29)	
Eye symptoms			
Mean	1.3	1.1	–0.1 to 0.4
SD	1.3	1.3	
Range	0.0 to 6.2	0.0 to 7.3	
(Missing)	(30)	(30)	
Headache			
Mean	0.4	0.4	–0.1 to 0.2
SD	0.9	0.7	
Range	0.0 to 6.0	0.0 to 4.0	
(Missing)	(30)	(31)	

a Symptoms were rated on a 10-point scale: 0 = absent to 9 = very severe.

Abbreviations: FPANS = fluticasone propionate aqueous nasal spray 200µg once daily in the morning; FPANS plus cetirizine = fluticasone propionate aqueous nasal spray 200µg once daily in the morning plus one tablet of cetirizine 10mg.

Table III. Proportion of symptom-free days[a] for the total population

	FPANS alone	FPANS plus cetirizine	95% Confidence interval
Total no. of patients	**227**	**227**	
Nasal symptoms			
Mean	0.45	0.46	–0.08 to 0.07
SD	0.38	0.4	
Range	0.0 to 1.0	0.0 to 1.0	
(Missing)	(30)	(29)	
Eye symptoms			
Mean	0.56	0.57	–0.09 to 0.05
SD	0.36	0.36	
Range	0.0 to 1.0	0.0 to 1.0	
(Missing)	(30)	(30)	
Headache			
Mean	0.86	0.85	–0.03 to 0.06
SD	0.22	0.25	
Range	0.0 to 1.0	0.0 to 1.0	
(Missing)	(30)	(31)	

a A score of 0 represents no days symptom-free, a score of 1 indicates that all days were symptom-free.

Abbreviations: FPANS = fluticasone propionate aqueous nasal spray 200µg once daily in the morning; FPANS plus cetirizine = fluticasone propionate aqueous nasal spray 200µg once daily in the morning plus one tablet of cetirizine 10mg.

Table IV. Proportion of days for which rescue medication[a] was not taken (total study population)

	FPANS alone	FPANS plus cetirizine	99% Confidence interval
Total no. of patients	**227**	**227**	
Mean	0.81	0.82	–0.05 to 0.10
SD	0.29	0.26	
Range	0.00 to 1.0	0.00 to 1.0	
(Missing)	(48)	(54)	

a A score of 0 indicates rescue medication was required, a score of 1 indicates medication was not required every day.

Abbreviations: FPANS = fluticasone propionate aqueous nasal spray 200μg once daily in the morning; FPANS plus cetirizine = fluticasone propionate aqueous nasal spray 200μg once daily in the morning plus one tablet of cetirizine 10mg.

Methods

At the initial clinic visit, investigators recorded demographic details for each patient together with a brief clinical history and an assessment of the severity of symptoms during the hayfever season of the previous year and the medication taken.

Patients were reassessed at clinic visits following 3 and 8 weeks' treatment.

Patients were issued with a daily diary card on which to record scores for their nasal and eye symptoms, and headache. These symptoms were scored on a 10-point categorical rating scale, where 0 = no symptoms, 1-3 = mild symptoms, 4-6 = moderate symptoms, and 7-9 = severe symptoms. Additionally, patients were asked to record their use of study medication, eye drops, and any other concurrent medication.

At the end of the study, patients were asked whether or not they felt that study medication had adequately controlled nasal and eye symptoms and headache. The investigator was also asked to assess the measure of success of the study treatment in controlling the symptoms of seasonal allergic rhinitis.

Table V. Percentage of patients reporting adequate control of symptoms

	FPANS alone (n = 227)	FPANS plus cetirizine (n = 227)
Nasal symptoms	88%	89%
Eye symptoms	75%	82%
Headache	83%	86%

Abbreviations: FPANS = fluticasone propionate aqueous nasal spray 200μg once daily in the morning; FPANS plus cetirizine = fluticasone propionate aqueous nasal spray 200μg once daily in the morning plus one tablet of cetirizine 10mg.

Analysis

Symptoms (nasal symptoms, eye symptoms and headache) collected in the daily diary cards for weeks 3 to 8 inclusive (the period during which pollen count was the highest) were used in the assessment of symptom scores and symptom-free days. Treatment groups were compared for all measures of efficacy using a normal test; confidence intervals, 95% (symptoms) or 99% (use of rescue medication and overall assessments), were calculated using the appropriate standard error.

For the analysis of the proportion of symptom-free days and daily symptom scores, p values ≤ 0.05 were considered to indicate a statistically significant result. For the analysis of the proportion of days free of relief medication and patient's and physician's assessment scores, p values ≤ 0.01 were considered to indicate a statistically significant result.

Results were analysed before and after excluding patients who violated the study protocol, and as the outcome of these analyses were similar, data collected for the total (intention-to-treat) population are presented in this paper.

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