

# Early treatment of perennial rhinitis with budesonide or cetirizine and its effect on long-term outcome

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Asthma, rhinitis,  
other respiratory  
diseases

**Background:** Perennial rhinitis is a common disease that has many similarities with bronchial asthma. Early treatment with inhaled steroids has improved asthma symptoms, lung function, and bronchial hyperreactivity, but it has not been studied in perennial rhinitis.

**Objective:** The main objective was to determine whether early introduction of long-term daily intranasal steroid treatment would have a positive effect on the clinical course and outcome of perennial rhinitis compared with the effect of an antihistamine. A secondary objective was to compare the clinical efficacy of intranasal budesonide and oral cetirizine.

**Methods:** One hundred forty-three adult patients with newly detected perennial allergic or nonallergic eosinophilic rhinitis of 1 to 3 years' duration were randomized to receive budesonide dry powder, 400 µg (delivered dose of 280 µg) intranasally, or cetirizine, 10 mg orally, once daily for 1 year. At the end of the double-blind treatment period, medication was stopped, and the patients were followed for another year, during which time they could use 14-day courses of intranasal budesonide as needed to control rhinitis relapses. The main outcome measures were the time to first relapse and the number of relapses during the second year. Nasal symptom scores, nasal smear eosinophilia, and nasal peak expiratory flow were used to compare the clinical efficacy of the 2 treatments.

**Results:** During the randomized phase of the study, budesonide was significantly more effective than cetirizine in relieving nasal symptoms. Nasal peak expiratory flow improved significantly in budesonide-treated patients compared with in patients receiving cetirizine. After discontinuation of randomized treatment, 38% of budesonide-treated and 56% of cetirizine-treated patients had a relapse within the first month ( $P = .04$ ). The median time to first relapse was longer in budesonide-treated patients than in cetirizine-treated patients (62 vs 20 days), although the difference was not significant. Fourteen-day courses of budesonide provided effective control of relapses; the mean number of relapses was 4.0 versus 5.4 in the groups previously treated with budesonide or cetirizine, respectively. Both treatments were well tolerated throughout the study.

**Conclusions:** Budesonide is significantly more effective than

cetirizine in controlling perennial rhinitis. After stopping treatment, budesonide better prevents relapses for 1 to 2 months compared with cetirizine. Periodic therapy with budesonide may be sufficient to control symptoms in most patients who have relapses. (*J Allergy Clin Immunol* 2002;109:426-32.)

**Key words:** Antihistamine, budesonide, cetirizine, corticosteroids, early intervention, perennial rhinitis

Perennial rhinitis is a common condition that significantly limits daily activities and may impair quality of life as much as mild or moderate asthma.<sup>1</sup> Both antihistamines and intranasal corticosteroids are effective in the treatment of perennial rhinitis<sup>2-5</sup> and are recommended for long-term treatment.<sup>6,7</sup> They have provided effective relief of nasal symptoms in perennial rhinitis. Recent meta-analyses of 21 studies have shown that in seasonal rhinitis topical corticosteroids control nasal symptoms more effectively than oral antihistamines and have a greater effect on nasal obstruction.<sup>8,9</sup> However, the meta-analyses include only 2 studies of perennial rhinitis. Both interventions lasted 4 weeks.<sup>10,11</sup> Another comparison of a nasal steroid with a nasal antihistamine in perennial rhinitis lasted 6 weeks.<sup>12</sup> No long-term comparisons of intranasal steroids and oral antihistamines in perennial rhinitis are available. Furthermore, the effect of early intervention with long-term steroid treatment on the outcome of perennial rhinitis is unknown, but such an approach might be beneficial.

Early treatment of asthma with inhaled corticosteroids improves asthma symptoms and, possibly, lung function.<sup>13,14</sup> The nose and bronchi have many structural and functional similarities,<sup>15,16</sup> and perennial rhinitis and asthma often coexist in the same patient. There is thus a rationale for early intervention with intranasal steroids in patients with perennial rhinitis. We therefore performed a 2-year randomized comparison of an intranasal corticosteroid (budesonide) and an oral antihistamine (cetirizine) in patients with newly diagnosed perennial rhinitis to compare the efficacy of the 2 treatments and to determine the length of effect when the medications were withdrawn during the second (follow-up) year of the study. During the follow-up year, 14-day courses of intranasal budesonide taken for exacerbations provided an opportunity to evaluate the effect of periodic treatment.

## METHODS

### Study population

Patients were eligible for the study if they were between 16 and 68 years of age and had symptoms of perennial rhinitis that had last-

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*Abbreviation used*

nPEF: Nasal peak expiratory flow

ed for 1 to 3 years. Rhinitis symptoms were required to be present for at least 1 hour on most days.<sup>17</sup> Patients had to have eosinophils present in nasal smear (score  $\geq 1$ ), a positive skin prick test response for at least one perennial allergen (see below), or both to be included in the study. Patients with severe seasonal rhinitis symptoms were excluded, as were women who were pregnant or lactating; women of childbearing age were required to use adequate contraception. Other exclusion criteria were as follows: upper respiratory infection during the 4 weeks before randomization; concomitant illness or medication that might interfere with the study; previous steroid treatment for more than 3 months at any time or within 1 month before randomization; systemic steroid therapy within 3 months or cutaneous application of steroids; and immunotherapy for seasonal or perennial rhinitis within the past 3 years. Antihistamines, if used, were discontinued 48 hours before randomization (2 months before randomization in the case of astemizole), and intranasal cromoglycate was discontinued 14 days before randomization.

At randomization, a physical examination and rhinoscopy were performed, and patients with nasal polyps or nasal deformities severe enough to cause obstruction or signs of chronic infectious sinusitis on sinus radiography were excluded. Patients with asthma or moderately to severely increased bronchial responsiveness at histamine challenge<sup>18</sup> were excluded to avoid confounds caused by asthma medication.

Informed written consent was obtained from each patient and from a parent if the patient was under 18 years of age. The study was carried out at the Skin and Allergy Hospital of the University of Helsinki, Finland, and was approved by the hospital's ethics committee.

## Study design

The study had a double-blind, double-dummy, randomized, parallel-group design during the first year. The randomization was stratified according to type of rhinitis (allergic or nonallergic, see below), and block size was 4 patients. The patients used either budesonide delivered by means of the Turbuhaler device and placebo tablets or placebo Turbuhaler and cetirizine tablets. The study was open during the second year, but the first year of treatment was kept blinded.

After a 2-week run-in period, patients were randomized to receive either intranasal budesonide (Rhinocort Turbuhaler), 400  $\mu\text{g}$ , (equivalent to a delivered dose of 280  $\mu\text{g}$ <sup>19</sup>), or oral cetirizine (Zyrtec) 10 mg. Both treatments were taken once daily in the morning for 1 year. No other regular medication for rhinitis or allergy was permitted during the study.

Study medication was withdrawn at the end of the first year, and patients were monitored for a further year. During this period, patients could receive a 14-day course of intranasal budesonide if they actively reported to the study personnel the need for medication for symptom control. The relapse was thus defined as a patient-derived need to start the medication in agreement with the study personnel. The patients took 400  $\mu\text{g}$  (2 doses of 100  $\mu\text{g}$  for both nostrils) once daily in the morning.

All patients were given an intranasal saline spray (Humidose) and phenylpropanolamine (Rinexin) tablets, 25 mg, for use as rescue medication if required. Patients who still experienced severe symptoms were examined by an ear, nose, and throat specialist (J.R. or M.S.), and a 5-day course of oral prednisolone, 25 mg daily, was given, if necessary, during the first year. Compliance of the patients was followed during the first study year by asking whether the patients had taken the medication as instructed and by counting the returned tablets at every visit. The patients were classified as com-

pliant if they had taken at least 70% of the prescribed doses. The percentage of compliant patients was 80.3% in the budesonide group and 79.2% in the cetirizine group according to this criteria. During the second study year, the compliance was based on the diary notes regarding the use of budesonide.

## Assessments

Patients were assessed at the beginning and end of the run-in period; after 1, 3, 6, 9, and 12 months' active treatment; and 1 week and 3, 6, and 12 months after stopping study medication. All assessments were performed by one of 2 ear, nose, and throat specialists (J.R. or M.S.), except assessment at 9 months during the first year, which was performed by a study nurse.

Nasal smears were taken from both nostrils at randomization and after 1, 12, and 24 months' treatment. Smears were obtained by gently rubbing the inferior turbinate with a cotton-covered stick, fixed, and stained with eosin and methylene blue. Eosinophil and neutrophil leukocyte counts were calculated as the mean of 6 fields of view and scored semiquantitatively<sup>20</sup> on a 5-point scale (eosinophils: 0 = no or very few cells, 0.5 = tract of 5-10 cells in 1-3 fields of view, 1 = tract of 5-10 cells in 3-5 fields of view or a single finding of 20-30 cells, 2 = several tracts of 20-30 cells, and 3 = rich tracts; neutrophils: 0 = no or very few cells, 0.5 = barely sufficient finding, 1 = moderate finding, 2 = several rather rich tracts, and 3 = plenty of tracts on the whole glass).

Skin prick tests (Solu-Prick SQ, 10 histamine-equivalent prick, ALK) were performed at randomization against 10 common inhalant allergens (birch, timothy, meadow fescue, mugwort, *Cladosporium herbarum*, cat, dog, horse, cow, and *Dermatophagoides pteronyssinus*). Patients were considered allergic if at least one allergen caused a wheal with a diameter of 3 mm and control solutions gave expected results.<sup>21</sup>

Patients recorded their symptoms (blocked nose, rhinorrhea, sneezing, and eye symptoms) every evening in diaries during the run-in period; the first, sixth, and twelfth months of the first year; and the first 3 months, the sixth month, and the twelfth month of the second year. Symptoms were recorded on a 6-point scale (0 = no symptoms, 1 = very mild symptoms, 2 = mild symptoms, 3 = moderate symptoms, 4 = severe symptoms, and 5 = very severe symptoms). Days with a total nasal symptom score equal to or less than 2 (maximum = 15) were considered rhinitis free, and the percentage of rhinitis-free days of the total number of days followed by symptom diaries was calculated in both treatment groups. If relapses requiring treatment occurred during the second year, patients kept diaries from the day before the start of the 2-week intranasal budesonide course to the end of the treatment episode.

Nasal peak expiratory flow (nPEF) was measured with a Vitalograph PEF meter (Vitalograph Cat. No. 43.000SD) with an Everseal mie face mask. Measurements were made in the evenings for the diary periods, and the best of 3 measurements was recorded in the patients' diaries. All medication used during the study was also recorded.

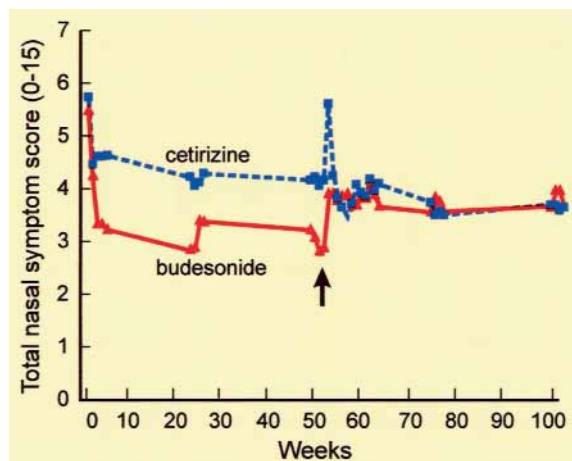
At the end of the first year, patients evaluated the overall efficacy of their treatment on a 5-point scale (4 = total control of symptoms, 3 = substantial control, 2 = minor control, 1 = no control, and 0 = aggravation of symptoms).

Details of adverse events were obtained throughout the first year of the study by means of a standard question: Have you had any health problems or symptoms not usually associated with your rhinitis since your last visit? Patients were asked to rate adverse events as mild, moderate, or severe, according to their effect on daily activities.

## Statistical analysis

Data were analyzed on an intention-to-treat basis. Mean values for each efficacy variable were calculated for each patient during the 2-week run-in period (baseline) and each subsequent measure-

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**FIG 1.** Mean weekly total nasal symptom score throughout the study with 12 months treatment with budesonide (solid red line) and cetirizine (dashed blue line). The arrow indicates the end of treatment and start of the 12-month follow-up period, during which both groups received 14-day courses of budesonide when needed.

**TABLE I.** Patient characteristics

	Budesonide	Cetirizine
No. of patients	71	72
Female/male ratio	43:28	46:26
Age, y (mean [range])	35.1 (17.3-67.5)	33.9 (16.7-64.6)
Duration of rhinitis		
1 y	27	33
2 y	33	32
3 y	11	7
Skin prick test responses, n		
Negative	18	17
Positive	53	55
Positive for perennial allergen(s)	49	51
Positive for seasonal allergen(s)	39	39
Positive for perennial and seasonal allergen(s)	35	35
No. of patients with mild bronchial hyperreactivity*	23	16
Eosinophils present in nasal smear	49	52
Mean nasal eosinophilia score (range, 0-3)	0.79	0.85
Mean serum IgE concentration, kU/L	118	168

\*Patients with moderate or severe hyperreactivity were excluded.

ment period. Changes in efficacy variables from baseline were analyzed by means of ANOVA, with the baseline mean value as a covariate. The consumption of rescue medication was analyzed with the Fisher exact test.

During the second year, the primary efficacy variable was the time to first relapse. Survival curves were calculated according to the Kaplan-Meier technique, and treatments were compared by means of a log-rank test. A global assessment of treatment efficacy at each visit was performed by means of ANOVA. All tests of significance were 2-tailed, and *P* values of less than .05 were considered significant.

## RESULTS

A total of 147 patients were enrolled in the study, of whom 3 were withdrawn during the run-in period, and

one randomized patient opted to discontinue before receiving any medication. Thus 143 patients entered the first year of the study, of whom 126 (88%) continued until the end of the first study year, and 113 (79%) completed the full 2 years.

Of the 143 patients who entered the study, 108 were classified as allergic on the basis of skin prick test responses (at least one positive reaction): 100 had positive skin prick test responses for perennial allergens (animals or house dust mite), and 8 had positive skin prick test responses only for seasonal allergens (pollens). There were no significant differences between the 2 treatment groups (Table I). The demographic characteristics of the 124 patients who remained in the study at the start of the second year were comparable with those of the overall study population.

## Effects on rhinitis symptoms

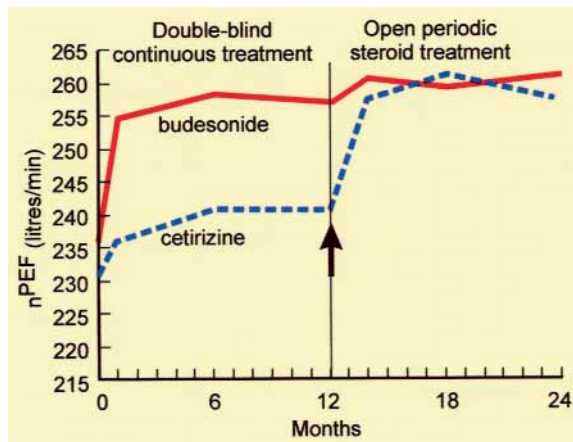
Both budesonide and cetirizine produced significant improvements in total and individual nasal symptom scores during the first year of the study (Table II), but the achieved reductions were consistently significantly greater with budesonide than with cetirizine, except for the score for blocked nose at 12 months (Table III). Patients with positive (allergic, *n* = 108) and negative (nonallergic, *n* = 35) skin prick test responses responded quite similarly to the treatment. For total nasal symptoms, budesonide was significantly more effective than cetirizine in both groups (*P* = .006 and *P* = .020, respectively).

An analysis of the weekly total nasal symptom scores (Fig 1) suggested that the maximal treatment effect with both drugs was achieved during the first 2 weeks and was maintained until the end of the year. The percentage of rhinitis-free days (Table II) was significantly higher in the budesonide group (45.1%) compared with that in the cetirizine group (25.9%). There was no significant difference between the groups in eye symptoms. Patients in the cetirizine group used significantly more phenylpropanolamine tablets as rescue medication than patients in the budesonide group (Table II). Altogether, 22 five-day courses of prednisolone, 25 mg/d, were prescribed to control breakthrough symptoms for 14 patients: 18 courses for 10 patients in the cetirizine group and 4 courses for 4 patients in the budesonide group. The difference between the treatment groups was significant (*P* = .002).

The patients' assessment of the overall efficacy of treatment also showed that budesonide was significantly more effective in controlling rhinitis symptoms than cetirizine. Substantial or total control of symptoms was achieved in 74% of budesonide-treated patients compared with in 50% of those receiving cetirizine (*P* = .0023).

## Effects on nasal patency

During the first year of the study, nPEF increased from a mean of 236 to 257 L/min (8.9%) in the budesonide group and from 231 to 241 L/min (4.3%) in the cetirizine group (Tables II and III and Fig 2). The difference in increase in nPEF between the groups was statistically significant (*P* < .05).



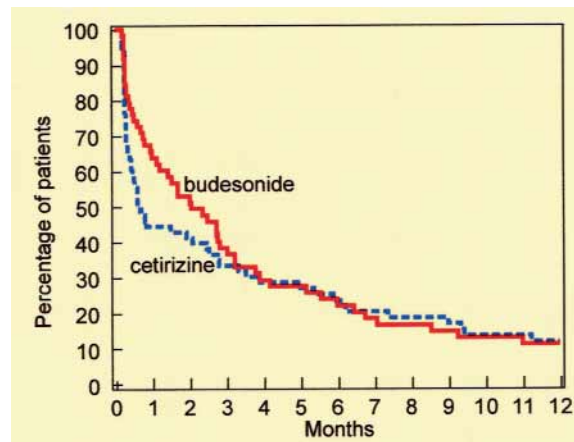
**FIG 2.** Mean nPEF throughout the study with 12 months treatment with budesonide (solid red line) and cetirizine (dashed blue line). The arrow indicates the end of treatment and start of the 12-month follow-up period, during which both groups received 14-day courses of budesonide when needed.

### Effects on nasal cytology

Nasal smear eosinophilia decreased to a greater extent in patients treated with budesonide than in those treated with cetirizine (Table II). In budesonide-treated patients the mean eosinophilia score at baseline was 0.79, and this score decreased to a mean of 0.16 at the end of the first year, whereas in cetirizine-treated patients, the mean eosinophilia score decreased from 0.85 to 0.54. The difference between the groups was statistically significant at 1 month ( $P < .001$ ), and it remained significant at 12 months ( $P < .01$ ). There was no significant difference in nasal smear neutrophil numbers between the 2 groups.

### Outcome after discontinuing treatment

After discontinuation of study treatment, symptoms returned in 90% of patients within 1 year (Fig 3). The proportion of patients experiencing a relapse within the first month after discontinuation of treatment was significantly smaller in the group treated with budesonide in the previous year than in the group previously treated with cetirizine (38% vs 56%, respectively;  $P = .04$ ). The median time to relapse was longer in the budesonide group than in the cetirizine group (62 vs 20 days; 62 vs 25 days in patients with positive skin test responses). These differences did not reach statistical significance. Similarly, the mean number of relapses during the follow-up year was smaller in the group previously treated with budesonide (4.0 vs 5.4), although the difference was not statistically significant ( $P = .089$ ). There were no significant differences in symptom scores between the groups during the second year (Table IV). The improvement in nPEF seen in budesonide-treated patients in the first year of the study was maintained during the second year (mean nPEF, 261 L/min at 12 months). In patients previously treated with cetirizine, mean nPEF increased during the second year from 241 to 257 L/min (6.6%), with 14-day courses of budesonide as the only treatment during relapse.



**FIG 3.** Kaplan-Meier plot showing the proportion of patients free from relapses during the second year of the study after discontinuation of 1 year's treatment with budesonide, 400  $\mu$ g once daily (solid red line), or cetirizine, 10 mg once daily (dashed blue line).

### Tolerability

Both treatments were well tolerated. Adverse events occurred in 65 budesonide-treated patients and 68 patients receiving cetirizine. The most common adverse events in each group were viral upper respiratory tract infections, which occurred in 48 budesonide-treated patients and 52 cetirizine-treated patients, blood in nasal secretion (ranging from blood-tinged mucus to nasal bleeding; 19 and 9 patients, respectively), conjunctivitis (8 and 5 patients, respectively), and headache (6 and 1 patients, respectively). Sinusitis was observed in 2 budesonide-treated patients and in one cetirizine-treated patient. Most adverse events were mild or moderate in intensity. Three budesonide-treated patients withdrew from the study at 6 months because of crusting of the nasal mucosa, bleeding, or both, and one cetirizine-treated patient withdrew because of drowsiness.

### DISCUSSION

This study is the first double-blind long-term comparison of an intranasal corticosteroid and an oral antihistamine in patients with perennial rhinitis. During the active treatment period, budesonide was consistently more effective than cetirizine in relieving nasal symptoms and improving nasal airflow. Thus this long-term study confirms the previous experience obtained in short-term comparisons of topical corticosteroids and antihistamines in perennial rhinitis.<sup>10-12</sup> The superior symptom relief obtained with budesonide was reflected in the patients' overall assessment of efficacy, in consumption of rescue medication, and in a higher proportion of rhinitis-free days in the budesonide group (45% vs 26%). The finding that 55% of the patients in the budesonide group and 74% in the cetirizine group were not free of symptoms shows a potential for further improvement in pharmacologic treatment of perennial rhinitis.



**TABLE II.** Mean symptom scores, percentage of rhinitis-free days, consumption of rescue medication, nPEF, and nasal smear eosinophilia during the first year of the study (active treatment with budesonide or cetirizine)

	Budesonide				Cetirizine				P value
	Baseline	1 mo	6 mo	12 mo	Baseline	1 mo	6 mo	12 mo	
Total nasal symptom score	5.47	3.54	3.03	3.05	5.74	4.50	4.06	4.19	<.001
Blocked nose	2.17	1.60	1.40	1.48	2.41	2.10	1.82	1.83	<.05
Runny nose	1.83	1.23	1.00	0.94	1.85	1.44	1.29	1.35	<.05
Sneezing	1.46	0.75	0.65	0.63	1.48	0.96	0.94	1.01	<.01
Eye symptoms	1.03	0.71	0.66	0.59	0.74	0.58	0.53	0.61	NS
Rhinitis-free days (% of total)	9.4		45.1†		9.9		25.9†		<.001
Rescue medication*									
Phenylpropanolamine tablets			1.2†				3.9†		<.05
Saline spray			2.9†				2.5†		NS
Prednisolone tablets			4 courses/4 patients†				18 courses/10 patients†		<.05
nPEF (L/min)	235.8	254.4	258.2	256.9	230.9	235.9	240.7	240.8	<.05
Nasal smear eosinophils (0-3)	0.79	0.14		0.16	0.85	0.67		0.54	<.001 at 1 mo, <.01 at 12 mo

The P value represents the comparison between the treatment groups during the whole treatment period.

\*The consumption of rescue medication is given for phenylpropanolamine tablets and saline spray as doses per week and for prednisolone tablets as number of 5-day courses per number of patients.

†Value represents the whole treatment period.

**TABLE III.** Adjusted mean changes in symptom scores and nPEF from baseline during the first year

	Budesonide	Cetirizine	Difference between budesonide and cetirizine (95% CI)	P value
Total nasal symptom scores				
1 mo	-1.97	-1.08	-0.89 (-1.37 to -0.41)	<.001
6 mo	-2.49	-1.51	-0.98 (-1.56 to -0.39)	.001
12 mo	-2.48	-1.40	-1.08 (-1.72 to -0.44)	.001
Blocked nose				
1 mo	-0.60	-0.22	-0.38 (-0.57 to -0.19)	<.001
6 mo	-0.82	-0.49	-0.33 (-0.57 to -0.08)	.009
12 mo	-0.74	-0.50	-0.24 (-0.050 to 0.03)	.086
Runny nose				
1 mo	-0.60	-0.37	-0.23 (-0.42 to -0.04)	.020
6 mo	-0.84	-0.52	-0.32 (-0.55 to -0.08)	.009
12 mo	-0.89	-0.47	-0.42 (-0.67 to -0.16)	.002
Sneezing				
1 mo	-0.76	-0.50	-0.26 (-0.43 to -0.08)	.005
6 mo	-0.82	-0.51	-0.31 (-0.50 to -0.11)	.002
12 mo	-0.83	-0.44	-0.39 (-0.61 to -0.17)	.001
nPEF (L/min)				
1 mo	18.6	3.4	15.2 (5.0 to 25.3)	.004
6 mo	22.6	8.1	14.5 (0.9 to 28.0)	.036
12 mo	21.3	8.2	13.1 (-1.7 to 28.0)	.081

95% CI, 95% Confidence interval.

**TABLE IV.** Mean symptom scores, percentage of rhinitis-free days, and nPEF during the second year of the study (after discontinuation of study medication)

	Originally treated with budesonide				Originally treated with cetirizine			
	End of treatment period	1-3 mo	6 mo	12 mo	End of treatment period	1-3 mo	6 mo	12 mo
Total nasal symptoms	3.05	3.84	3.72	3.72	4.19	3.99	3.49	3.55
Blocked nose	1.48	1.61	1.54	1.55	1.83	1.61	1.50	1.47
Runny nose	0.94	1.25	1.23	1.23	1.35	1.29	1.09	1.18
Sneezing	0.63	0.98	0.96	0.95	1.01	1.09	0.91	0.90
Eye symptoms	0.59	0.68	0.75	0.75	0.61	0.56	0.53	0.52
Rhinitis-free days (% of total)		34.4*				32.6*		
nPEF (L/min)	256.9	260.5	259.3	261.3	240.8	257.1	261.3	257.2

\*Value represents the whole second year of the study

There was no difference between treatments regarding effect on eye symptoms. However, the baseline scores for eye symptoms were low in these patients, as they often are in perennial rhinitis.<sup>6</sup> A meta-analysis of published comparisons of nasal corticosteroids and antihistamines has shown that both treatments are equally effective in relieving eye symptoms,<sup>9</sup> despite the widespread view that systemic antihistamines should be more effective than topical steroids in this respect.

When the 1-year treatment period was ended, symptom scores rapidly returned to baseline levels in patients who had been treated with cetirizine, whereas in patients randomized to budesonide, the treatment effect persisted for several weeks to months (Figs 1 and 3). As a result, the median time to relapse was longer in patients previously treated with budesonide, regardless of atopic sensitization, as judged with skin prick testing. The difference between treatments did not reach significance but is likely to be clinically valuable. The somewhat better preventive effect of budesonide against relapses in the beginning of the follow-up year was presumably caused by the anti-inflammatory actions of topical corticosteroids.<sup>22</sup> Evidence for this comes from the finding that nasal eosinophilia was reduced significantly more in budesonide-treated patients than in patients receiving cetirizine.

The definition of relapse can be criticized, but symptom increase leading to specialist consultation is close to the real-life situation. There is no validated definition for rhinitis relapse.<sup>6,17</sup>

However, disease remissions after 1 year of treatment were shorter than those seen when asthma was treated for 2 years with a topical steroid.<sup>13,14</sup> Thus the early introduction of anti-inflammatory steroid treatment in perennial rhinitis does not seem to significantly modify the outcome of the disease. The difference in the disease-modifying effect in asthma and in rhinitis may be related to the progressiveness of asthma, with airway remodeling caused partly by hypertrophy of the bronchial wall smooth muscle.<sup>23</sup> Such a phenomenon does not occur in rhinitis because there is no smooth muscle in the nasal mucosa, except in the vascular bed.

The corticosteroid effect reached a plateau 2 weeks after the start of treatment in the first year (Fig 1). During the second year of the trial, all patients would receive periodic treatment with budesonide to control relapses, irrespective of their original randomized treatment. Nasal symptom scores during the follow-up year remained lower than at baseline. Similarly, measurements of nPEF during the second year of the study showed that 14-day courses with budesonide maintained the improvement of nasal patency obtained by regular treatment with budesonide during the first year. In patients previously treated with cetirizine, nPEF tended to increase during the second year, when relapses were treated with 14-day courses of budesonide. These findings suggest that periodic treatment with intranasal corticosteroids may be an alternative strategy to treat patients with perennial rhinitis and even as effective as daily antihistamine. The study was not, however, designed to compare periodic with continuous treatment.

Both treatments were well tolerated. The adverse event profile was the same as that seen in short-term studies with intranasal steroids or oral antihistamines<sup>5,24,25</sup>; the number of events observed is presumably related to the long duration of the study. Blood-tinged nasal secretions and nosebleeds were more common in patients treated with budesonide. Such events were not usually troublesome, but 3 (4.2%) budesonide-treated patients withdrew from the study because of adverse events. One cetirizine-treated patient withdrew from the study because of drowsiness, which is known to occur sometimes during cetirizine treatment.<sup>26</sup>

In conclusion, this study has shown that intranasal budesonide (400 µg once daily) is significantly more effective than oral cetirizine (10 mg) in controlling nasal symptoms in patients with perennial allergic or nonallergic eosinophilic rhinitis. Although neither treatment significantly affected the long-term outcome of the condition, the time to relapse after discontinuation of therapy was longer with budesonide, which suggests that anti-inflammatory treatment has a prolonged effect. Furthermore, periodic treatment with budesonide may be a promising treatment strategy in perennial rhinitis.

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