

Efficacy of an oral antihistamine, astemizole, as compared to a nasal steroid spray in hay fever

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The efficacy and side effects of the oral H₁-antihistamine, astemizole, were compared with those of nasal beclomethasone in 158 adult birch-pollen allergic hay fever patients. 148 patients completed the 5-week, controlled trial which took place in Stockholm, May 1986, during the birch pollen season. Daily pollen counts were found to be at a rather low level throughout the study period. The effect and tolerability of both drugs were found to be excellent, although beclomethasone reduced nasal symptoms (sneezing, rhinorrhoea, blocked nose) significantly more effectively than astemizole. Eye symptoms were mild and equal in both groups. The results indicate that oral astemizole is an effective non-sedating antihistamine, though less so than nasal beclomethasone, in the treatment of nasal hay fever symptoms.

Key words: antihistamine; astemizole; beclomethasone dipropionate; glucocorticoid treatment, hay fever.

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Two of the most frequently prescribed drugs in the treatment of hay fever are oral antihistamines and steroid nasal spray.

Although antihistamines have a long tradition and a well-documented effect, their use is somewhat limited due to the frequently occurring sedative side effect. In recent years some non-sedating antihistamines have been synthesized, of which astemizole is one of the most specific H₁-blockers (4). Astemizole has been studied in both allergic and non-allergic rhinitis (6, 12), and its efficacy has been established in comparison to placebo, DSCG, traditional antihistamines and terfenadine (1, 2, 3, 5, 10, 12, 13, 14), another non-sedating antihistamine. When compared with nasal steroid spray, some studies have shown equal effect (7, 15) and some have favoured nasal steroids (12).

Nasal steroid spray is increasingly used for relief of allergic rhinitis and has been proven efficacious and safe (8, 9). Our aim was to compare nasal beclomethasone with oral aste-

mizole in the treatment of patients with birch pollen allergy.

MATERIAL AND METHODS

The study was carried out at two centres in Stockholm during the 5-week period of the birch pollen season starting April 28, 1986. A total of 158 patients with a previous clinical history of hay fever due to birch pollen were selected. One patient was excluded from analysis because of inadequate compliance and thus no treatment data.

Apart from a positive clinical history, a positive skin prick test (≥ 3 mm) and a positive RAST (RAST class ≥ 2) were required. Pregnant or lactating patients were excluded, as well as those with a history of perennial rhinitis or asthma requiring more than occasional β_2 -spray therapy. As a safety precaution patients in "sedation risk groups", such as bus-drivers, were excluded, as well as patients receiving specific immunotherapy.

The protocol was approved by the National Board of Health and Welfare and the local Ethics Committee, and all patients gave verbal informed consent. The patients were randomly allocated into two groups and given parallel treatment with either astemizole tablets 10 mg once daily or Becotide Nasal® 50 µg/ml, 2 puffs in each nostril twice daily. Double-blind double-dummy technique was used. Beclomethasone dipropionate or placebo was administered by nasal spray with mechanical pump. DSCG eye-drops were prescribed as rescue medication for eye symptoms, and occasional β_2 -adrenergic spray was also allowed in the case of asthmatic symptoms.

The patients were seen by a physician immediately before and after the treatment period, and kept a standardized diary upon which evaluation of the treatment is based. To obtain the best possible patient compliance, the diary consisted of weekly cards which were sent to the investigators by post once a week. The parameters recorded by the patients are listed in Table 1. Any extra medication, such as DSCG eyedrops and β_2 -adrenergic spray, was recorded on the diary cards. The patients also made an assessment of their total allergic symptoms during each week, using a visual analogue scale. At the end of the study the patients were asked to give a global evaluation, using a three-stepped scale: excellent, satisfactory or bad effect of treatment. Besides evaluation of therapeutic effects body weight was measured before and after the study and consumed drugs controlled. The nasal sprays were weighed before and after the treatment period, and any remaining tablets were counted. Blood samples were drawn before and shortly after the study, and were analysed for haemoglobin, sedimentation rate, red and white blood cell count, platelets, asparto-aminotransferase (ASAT), alanine-aminotransferase (ALAT), bilirubin, alkaline phosphatases and creatinine. Astemizole concentration in plasma was analysed from samples drawn within 1 week from the end of the trial. The pollen count in Stockholm was recorded throughout the study, using a Burkard pollen trap.

Statistics

Statistic evaluation was made using two-tailed Mann-Whitney, U-test and chi-square test. All patients, drop-outs included, were analysed when data was available.

Table 1
Parameters recorded

Parameter	Assessment	
Sneezing	No./day	<i>Scale</i>
Runny nose	scale 0-3	0 = no symptoms
		1 = slight symptoms
Blocked nose	scale 0-3	2 = moderate symptoms
		3 = severe symptoms
Eye symptoms	scale 0-3	
Use of DSCG eyedrops	times/day	
Side effects		
Sedation	scale 0-3	
Other	type	

Table 2
Reason for drop-out

	Astemizole	Beclomethasone
Unknown		1
Forgot medication		2
Nose bleeding	1	
Tiredness	1	
Lack of effect	2	1
Other disease		1
	4	5

Table 3
Patient characteristics

	Astemizole	Beclomethasone
No patients	80	77
Male/Female	38/42	33/44
Age: mean + SD	31.2 + 8.9	23.3 + 8.3
median (extrem.)	31.5 (18-55)	29 (16-49)
Weight: mean + SD	68.4 + 12.6	66.9 + 12.1
median (extrem.)	67.6 (47-116)	65.6 (45-99)

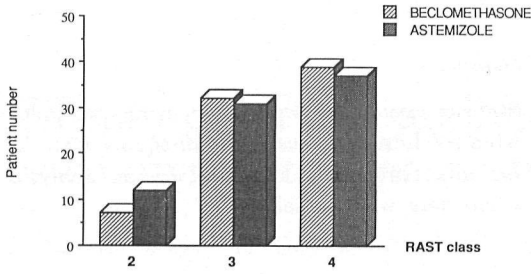


Fig. 1. RAST results.

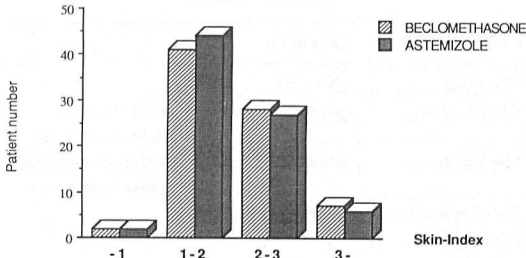


Fig. 2. Skin-index = ratio birch/histamine

RESULTS

The pollen count was generally low, with only five peaks above 100 grains/m³, between May 7 and 15. A total of 148 patients completed the study correctly. Nine subjects, five in the beclomethasone and four in the astemizole group, did not finish treatment. However, all but four of these patients gave their global evaluation. Reasons for drop-out varied and did not follow any specific pattern (Table 2). The average age of the patients was 30 years, and in both groups the distribution of age, sex and body weight was even (Table 3) with no statistically significant differences. The two groups were comparable regarding RAST classes and skin prick test (see Figs. 1, 2).

Nasal symptoms in both groups were relatively mild, although beclomethasone had a significantly better effect ($P < 0.05$) on all three recorded symptoms (Fig. 3a-c). Eye symptoms (Fig. 4) and consumption of DSCG eye-drops showed no difference between the groups.

The result of the weekly visual analogue scales was statistically in favour of beclomethasone

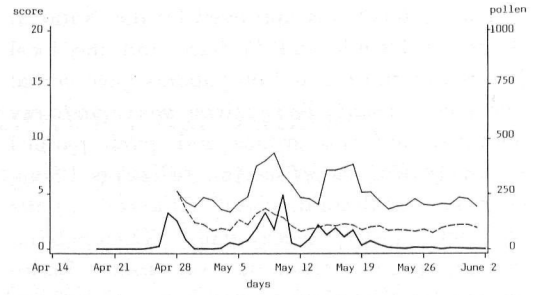


Fig. 3a. Sneeze.

— Pollen concentration
--- Astemizole
- - - Becotide nasal

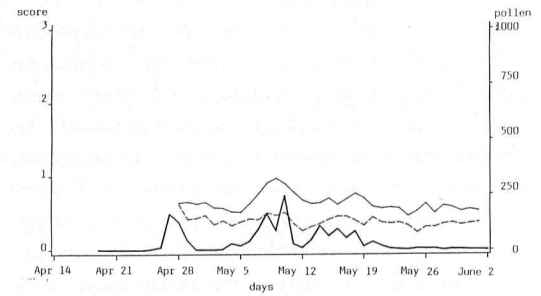


Fig. 3b. Runny nose.

— Pollen concentration
--- Astemizole
- - - Becotide nasal

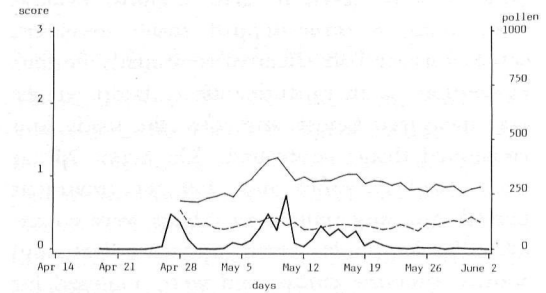


Fig. 3c. Blocked nose.

— Pollen concentration
--- Astemizole
- - - Becotide nasal

weeks 2-5 ($P < 0.05$) (Fig. 5). The patients' global evaluation gave good scores for both treatments, but a significantly better result for the beclomethasone group ($P < 0.01$) (Fig. 6).

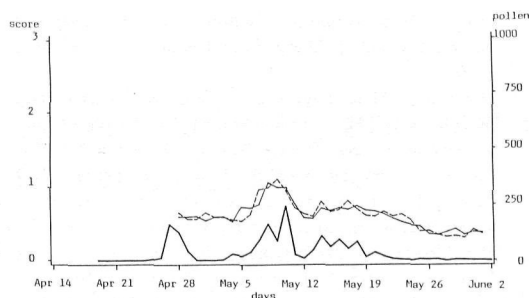


Fig. 4. Swollen eyes

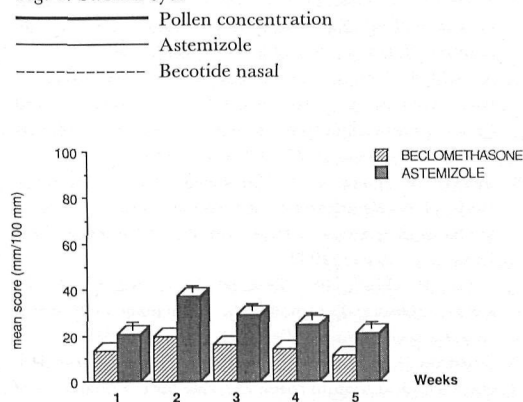


Fig. 5. Visual analogue scales. (standard error)

Adverse effects were mild and transient in both groups. A total of 41 different minor complaints were reported approximately equally in both groups – 47 and 48, respectively. Headache was reported by 15 patients in the beclomethasone, and three in the astemizole group. The sedation effect was generally mild and did not differ between the treatments (Fig. 7).

Body weight showed a slight decrease in the beclomethasone group (median 0.5 kg), while the astemizole group showed a slight increase (median 0.6 kg). These effects resulted in a statistically significant intergroup difference ($P < 0.01$). Considering only those patients whose body weight changed at least 2.0 kg, 12 (15%) in the astemizole group and one (1%) in the beclomethasone group increased in weight, while three (4%) in the astemizole and 15 (20%) in the beclomethasone group decreased.

The haematological and biochemical para-

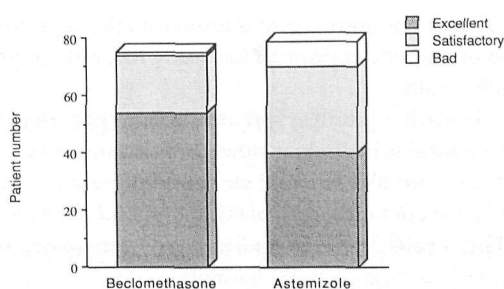


Fig. 6. Global evaluation.

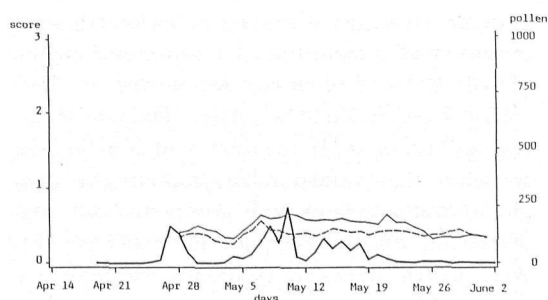


Fig. 7. Tiredness.

— Pollen concentration
 — Astemizole
 — Becotide nasal

meters remained normal after both treatments. The concentration of astemizole and its hydroxylated metabolites in plasma as determined by radioimmunoassay showed a mean of 2.5 ng/ml in the astemizole-treated group. None of the 11 patients with plasma concentrations exceeding 4 ng/ml had a weight increase of ≥ 2 kg.

DISCUSSION

The low pollen count during the season probably influenced the study to such an extent that the allergic symptoms were generally milder than could be expected in both groups. Before the birch-flowering season in Sweden, birch pollen counts in the days just prior to the present study were already rather high (up to 160 grains/m³). This was considered due to the "import" of pollens by strong winds from eastern Europe and was coincident with the nuclear plant disaster at Chernobyl. It is difficult to evaluate to what extent the lack of

"run-in" period in combination with the exposure to birch pollens prior to the study has influenced the results.

In earlier studies, astemizole has been shown comparable not only to other antihistamines (1, 3, 5, 14), but also to nasal steroid treatment (7, 12, 15), except for the lack of effect on nasal blockage. The results in these studies have been based on material from 45 to 90 patients.

Using a patient material large enough to prove a possible equal treatment effect at a confidence level of 5% and a power of 80%, we have been able to demonstrate the advantage of beclomethasone over astemizole regarding nasal symptoms and the global patient evaluation. Astemizole has previously been shown to be a potent and non-sedating antihistamine. In the treatment of pollinosis, we believe that the favourable symptom scores and global evaluations in both groups indicate that astemizole may be adequate for many patients when pollen counts are moderate, and may be a preferable supplementary to topical steroids during intense pollen seasons or in patients with severe hay fever. We found a slight, but significant weight increase in the astemizole group. This tendency has been described in other trials (12, 13) and may be the result of increased appetite. In a previous study this was shown not to be a problem in long-term treatment, possibly because the patients were warned about this side effect (12). The loss of weight in the beclomethasone group is in accordance with studies of seasonal variation in body weight in both healthy and over-weight populations (11, 16). A minor weight reduction during spring has been shown to be a normal finding.

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