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Astemizole in combination with pseudoephedrine in the treatment of seasonal allergic rhinitis*

Markku Simola[1], Ilmari Böss[1], Eino Holopainen[1], Henrik Malmberg[1], Pirkko Ruoppi[2], Juha Seppä[2], Lasse Siivonen[3], Jouko Suonpää[3], Tapani Piepponen[4]

[1] Department of Otorhinolaryngology, University Central Hospital, Helsinki, Finland
[2] Department of Otorhinolaryngology, University Hospital, Kuopio, Finland
[3] Department of Otorhinolaryngology, University Central Hospital, Turku, Finland
[4] Research Centre, Orion Pharmaceutica, Espoo, Finland

SUMMARY

The efficacy and side effects of once-daily astemizole-D, a combination of 10 mg astemizole and 240 mg pseudoephedrine, were compared with those of twice-daily brompheniramine-D, a combination of 12 mg brompheniramine and 50 mg phenylpropanolamine (Lunerin®), in 64 patients with seasonal allergic rhinitis caused by birch pollen. Efficacy was monitored by patient's diary scores, investigator assessments of nasal and eye symptoms and need of rescue medication during the 4-week study period. Both astemizole-D and brompheniramine-D reduced nasal and eye symptoms of allergy. There were no significant differences between the treatment groups regarding obstruction, but brompheniramine-D alleviated symptoms of rhinorrhoea and itchy eyes significantly more than astemizole-D. On the other hand, the patients in the brompheniramine-D group reported dry mouth, tiredness and drowsiness more often than those in the astemizole-D group. The results indicate that the two drugs are effective in the treatment of seasonal allergic rhinitis, but astemizole-D is better tolerated than brompheniramine-D.

Key words: allergic rhinitis, astemizole, antihistamines, sympathomimetics, nasal congestion

INTRODUCTION

Many classical H_1-antihistamines for treatment of seasonal allergic rhinitis have been successfully combined with sympathomimetics, partly to compensate the sedative effect of the antihistamine but, more importantly, to enhance the effect on nasal congestion. With the introduction of the non-sedative H_1-receptor antagonists, sedation and anticholinergic side effects are no longer a problem, but the control of nasal congestion symptoms is still poor. Astemizole is a well-documented, non-sedative H_1-antihistamine which has been shown to be effective on symptoms of allergic rhinitis (Malmberg et al., 1983; Juniper et al., 1988; LASAR, 1992). A combination with a sympathomimetic could be expected to improve the effect on nasal stuffiness (Nuutinen et al., 1989). To date, studies of second-generation antihistamines and sympathomimetics have seldom been reported. This pilot study describes a comparison of astemizole combined with pseudoephedrine, i.e. astemizole-D, and a well-known preparation consisting of brompheniramine and phenylpropanolamine (Lunerin®) in the treatment of seasonal nasal allergy.

PATIENTS AND METHODS

Sixty-four patients (38 female and 26 male, aged 12–60 years) who had a positive skin test or RAST reaction to birch pollen and a history of birch-pollen-induced rhinitis for at least one year, were enrolled in the study in three cities, Helsinki, Turku and Kuopio (Table 1). To avoid possible carry-over effects, all medication which could influence nasal symptoms was withheld for 2–8 weeks before admission to the study. Patients with vasomotor rhinitis, rhinitis medicamentosa, active upper respiratory tract infection (URTI), obstructive nasal polyps or contraindications to oral sympathomimetic therapy (severe hypertension, severe coronary artery disease, hyperthyreosis, or pheochromocytoma) were not accepted. The patients were not allowed to use monoamine-oxidase inhibitors. Informed consent was obtained from all patients and the study was approved

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Table 1. Summary of demographic data.

therapy group	astemizole-D	brompheniramine-D
n	30	34
sex	14 male/16 female	12 male/22 female
mean age (years)	30.7	31.6
mean duration since diagnosis of allergic rhinitis (years)	13.4	14.8

by the Ethics Committee of the hospital. The patients were allocated at random to two parallel treatment groups. The astemizole-D group (30 patients) received a capsule consisting of 10 mg astemizole and 240 mg pseudoephedrine as extended-release beads (Janssen Pharmaceutica, Belgium) in the morning, and a capsule of placebo in the evening. The brompheniramine-D group (34 patients) received a tablet of 12 mg brompheniramine and 50 mg phenylpropanolamine (Lunerin®, Draco, Sweden), twice daily. The trial was single-blind, i.e. the clinicians did not know whether the patients took capsules or tablets, and the patients were not informed of the constitution of their treatments. The patients reported for baseline examination, when nasal blockage and at least one other nasal or ocular symptom had become moderate or severe (2 respectively 3 points on the scale from 0 to 3). The medication was started on the following day. The duration of the treatment was four weeks. The patients were allowed to use cromoglycate eye drops as rescue medicine for severe ocular symptoms. To assess the efficacy of the therapy, the patients were asked to rate the severity of their nasal symptoms of sneezing, itching, obstruction and running, and ocular symptoms of itching, watering, redness and oedema on a 4-point scale from 0 to 3 and to record the results daily in a symptom score diary. The overall severity of symptoms was assessed on a visual analogue scale. Possible side effects and rescue medication were also recorded.

Clinical check-ups were done at baseline, at two weeks and at the end of treatment (at four weeks or discontinuation). The above-mentioned symptoms, ocular signs (redness, swelling) and rhinoscopy findings (swelling, secretion) were also scored on a 4-point scale and recorded by the clinician. Birch pollen data were recorded by the Finnish Aerobiology Group using pollen collectors, one at each study centre.

The results were analyzed statistically with the Mann-Whitney U test and the Wilcoxon test.

RESULTS

Birch pollen data

The levels of airborne birch pollen were fairly low throughout the season, the peak densities reaching 3,392 grains/m^3 at one centre, but only 1,550 and 307, respectively, at the other two centres. The daily mean pollen densities are shown in Figure 1.

Symptom severity assessments

At baseline, nasal and ocular symptom severity did not differ significantly between the two groups. The severity of allergy

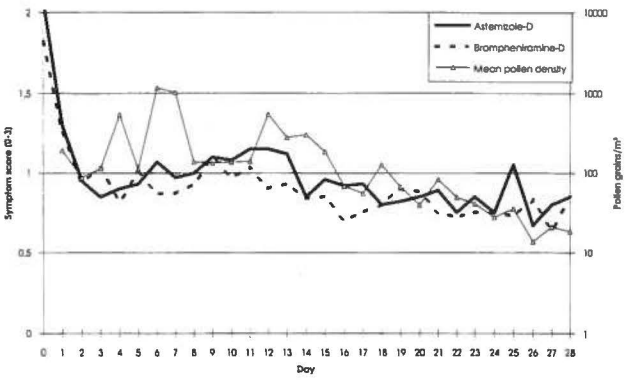

Figure 1. Mean pollen density in the three cities and daily nasal obstruction score as assessed by the patient after start of therapy.

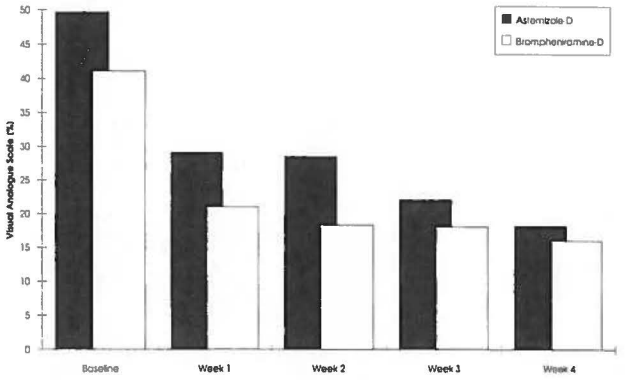

Figure 2a. Severity of all allergy symptoms as assessed by the patient.

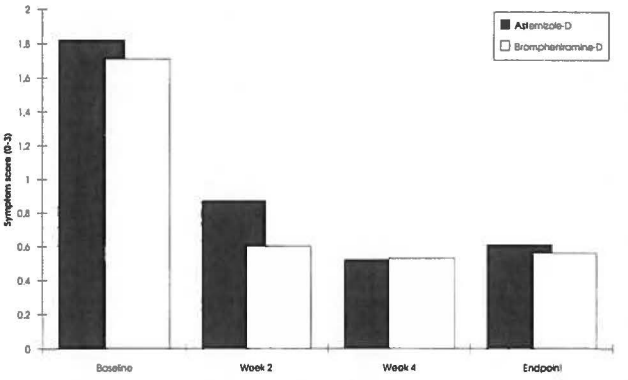

Figure 2b. Severity of all nasal symptoms as assessed by the clinician.

symptoms at baseline and during the four trial weeks, as recorded by the patients on the visual analogue scale, is shown in Figure 2a. Figure 2b shows the symptom severity as assessed by the clinician. A significant reduction in all (i.e., nasal and ocular) symptoms was observed in both therapy groups ($p < 0.001$), but differences between the therapy groups were not significant. In the analysis of the daily symptom scores for nasal itching, sneezing, running, stuffiness and eye symptoms, the curve for each symptom was drawn and the area under the curve (AUC) calculated as a percentage of the whole area. AUC values were then compared between the two therapy groups. Brompheniramine-D was found to be significantly more effective than astemizole-D in reducing the symptoms of rhinorrhoea,

the AUC values being 32.4% versus 23.1% (p=0.040). This was also true of itching of the eyes; AUC 23.9% versus 14.1%, respectively (p=0.018). Scores for nasal obstruction did not differ between the groups; AUC: 32.8% versus 29.5% (p=0.53; Figure 1). Nor were significant differences observed in itching of the nose (AUC: 23.4% and 20.6%, p=0.15), or sneezing (AUC: 21.4% and 15.6%, p=0.15). Cromoglycate eye drops were used by four patients in the astemizole-D group and by two in the brompheniramine-D group.

Most of the patients, 69% in the astemizole-D group and 72% in the brompheniramine-D group, reported that the action of the drug began within 30 to 120 min of ingestion. According to the patient's assessment at the end of the trial, the effect on nasal symptoms was rated excellent or good by 85.3% of the brompheniramine-D patients and by 85.8% of the astemizole-D patients. For ocular symptoms, the proportions were 73.5% and 75%, respectively.

Adverse events

Eleven patients discontinued the trial: four in the astemizole-D group (insomnia: 1; URTI: 1; no symptoms: 1; lost from trial: 1) and seven in the brompheniramine-D group (dizziness: 1; dry mouth and palpitation: 1; tiredness: 4; no symptoms: 1). Adverse events were spontaneously reported by 9 of the 30 (30%) astemizole-D patients and by 14 of the 34 (41.2%) brompheniramine-D patients. The most frequent complaints are listed in Table 2. The patients were asked about tiredness at each visit. In the astemizole-D group, the proportion of patients giving affirmative answers diminished from 50% at the baseline to 38% at week 4. In the brompheniramine-D group the situation was reversed: 39% complained of tiredness at the baseline and 56% at the end of week 4.

Table 2. Adverse events spontaneously reported by the patients.

adverse event (AE)	astemizole-D group (n=30)	brompheniramine-D group (n=34)
	no. patients with AE (%)	no. patients with AE (%)
tiredness	3 (10.0)	5 (14.7)
dry mouth	1 (3.3)	5 (14.7)
insomnia	1 (3.3)	0 (0)
drowsiness	0 (0)	3 (8.8)
dizziness	0 (0)	1 (2.9)
headache	2 (6.7)	2 (5.9)
palpitation	1 (3.3)	2 (5.9)

DISCUSSION

During the season covered by the present trial, the levels of airborne pollen were relatively low, although density peaks in excess of 2,000 grains/m^3 occurred and the days with less than 30 grains/m^3 were very few. The patients did not start the medication until a clear worsening of hay fever symptoms had been established at the baseline visit and it may, therefore, be assumed that they were sensitive enough to allow assessment of the efficacy of the treatment. In order to achieve a better control of symptoms of nasal stuffiness, astemizole has been combined with 240 mg pseudoephedrine in an "extended-release form." This pseudoephedrine preparation is taken once daily and has been shown to be well tolerated, better indeed than 60 mg q.i.d. or 120 mg b.i.d. (Janssens et al., 1990). In our comparison with the well-documented combination of brompheniramine and phenylpropanolamine (i.e., brompheniramine-D), astemizole combined with 240 mg pseudoephedrine (i.e. astemizole-D) seemed to have not only a fast but also a long-lasting effect on nasal congestion. Differences between the antihistamine effects could be seen in this study. Brompheniramine had a better effect on rhinorrhoea and itching of the eyes but, on the other hand, drowsiness and other side effects, were commoner in this group. Six brompheniramine patients discontinued medication because of adverse effects, as compared with only one patient in the astemizole group.

Our results indicate that both astemizole-D and brompheniramine-D reduced nasal symptoms and most of the eye symptoms rapidly and effectively, but astemizole-D was better tolerated than brompheniramine-D.

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Markku Simola, MD
Helsinki University Central Hospital
Dept. of Otorhinolaryngology
Haartmaninkatu 4E
FIN-00290 Helsinki
Finland