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# Cetirizine and pseudoephedrine retard, given alone or in combination, in patients with seasonal allergic rhinitis*

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SUMMARY

*We compared the efficacy and safety of cetirizine (5 mg), pseudoephedrine retard (120 mg), and the combination of cetirizine (5 mg) with pseudoephedrine retard (120 mg), each given twice daily for two weeks to subjects with pollen-associated allergic rhinitis. The study was multicentre and of randomized, double-blind, parallel-group design. Five rhinitis symptoms were rated according to severity on a scale of 0-3, daily by patients and at each clinic visit by investigators. A total of 687 patients, aged 9-66 years (mean: 32 years) was randomised to treatment (cetirizine: 231; pseudoephedrine: 226; combination: 230). On entry, the three groups were comparable in relevant respects. The primary outcome measure was based on the five symptoms assessed by the patients over the 2-week treatment period. The combination was more effective, providing at least 20% more "comfortable days" (symptoms absent or at most mild) than cetirizine or pseudoephedrine given alone (median values: 53.3%, 30.8%, and 33.3%, respectively; $p<0.001$). For nasal obstruction, the combination (mean score: 1.19) was more effective than cetirizine (mean score: 1.43; $p=0.0005$), but there was little difference between the combination and pseudoephedrine (mean score: 1.22; not significant). Sneezing, rhinorrhoea, nasal and ocular pruritus were better controlled by combination (mean 4-symptom score: 0.77) than by pseudoephedrine alone (mean 4-symptom score: 1.12; $p<0.001$) and also better than by cetirizine alone (mean 4-symptom score: 0.93; $p<0.001$). No unexpected adverse reactions were observed. A combination of cetirizine and pseudoephedrine retard is well tolerated and superior to each given alone for moderate to severe allergic seasonal rhinitis, especially when nasal obstruction is a predominant symptom.*

*Keywords: cetirizine, pseudoephedrine, seasonal rhinitis, allergic rhinitis*

## INTRODUCTION

The treatment of symptoms of seasonal allergic rhinoconjunctivitis often requires the use of an antihistamine to control symptoms primarily mediated by histamine, such as sneezing, rhinorrhoea, nasal and ocular pruritus, together with a decongestant to improve nasal congestion when it is a prominent symptom.

Each new fixed-combination product must be shown to be more effective than its components given as sole therapy. More precisely, the combination must at least provide better control of nasal obstruction than the antihistamine alone, and be superior to pseudoephedrine alone in treating the other symptoms of rhinitis.

Cetirizine is a potent, selective $H_1$-antagonist of established efficacy and good tolerability in the treatment of seasonal and perennial allergic rhinitis (Falliers et al., 1991; Mansmann et al., 1992; Masi et al., 1993; Jobst et al., 1994). Cetirizine is normally taken as a single daily dose of 10 mg, but a dose of 5 mg twice daily has been shown to be as effective (Wassemlan et al., 1991).

Relief of nasal congestion by pseudoephedrine, taken orally, is well documented, both when it is taken alone (Roth et al., 1977; Hamilton et al., 1982) and in combination with an $H_1$-antagonist agent (Backhouse et al., 1990; Bronsky et al., 1995; Bertrand et al., 1996; Dockhorn et al., 1996). The maximal daily dose of pseudoephedrine is 240 mg, in adults and children 12 years and over, even in over-the-counter products in the United States (USCFR, 1996).

The present study examined the efficacy and safety of cetirizine (5 mg) and pseudoephedrine retard (120 mg), each given twice

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daily, with a combination formulation of cetirizine and pseudoephedrine in subjects with pollen-associated allergic rhinitis. A placebo group was not considered to be needed as the trial aimed at evaluating the superiority of the combination over each of its components.

## MATERIAL AND METHODS

### *Patients*

The study was multicentre and of double-blind design. Patients were allocated, in blocks of three, stratified by centre, from a computer-generated randomisation list, to one of three treatments: 5 mg cetirizine alone; 120 mg pseudoephedrine retard alone; and the same doses of both agents in combination. Treatment with each regimen was given twice daily for two weeks to subjects with pollen-associated allergic rhinitis. A total of 43 centres participated in the study, 30 in France and 13 in Germany. The study was performed between March and September 1992, when pollen counts were high (data not shown).

The study was conducted in accordance with the amended Declaration of Helsinki (Tokyo, 1991) and the European Community Guidelines on Good Clinical Practice (1990). Patients, their parents or guardians gave their written informed consent and the study protocol was approved by relevant Ethics Committees in France and Germany.

The study required three visits of the patient: on entry, review after one week, and a final visit after two weeks' treatment. Male and female out-patients (aged 12-65 years) with a documented history of pollen-associated allergic rhinitis for at least one year and skin or RAST tests positive to seasonal allergens were admitted to the study. Women of childbearing potential had to be using a medically acknowledged method of contraception and a negative pregnancy test was required prior to enrollment. On entry, all patients presented with nasal obstruction together with at least two of the following symptoms of rhinitis: sneezing, rhinorrhoea, nasal pruritus, or ocular pruritus. Symptoms were scored on a 4-point scale: "0": absent; "1": mild (present but not disturbing); "2": moderate (disturbing but not hampering daily activities or sleep); and "3": severe (hampering daily activities and/or sleep). Nasal obstruction on the day of admission was at least moderate in degree (score 2) and the total score for the five symptoms was at least 8 (of a possible 15), indicating rhinitis of moderate to severe degree.

Patients to whom any of the following criteria applied were not eligible for inclusion: (1) asthma, requiring either a change in treatment, or systemic or inhaled corticosteroids in a dose more than 400 µg/day; (2) atopic dermatitis or urticaria requiring antihistamines or systemic or topical corticosteroids; (3) an upper respiratory tract infection present on the day of admission; (4) obstructive nasal polyps or significant septal deviation; (5) relevant renal, hepatic or cardiovascular disease requiring treatment; (6) hypertension; (7) hyperthyroidism; (8) diabetes; (9) glaucoma; (10) prostatic hypertrophy; (11) urinary retention; (12) hypersensivity to cetirizine or pseudoephedrine; and (13) an infection requiring antibiotic treatment. Other reasons for exclusion were: (1) clinically relevant abnormalities unrelated to allergic rhinitis; (2) escalating doses of desensitization therapy; and (3) participation in another drug trial during the preceding three months. Pregnant or lactating women were not included.

Patients who had taken any of the following medications within the periods specified were excluded from entry: (1) astemizole (6 weeks); (2) systemic corticosteroids, ketotifen or MAO inhibitors (2 weeks); (3) topical corticosteroids or sedatives (1 week); or (4) nasal decongestants, antihistamines other than astemizole and ketotifen, and nasal or ocular cromoglycate (2 days). Concomitant use of any of these agents during the trial led to withdrawal, as well as other protocol violations, inefficacy, adverse events or personal reasons.

### *Treatment*

Patients were randomized to one of the following treatment regimens: (1) cetirizine (5 mg) and pseudoephedrine retard placebo; (2) pseudoephedrine retard (120 mg) and cetirizine placebo; and (3) cetirizine (5 mg) and pseudoephedrine (120 mg). All medications were in capsules of identical appearance and taken twice daily with meals. No rescue medication was provided.

Medications prohibited during the study were corticosteroids (except inhaled steroids in a dose ≤400 µg/day), sedatives, topical nasal and ocular medications, appetite suppressants, amphetamine CNS stimulants, cromones other than by inhalation, and MAO inhibitors.

Medications for the treatment of asthma (theophylline, ß2-sympathomimetic drugs, inhaled cromoglycate, nedocromil, inhaled corticosteroids in a dose ≤400 µg/day) and non-steroidal topical agents for atopic dermatitis could be taken, provided that dosage remained unchanged.

### *Assessments*

On entry to the study, the findings from history and physical examination were recorded. On entry, at review one week later and at the final visit, investigators evaluated the following symptoms of allergic rhinitis: nasal obstruction, sneezing, rhinorrhoea, nasal pruritus, and ocular pruritus - using the 4-point scale described above.

Patients evaluated the same symptoms (sneezing, runny nose, blocked nose, itchy nose, and itchy eyes) each day using the same 4-point scale and the results, entered in the patients' diaries, constituted the primary efficacy variables. At the final assessment, the investigator made a global evaluation of the effect of treatment using the following 5-point scale: "0": worse; "1": no change; "2": slight improvement; "3": marked improvement; and "4": symptom-free.

Heart rate and blood pressure were checked at each visit; all adverse events together with outcome, severity, duration and possible causal relationship with the study drugs were recorded and classified according to the COSTART dictionary (DHHS, 1989). Blood was taken for routine laboratory safety tests (full blood count, haematocrit, SGOT, SGPT, total serum bilirubin, blood urea, and plasma creatinine) at the first and last visits.

Returned tablets were counted to determine compliance with study medication, which was required to be between 80 and 120%.

*Statistical considerations*

*Patients' evaluations*: The primary efficacy measure was based on the scores for the five symptoms, as assessed by the patients, over the total treatment period. The highest score of any one of the five symptoms, i.e. the score of the most severe symptom, was calculated each day for each patient, and this was called the "maximal symptom score." The percentage of days with a maximal score of 0 or 1, called "comfortable" days, was computed from the second day of treatment to the day before the last visit. This primary outcome measure was selected since in our opinion it provides the most clinically relevant global measure of effective treatment of rhinitis, i.e. when symptoms do not disturb daily activities or sleep.

The Kruskal-Wallis test was used to compare the distribution of this variable between study groups, with a significance level of 5%. Comparisons of each of cetirizine and pseudoephedrine with the combination were performed using the Wilcoxon rank sum test, with a significance level of 3%.

Secondary efficacy variables were the mean 5-symptom score, the mean 4-symptom score (excluding nasal congestion) and individual mean symptom scores, over the whole treatment period. Global comparisons were performed on the variable using one-way analysis of variance, and two-by-two comparisons were performed using Student's t test.

*Investigators' evaluations:* The severity of rhinitis at each visit was assessed by selecting the highest score of the five symptoms. They were compared at each visit using the Cochran-Mantel-Haenszel (CMH) test stratified according to baseline (highest score at visit 1). Investigators' global evaluations at the end of the study were also compared using the CMH test.

*Safety:* The number of patients in each treatment group with none, one, two, three or more adverse events was compared using the CMH test.

Data from all patients receiving treatment were analysed on an intention-to-treat basis. Analyses were performed using SAS software, Versions 6.07 and 6.09 for VMS.

## RESULTS

Of 687 patients with pollen-associated allergic rhinitis randomized in the study by 43 investigators, 231 were randomized to cetirizine, 226 to pseudoephedrine and 230 to combination treatment with cetirizine and pseudoephedrine (Table 1). Three patients in each group did not return their daily record cards. A total of 616 patients (89.7%) evenly distributed between the three treatment groups completed the study. The reasons for withdrawal in 71 patients were lack of efficacy (30 patients); adverse events (22 patients); and other reasons unrelated to study drugs, mostly protocol deviations (19 patients; Table 1).

The three groups were closely comparable in baseline characteristics: age, sex, body weight, allergies, duration of rhinitis, and severity of symptoms (Table 2). Since all patients had to have at least one symptom of moderate severity to be eligible, there were no "comfortable days" at baseline. As requested, nasal obstruction was of moderate to severe degree and a prominent symptom with mean scores of 2.2-2.3 across the three groups (Table 2).

Table 1. Patients enrolled and completing the study: Reasons for withdrawal.

| | cetirizine | pseudo-ephedrine | combination | totals |
|---|---|---|---|---|
| number enrolled | 231 | 226 | 230 | 687 |
| number | 208 | 198 | 210 | 616 |
| completed (%) | (90) | (87.6) | (91.3) | (89.7) |
| number | 23 | 28 | 20 | 71 |
| withdrawn (%) | (10) | (12.4) | (8.7) | (10.3) |
| reasons for withdrawal: | | | | |
| – lack of | 11 | 13 | 6 | 30 |
| efficacy (%) | (4.8) | (5.8) | (2.6) | (4.4) |
| – adverse | 6 | 7 | 9 | 22 |
| event (%) | (2.6) | (3.1) | (3.9) | (3.2) |
| – other (%) | 6 | 8 | 5 | 19 |
| | (2.6) | (3.5) | (2.2) | (2.8) |

Table 2. Patients' characteristics at baseline.

| | cetirizine (n=231) | pseudo-ephedrine (n=226) | combination (n=230) |
|---|---|---|---|
| *sex (%):* | | | |
| M | 48 | 49 | 53 |
| F | 52 | 51 | 47 |
| *age (years):* | | | |
| mean | 32 | 34 | 31 |
| range | 12-66 | 12-65 | 9-65 |
| *weight (kg):* | | | |
| mean | 66 | 65 | 66 |
| range | 34-115 | 35-94 | 27-100 |
| *positive allergy tests* (% patients):* | | | |
| grass | 83 | 84 | 84 |
| trees | 54 | 58 | 56 |
| weeds | 41 | 41 | 37 |
| mites, animal danders, moulds | 22 | 24 | 23 |
| *duration of rhinitis (years):* | | | |
| mean | 8 | 8 | 9 |
| *severity of rhinitis (mean scores from patient diaries):* | | | |
| • sneezing | 2.02 | 1.99 | 1.93 |
| • runny nose | 2.07 | 2.00 | 1.99 |
| • itchy nose | 1.76 | 1.79 | 1.71 |
| • itchy eyes | 1.83 | 1.75 | 1.68 |
| • blocked nose | 2.28 | 2.24 | 2.29 |
| • 5 symptoms | 1.99 | 1.96 | 1.92 |
| • 4 symptoms** | 1.92 | 1.88 | 1.83 |

*: not all allergens were tested in every patient; **: excluding blocked nose

Average compliance with treatment was estimated at 97-99%. The numbers and types of concomitant therapies prescribed during the study were also similar in the various groups and consisted chiefly of anti-asthmatics (28-32 in each group), topical nasal preparations (13-15 in each group), ophthalmic preparations (9-15 in each group) and maintenance desensitization (11-13 in each group).

*Patient assessments*

*Five symptoms:* At baseline, all patients had moderate to severe symptoms and mean scores were comparable (Table 2). During the 2-week treatment period, the proportion of "comfortable" days (symptoms absent or mild at the most) was significantly ($p<0.001$) greater with the combination than with either cetirizine or pseudoephedrine alone; the median values were 53.3%, 30.8% and 33.3%, respectively, and the mean values 50.5%, 39.8% and 37.2%, respectively (Figure 1). The same conclusion was reached for the mean 5-symptom scores which were 0.85, 1.03 and 1.14, respectively (Table 3).

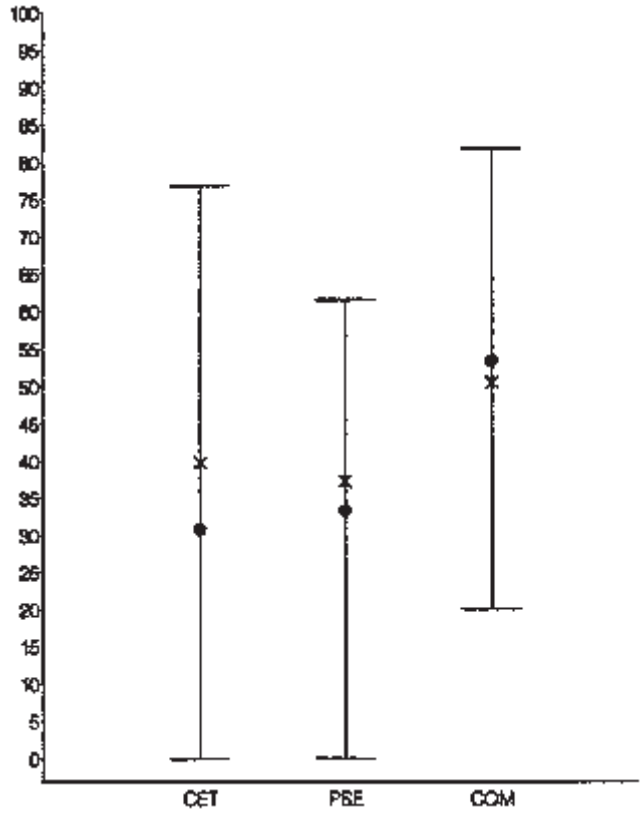


Figure 1. Percentage of "comfortable" days (no or only mild symptoms); •: median; ×: mean; bars represent the first and third quartile; CET: cetirizine; PSE: pseudoephedrine; COM: combination.

Table 3. Mean scores over total treatment period for five symptoms, four symptoms and individual symptoms (daily record cards).

| | cetirizine (n=228) | pseudo-ephedrine (n=223) | combination (n=227) |
|---|---|---|---|
| 5 symptoms | 1.03*** | 1.14*** | 0.85 |
| 4 symptoms (excluding blocked nose) | 0.93*** | 1.12*** | 0.77 |
| blocked nose | 1.43*** | 1.22 | 1.19 |
| sneezing | 0.91** | 1.20*** | 0.74 |
| runny nose | 1.11*** | 1.25*** | 0.90 |
| itchy nose | 0.90** | 1.06*** | 0.75 |
| itchy eyes | 0.81 | 0.94*** | 0.67 |

comparisons versus combination: **$0.001<p\leq0.01$;***$p<0.001$

*Four symptoms:* The mean score of the four symptoms (sneezing, rhinorrhoea, nasal and ocular pruritus) over the total treatment period was significantly ($p<0.001$) lower for the combination (0.77) than for cetirizine (0.93) or pseudoephedrine (1.12) alone (Table 3).

*Individual symptoms:* Baseline scores for all symptoms were similar in the three groups (Table 2). The pattern and time-course of improvement in mean scores is shown in Figure 2 (graphs 1-5). Improvement was significantly ($p\leq0.01$) greater with combination treatment than with cetirizine for all symptoms (except itchy eyes) and greater than pseudoephedrine alone for all symptoms, except nasal congestion (Table 3).

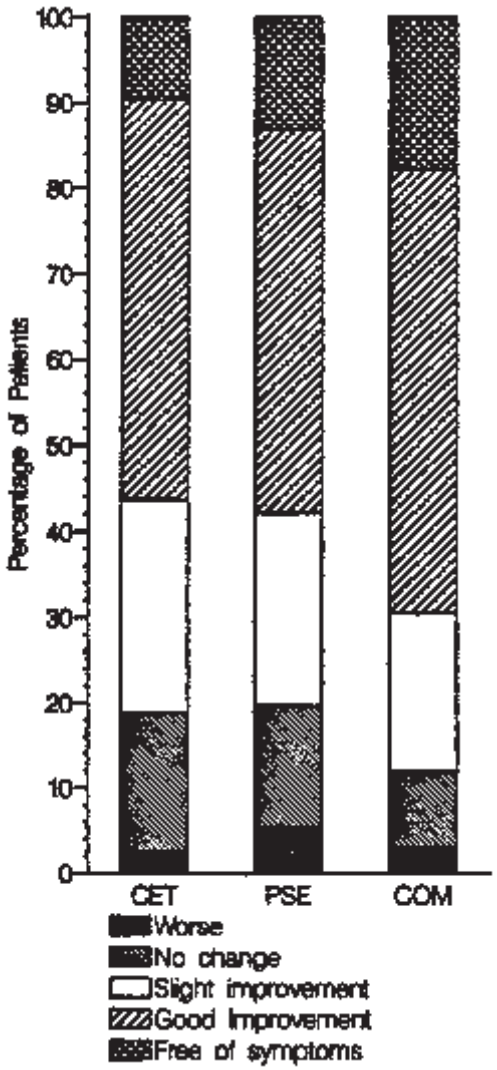


Figure 3. Global evaluation of treatment by investigators (CET: cetirizine; PSE: pseudoephedrine; COM: combination).

*Investigators' assessments*

*Maximal symptom scores:* The mean maximal score of the five symptoms as assessed by investigators was calculated for each visit. Baseline values were similar in the three groups (2.77-2.78). Investigators judged combination therapy (mean maxi-

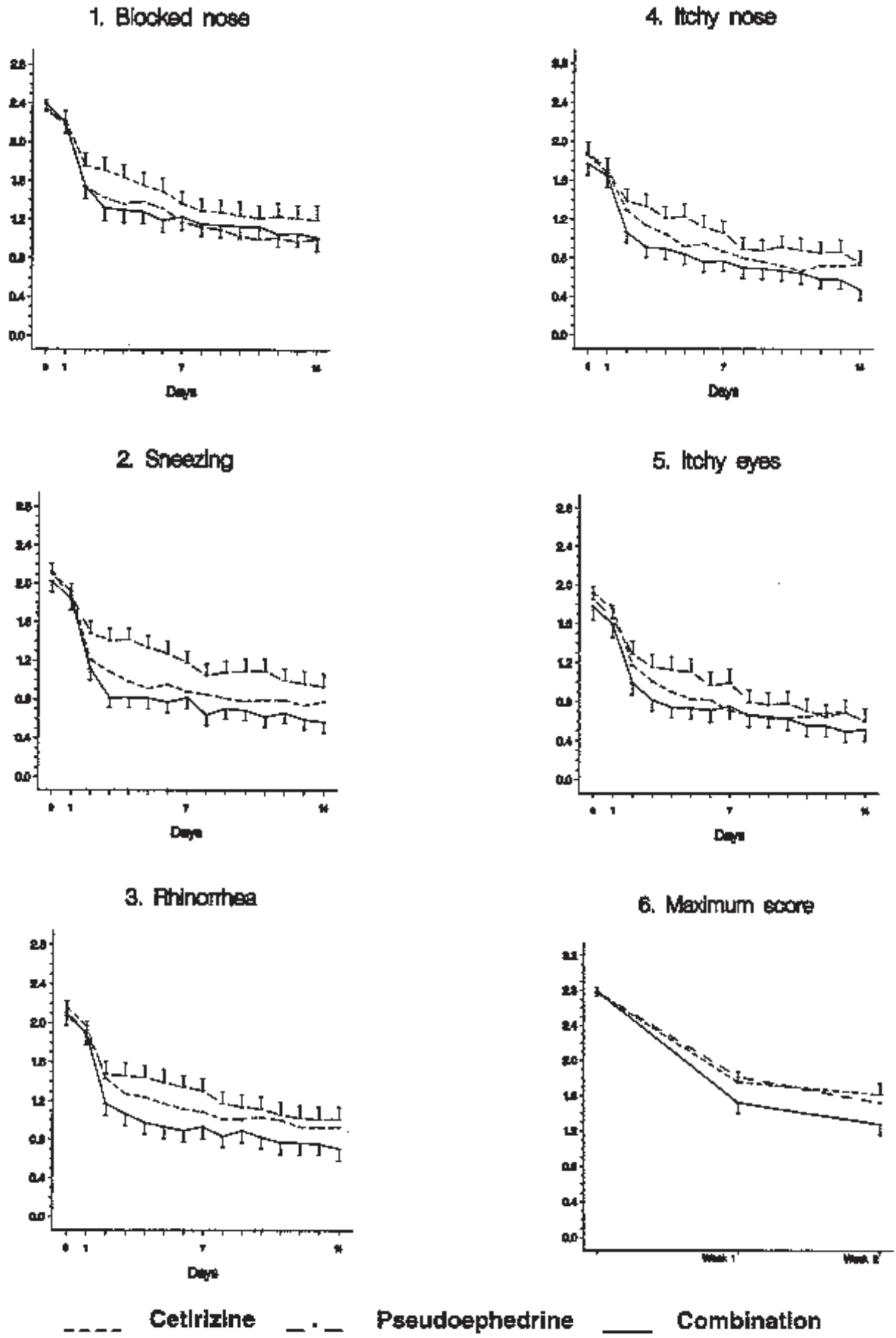


Figure 2. Graphs 1-5: Mean individual symptom scores rated daily by patients. Graph 6: Mean maximal symptom scores rated by investigators at the visits (bars represent two standard errors).

mum score: 1.53) to be significantly more effective than either cetirizine or pseudoephedrine (mean maximum score: 1.76 and 1.82, respectively; $p<0.01$) as sole therapy after the first week and also after the second week (combination: 1.29; cetirizine: 1.63, [$p<0.001$]; pseudoephedrine: 1.53 [$p=0.031$]). The pattern of response for the mean maximal score of the five symptoms is apparent in Figure 2 (graph 6). Nasal obstruction scores with combination treatment were significantly lower than after cetirizine ($p<0.001$) but not pseudoephedrine, after both one and two weeks (data not shown).

*Global evaluation of treatment:* Analysis of investigators' global evaluations of treatment also confirmed that combination therapy was significantly more effective than either cetirizine ($p=0.001$) or pseudoephedrine ($p=0.007$) taken alone (Figure 3). Good to excellent results were reported by 69% of the patients in the combination group, in 56% of the patients in the cetirizine group, and in 58% in the pseudoephedrine group.

*Safety*

Adverse events (Table 4), whether or not considered drug-related, were reported by 54 patients (23.4%) taking cetirizine, 68 patients (30.1%) with pseudoephedrine, and 68 patients (29.6%) with combination treatment (not significant). There were no serious adverse events. Adverse events were infrequently considered severe and led to withdrawal from the study in 6 patients (2.6%) on cetirizine, 7 patients (3.1%) on pseudoephedrine, and 9 patients (3.9%) on combination treatment.

Table 4. Summary of adverse events.

| | cetirizine (n=231) No. (%) | pseudo-ephedrine (n=226) No. (%) | combination (n=230) No. (%) |
|---|---|---|---|
| number of patients with adverse events | 54 (23.4) | 68 (30.1) | 68 (29.6) |
| number of patients with severe adverse events* | 7 (3) | 15 (6.6) | 17 (7.4) |
| number of patients withdrawn because of adverse events | 6 (2.6) | 7 (3.1) | 9 (3.9) |
| number of patients (%) with most frequent adverse events: | | | |
| asthenia | 9 (3.9) | 0 | 5 (2.2) |
| headache | 10 (4.3) | 16 (7.1) | 9 (3.9) |
| somnolence | 14 (6.1) | 7 (3.1) | 3 (1.3) |
| insomnia | 0 | 25 (11.1) | 16 (6.9) |
| nervousness | 0 | 5 (2.2) | 3 (1.3) |
| dry mouth | 4 (1.7) | 10 (4.4) | 17 (7.4) |
| abdominal pain | 3 (1.3) | 6 (2.7) | 1 (0.4) |

*possibly drug-related adverse events: cetirizine: 2; pseudoephedrine: 17; combination: 15

Adverse events reported most frequently were somnolence (6.1%) and headache (4.3%) with cetirizine, and in those on pseudoephedrine and combination treatment, headache (pseudoephedrine 7.1%; combination 3.9%), sleep disorders, mostly insomnia (pseudoephedrine 11.1%; combination 6.9%) and dry mouth (pseudoephedrine 4.4%; combination 7.4%). Minor laboratory test abnormalities in 7 patients were not considered clinically relevant. Mean heart rate increased by 2.2 and 3.2 beats/min, between the first and the last visit, respectively in the pseudoephedrine and combination groups.

## DISCUSSION

These results in a large group of patients with pollen-associated allergic rhinitis of moderate to severe degree show that combined treatment with cetirizine and pseudoephedrine provides greater symptom relief than either agent alone. The combination led to more improvement than pseudoephedrine alone in "histamine-induced" symptoms of sneezing, rhinorrhoea, nasal and ocular pruritus. Compared with cetirizine, the combination was, as anticipated, more effective in relieving nasal congestion, but also the other three nasal symptoms (sneezing, rhinorrhoea and nasal pruritus). A likely explanation for this finding is a "carry-over" effect due to the good relief from the nasal congestion on the evaluation of the other nasal symptoms.

We defined the primary criterion of efficacy as the overall effect of treatment over the 2-week study period and expressed this as the percentage of "comfortable days", i.e. days when patients were without symptoms, either moderate or severe in intensity. We have previously explained why we believe this analysis is to be preferred (Masi et al., 1993; Jobst et al., 1994) to a more conventional analysis of mean (or total) symptom scores. This analysis is more demanding since it is driven by the least responsive symptom, but in the present instance it helped in separating the effects of the three treatments. However, we also analysed the mean scores to confirm our findings and again found the combination to be more effective than either of its components.

The results of investigators' evaluations, made at review visits after one and two weeks, also confirmed the greater efficacy of combination treatment. For this analysis we used again the maximal scores, i.e. the scores of the most severe symptom, to characterize disease severity. Global evaluations by investigators at the end of the study also favoured combination treatment over the single agents.

The incidence of adverse events was in line with the known safety profiles of the agents and there were no unexpected or serious adverse events. The incidence of severe adverse events was twice as high with combination treatment compared to cetirizine alone. This is the price which must be paid for increased efficacy, as suggested by the drop-out rates: more withdrawals because of adverse events with combination treatment and, by contrast, more due to lack of efficiency with the single agents.

The results of this trial are consistent with those of comparable combination products (Backhouse et al., 1990; Bronsky et al., 1995; Dockhorn et al., 1996) and of a previous study in which cetirizine and pseudo-ephedrine alone were compared with the combination in patients with perennial allergic rhinitis (Bertrand et al., 1996). We conclude that a combination of cetirizine (5 mg) and pseudoephedrine retard (120 mg), both given twice daily over a 2-week period, is a well tolerated and effective treatment for the symptoms of seasonal allergic rhinitis, particularly when nasal congestion is a prominent symptom.

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REFERENCES

1. Backhouse Cl, Rosenberg RM, Fidler C (1990) Treatment of allergic rhinitis: A comparison of a combination tablet of terfenadine and pseudoephedrine with individual ingredients. Br J Clin Pract 44: 274-279.
2. Bertrand B, Jamart J, Marchal JL, Arendt C (1996) Cetirizine and pseudoephedrine retard alone and in combination in the treatment of perennial allergic rhinitis: A double-blind multicentre study. Rhinology 34: 91-96.
3. Bronsky E, Boggs P, Findlay S, Gawchik S, Georgitis J, Mansmann H, Sholler L, Wolfe J, Meltzer E, Morris R, Munk Z, Paull B, Pleskow W, Ratner P, Danzig M, Harrison J, Lorber R (1995) Comparative efficacy and safety of a once daily loratadine/pseudoephedrine combination versus its components alone and placebo in the management of seasonal allergic rhinitis. J Allergy Clin Immunol 96: 139-147.
4. DHHS (1989) "COSTART" Coding Symbols for Thesaurus of Adverse Reaction Terms. Department of Health and Human Services/Food and Drug Administration, Washington, USA.
5. Dockhorn RJ, Williams BO, Sanders RL (1996) Efficacy of acrivastine with pseudoephedrine in treatment of allergic rhinitis due to ragweed. Ann Allergy Asthma Immunol 76: 204-208.
6. Falliers CJ, Brandon ML, Buchman E, Connell JT, Dockhorn R, Leese PT, Miller J, Wasserman Sl, Zeterberg JM, Altman R, Love S, Samuels LL (1991) Double-blind comparison of cetirizine and placebo in the treatment of seasonal rhinitis. Ann Allergy 66: 257-262.
7. Hamilton LH, Chobanian SL, Cato A, Perkins JG (1982) A study of sustained action pseudoephedrine in allergic rhinitis. Ann Allergy 48: 87-92.
8. Jobst S, Van den Wijngaart W, Schubert A, Van de Venne H (1994) Assessment of the efficacy and safety of three dose levels of cetirizine given once daily in children with perennial allergic rhinitis. Allergy 49: 598-604.
9. Mansmann Jr. HC, Altman RA, Berman BA, Buchrnan E, Dockhorn RJ, Leese PT, Love SJ, Middleton Jr E (1992) Efficacy and safety of cetirizine therapy in perennial allergic rhinitis. Ann Allergy 68: 348-353.
10. Masi M, Candiani R, Van de Venne H (1993) A placebo-controlled trial of cetirizine in seasonal allergic rhinoconjunctivitis in children aged 6 to 12 years. Pediatr Allergy Immunol 4 (Suppl 4): 47-52.
11. Roth RP, Cantekin EI, Bluestone CD, Welch RM, Cho YW (1977) Nasal decongestant activity of pseudoephedrine. Ann Otol 86: 235-242.
12. USCFR (1996) Labeling of Nasal Decongestant Drug Products. Code of Federal Regulations 21/CFR341.80, p. 258.
13. Wassemlan SI, Broide DH, Marquardt DL (1991) Cetirizine therapy for seasonal allergic rhinitis: Alternative dosage schedules. Clin Ther 13: 707-713.

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