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Treatment of seasonal allergic rhinitis – a double blind, group comparative study of terfenadine and dexchlorpheniramine

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SUMMARY

In order to evaluate the efficacy of and adverse reactions to terfenadine compared to dexchlorpheniramine, a double blind, group comparative study was carried out in 42 patients suffering from grass-pollen induced allergic rhinitis. The treatment was either terfenadine tablets 60 mg twice daily or dexchlorpheniramine tablets 6 mg twice daily. Nasal and eye symptoms as well as tiredness were rated daily on a scale from 0 (absent) to 3 (severe). Terfenadine and dexchlorpheniramine performed almost equally well in keeping symptoms at a mild level with a superiority of dexchlorpheniramine in the control of runny nose. Dexchlorpheniramine was associated with a significant increase in the score for tiredness in contrast to terfenadine which caused no significant change. Two patients in the group treated with dexchlorpheniramine stopped treatment because of tiredness. Other adverse reactions were few, mild and transient.

INTRODUCTION

Antagonists of H_1-receptors (antihistamines) are widely used in the treatment of allergic rhinitis. However their therapeutic value is limited by central nervous system effects, especially sedation.

Terfenadine is a new antihistamine (Hüther et al., 1977), free from CNS effects (Clarke et al., 1978; Kulshrestha et al., 1978). This is probably due to the fact that the drug does not cross the blood-brain barrier. (Rose et al., 1982; Wiech and Martin, 1982).

The incidence of drowsiness with terfenadine is found to be similar to that with placebo (Backhouse et al., 1982; Brandon and Weiner, 1982; Brewster, 1982). Moreover, terfenadine does not potentiate the sedative effect of alcohol or diazepam (Moser et al., 1978).

A number of clinical trials have demonstrated the efficacy of terfenadine in the treatment of seasonal and perennial allergic rhinitis, both in comparison with other antihistamines and with placebo (Sorkin and Heel, 1985).

The aim of this study was to compare the efficacy of and adverse reactions to terfenadine and dexchlorpheniramine (Polaramin®) in patients suffering from seasonal allergic rhinitis.

MATERIAL AND METHODS

42 patients, aged 15 years or more, with a clinical diagnosis of grass-pollen induced allergic rhinitis were recruited to the study.

The rhinitis should have a duration of at least two seasons and be confirmed by a positive skin prick test. Patient characteristics are given in Table 1.

Exclusion criteria were: 1. Use of antihistamines within 3 days prior to start of the trial. 2. Use of DSCG (Lomudal®) 3 days prior to start of the trial medication. 3. Corticosteroid therapy (oral corticosteroids not allowed for two weeks prior to start of the trial medication and depot corticosteroids not allowed for eight weeks). 4. Hyposensitization therapy given during the previous 12 months. 5. Pregnancy or nursing.

The trial was carried out during summer 1985 as double-blind group comparative study. The trial started with a seven day run-in period, followed by a treatment period of three weeks, all patients beginning treatment on June 1st. Anamnestic and objective data were recorded at study entry and after the treatment. The patients were randomized and received one of the following treatments twice daily using a double-dummy technique: 60 mg terfenadine + placebo dexchlorpheniramine or 6 mg dexchlorpheniramine + placebo terfenadine.

Table 1. Patient characteristics.

		dexchlor-pheniramine	terfenadine
no. of patients entered		21	21
withdrawn/excluded		3	1
no. of patients in the analysis of efficacy		18	20
sex ratio (male/female)		10/8	8/12
age (years)	mean	31.8	31.1
	range	19–63	18–49
duration of disease (years)	mean	14.4	16.0
	range	7–30	5–30

No further medication for allergic rhinitis was permitted during the trial. However, if the symptoms became intolerable during the run-in period the patients could use eye drops (antazoline 5 mg/ml + naphazoline 0.25 mg/ml) or clemastine tablets 1 mg. If additional medication for allergic rhinitis was used for five days or less during the treatment period only these days were omitted from analysis. When eye-drops were used, the scores for eye symptoms were not used. Each patient was provided with diary cards on which the following symptoms

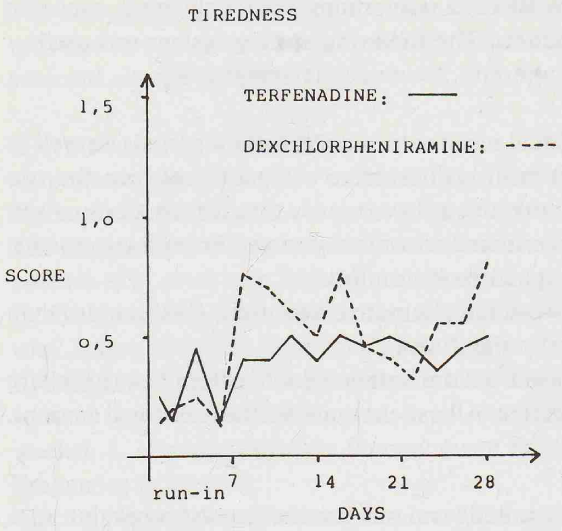
were to be recorded every day: Blocked nose, runny nose, itchy nose, sneezing bouts, eye symptoms and tiredness. The following scoring system was used:
0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms,
3 = severe symptoms.
For different scores, the individual mean value during certain periods, as well as individual differences of such mean values, were compared between the two treatment groups. Wilcoxon's rank sum test was used in the analysis. Comparison was also made between the run-in and treatment periods for both treatments, separately, using Wilcoxon's signed rank sum test.
In any test of significance a two-sided alternative was used. *P*-values less than 0.05 were considered statistically significant.
Approval of the trial was obtained from the National Board of Health and Welfare and from the local ethics committee. All patients gave written informed consent.

RESULT

Due to a cold and wet summer pollen level was low the first 2½ week, but rose towards the end of the study period. The mean scores for nasal and ocular symptoms were regarded as about "mild" (score 1) during the run-in period in both treatment groups with a slight increase in symptom severity towards the end of the period. A tendency towards higher scores in the dexchlorphendiramine group was seen, but no difference was significant (Table 2). Symptom scores remained at a low lovel during treatment in both grtoups also when the days with increased pollen levels were considered separately. When the symptom scores were compared, it was found that dexchlorpheniramine significantly reduced the scores for

Table 2. The mean symptom score during the run-in and treatment periods.

		dexchlor	terfenadine	mean diff. between treatments
blocked nose	run-in	0.66	0.63	NS
	treatment	0.55	0.63	NS
	mean diff. vs. run-in	NS	NS	
itchy nose	run-in	0.80	0.66	NS
	treatment	0.37	0.53	NS
	mean diff. vs. run-in	$p < 0.01$	NS	
sneezing	run-in	0.92	0.64	NS
	treatment	0.58	0.65	NS
	mean diff. vs. run-in	NS	NS	
tiredness	run-in	0.23	0.24	NS
	treatment	0.50	0.38	NS
	mean diff. vs. run-in	$p < 0.001$	NS	



Fugure 1.
The mean scores for tiredness during the "run-in" and treatment periods.

itchy nose (Table 2), runny nose and eye symptom. No changes were significant in the terfenadine group.

There was no significant difference between the scores for tiredness during the run-in and the terfenadine medication period, while dexchlorpheniramine treatment was associated with a significant increase of symptoms (Table 2 and Figure 1). The mean scores were lower during terfenadine than during dexchlorpheniramine treatment, but did not reach statistical significance.

Six patients in the terfenadine group scored for tiredness during some days of the run-in period and 11 scored during the actual treatment. The corresponding figures for the dexchlorpheniramine group was four and 18. Six out of these 18 patients found the tiredness severe and two of them withdrew from the study after three and eight days of treatment, respectively. Two patients in the terfenadine group scored their tiredness as severe on some occasion during treatment.

Two patients, one from each treatment group were excluded from the analysis because of protocol violations (lost diary card, continuous use of additional antihistamine).

DISCUSSION

In spite of the low pollen levels during the first part of the trial, symptom severity was reduced in both groups when treatment commenced. Both treatments controlled the symptoms of allergic rhinitis very well, also during the period of high pollen levels. This confirms the results of several other studies (Sorkin and Heel, 1985). Although some differences in symptom severity existed between the groups during the run-in period, they were too small to be of clinical relevance

and the two groups are regarded as fully comparable.
A better symptom control with dexchlorpheniramine was seen in some symptoms, but the difference is presumably of minor importance since symptom severity in both groups were mild during the whole treatment period. Although dexchlorpheniramine is viewed as a mild sedating antihistamine it was associated with more sedation than terfenadine. In the first few days of dexchlorpheniramine treatment there was a marked increase in mean symptom score for tiredness (Figure 1). The clinical relevance of this finding is shown by the fact that more patients regarded their tiredness as severe in the dexchlorpheniramine than in the terfenadine group. In fact, two patients on dexchlorpheniramine left the study because of tiredness. However, judging from the day-by-day recording of scores for tiredness a tolerance to the sedative effects of dexchlorpheniramine may have developed after about one week of treatment and no difference in sedation was evident during the last half of the three week treatment period. Nevertheless, the difference in sedative properties between dexchlorpheniramine and terfenadine is important, since antihistamines are mainly used symptomatically and patients compliance is crucial during the first days of treatment.
The conclusion of this trial is that terfenadine and dexchlorpheniramine show almost comparable efficacy in the treatment of seasonal allergic rhinitis. Dexchlorpheniramine is associated with more sedation than terfenadine.

ZUSAMMENFASSUNG

Um den Effekt und die Nebenwirkungen auf Terfenadine verglichen mit Dexchlorpheniramine zur beurteilen, wurde eine doppel-blinde, vergleichende Untersuchung bei 42 Patienten ausgeführt, die an einem von Gras-Pollen verursachten allergischen Rhinitis leideten. Die Behandlung wurde entweder mit 60 mg Terfenadine-Tabletten zweimal täglich oder mit 6 mg Dexchlorpheniramine-Tabletten zweimal täglich durchgeführt. Nasen- und Augensymptome sowie Müdigkeit wurden täglich von 0 (keinen) bis 3 (schweren) registriert. Terfenadine und Dexchlorpheniramine waren fast gleich wirksam, indem beide Medikamente die Symptome auf einer niedrigen Ebene hielten, jedoch erwies sich Dexchlorpheniramine ein bisschen effektiver in der Verhinderung von laufender Nase. Dexchlorpheniramine war mit einer gesteigerten Müdigkeit verbunden, im Gegensatz zu Terfenadine, das keine signifikante Veränderung verursachte. Zwei Patienten aus der mit Dexchlorpheniramine behandelten Gruppe hörten wegen Müdigkeitserscheinungen mit der Behandlung auf. Sonstige Nebenwirkungen waren wenig, mild und vorübergehend.

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