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A DOUBLE-BLIND, MULTICENTRE STUDY OF THE EFFICACY AND SAFETY OF CETIRIZINE (0.2 or 0.6 mg/kg/day in 2 divided doses for 4 weeks) IN THE TREATMENT OF POLLEN-INDUCED ASTHMA IN CHILDREN BETWEEN 6 AND 14 YEARS OF AGE (Protocol PCF89B092)

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SUMMARY

Sixty-three children between 6 and 14 years of age, suffering from pollen-induced asthma, were included in this double-blind, randomized study which compared two doses of cetirizine (0.2 and 0.6 mg/kg/day) administered for 4 weeks.

Forty-nine patients were evaluable for efficacy of treatment after the first 2 weeks of treatment; 42 patients were evaluable for the full 4 weeks of treatment. The main cause of nonevaluability for efficacy was nonrespect of the prescribed dose (10 cases), due either to poor patient compliance or a mistake in the dose given. All patients were included in the analysis of safety, with the exception of one patient who never started treatment. Rhinconjunctivitis symptoms were consistently less severe in the group treated with the 0.6 mg/kg/day dose, but this difference was not statistically significant. Global evaluations of rhinconjunctivitis symptoms using a visual analogue scale, and global evaluations for the efficacy of treatment (by the patient and investigator) did not show any difference between the 2 treatment groups.

The daytime asthma score for the group treated with 0.6 mg/kg/day was significantly better on the first 2 days and 1st week of treatment. This difference disappeared during the 2nd, 3rd and 4th weeks of treatment. Furthermore, there was no statistically significant difference between the 2 treatment groups for any of the other parameters of efficacy of treatment of asthma (nocturnal asthma, ß-mimetic consumption, global asthma index, proportion of patients presenting with asthma symptoms at visits, severity of asthma symptoms at visits, global evaluation of efficacy of treatment by the patient and the investigator, global evaluation of asthma symptoms by the patient on a visual analogue scale). Taken as a whole, these data do not show the superiority of the 0.6 mg/kg/day dose as compared to 0.2 mg/kg/day.

The safety of the study drug was excellent. Only 2 adverse effects, for which a relationship with the study drug was considered to be possible or probable by the investigator, were reported: 1 case of somnolence at the 0.6 mg/kg dose, and 1 case of joint pain at the 0.2 mg/kg dose. In the latter case, the investigator cited growth pain as a possible cause for the adverse event. No serious laboratory test abnormality was seen.
I. INTRODUCTION

Cetirizine, a metabolite of hydroxyzine, is a powerful and specific antihistamine (anti-H) devoid of significant antiserotonergic, anticholinergic, antiadrenergic, parasympathomimetic, anesthetic or analgesic actions (1). Cetirizine inhibits the recruitment and activation of eosinophils and neutrophils at allergic reaction sites (2-4). It is possible that by this latter mechanism cetirizine inhibits the inflammatory reaction which characterizes the late phase of the allergic response. Cetirizine is registered in several countries for the treatment of pollen-induced allergic rhinitis, perennial allergic rhinitis and chronic urticaria in the adult. The recommended dose for the adult is 10 mg/day. In children between 6 and 12 years of age, cetirizine has been shown to be effective, at a dose of 10 mg/day or 2 x 5 mg/day, in the treatment of perennial allergic rhinitis and seasonal allergic rhinitis.

Today, asthma is considered to be a chronic inflammatory disease of the bronchial tract, with acute exacerbations (5, 6). The antihistamine properties of cetirizine, and its action on neutrophils and eosinophils, constitute two good reasons for investigating the drug's action in asthmatic patients.
The present study was conducted only in France, where the pollen count was considered to be sufficiently high and stable. Only the 0.2 and 0.6 mg/kg/day doses were studied. The objective was to recruit a sufficiently high number of children suffering from pollen-induced asthma so that a statistically and medically significant difference of efficacy between the 2 dosage schedules could be detected. Another important objective was to study the safety of cetirizine at these doses.
II. METHODS

1. Organization of the study

The patients were randomized into 2 parallel groups using the double-blind technique. One group of patients received cetirizine at a dose of 0.2 mg/kg/day in 2 divided doses (CTZ 0.2 group); the other group received cetirizine at a dose of 0.6 mg/kg/day in 2 divided doses (CTZ 0.6 group). In principle, all patients were treated for a total of 4 weeks (limits of 27 to 31 days) in 2 consecutive periods of 2 weeks (limits of 13 to 17 days). The hypothesis to be tested was that both regimens were active on rhinoconjunctivitis symptoms but that only the higher dose (0.6 mg/kg/day) was active on asthma symptoms.
2. Selection of patients

The patients had to be suffering from grass pollen-induced asthma of recent onset (duration of symptoms less than 96 hours). Such a diagnosis could coexist with a diagnosis of perennial asthma. The allergy to grass pollen had to be proven by a skin test or RAST test.

The patients could be either male or female, had to be between 6 and 14 years of age and had to weigh more than 20 kg.

The patients were not to have had, in the 2 weeks preceding inclusion in the study, infections of the ENT system, the upper respiratory tract or the lower respiratory tract.

A treatment-free period was necessary for the following drugs:
- systemic corticosteroids: 6 weeks
- astemizole: 4 weeks
- theophylline and its derivatives, oral β₂-mimetics, anticholinergics, inhaled topical corticosteroids, inhaled cromoglycate, ketotifen: 2 weeks
- nasal topical corticosteroids: 1 week
- other antihistamines had to be interrupted on inclusion in the study
Furthermore, the patients were not allowed to use drugs likely to interfere with the evaluation of efficacy and/or safety of cetirizine: sedatives, psychotropic drugs, anti-inflammatory agents, etc.

The following past history and/or concomitant diseases excluded a patient from the study: a history of status asthmaticus requiring artificial ventilation; chronic obstructive airways disease; hepatic, renal or cardiac insufficiency; a clinically relevant laboratory test abnormality; allergy to hydroxyzine, cetirizine or any other diphenylpiperazine.

Patients in whom there was a high risk of withdrawal from the study or of noncompliance with the conditions of the study were excluded. Patients were not to have participated in another clinical study in the month preceding the present study.

All patients, or their legal representatives, were required to give written consent before participation in the study was authorized.

3. Treatments

3.1 Study drug and dose

The study drug was administered in the form of tablets of identical aspect containing 2.5 mg (batch N°49) or 7.5 mg (batch N°48) of cetirizine. The patients in the CTZ 0.2 group were given 2.5 mg tablets; the patients in the CTZ 0.6 group were given 7.5 mg tablets.

Patients weighing less than 30 kg were given 1 tablet in the morning and 1 tablet in the evening; patients weighing between 30 and 40 kg were given 1.5 tablets in the morning and 1.5 tablets in the evening; patients weighing more than 40 mg were given 2 tablets in the morning and 2 tablets in the evening.
3.2 Concomitant medications

The following concomitant medications were forbidden: corticosteroids (systemic or topical), antihistamines, theophylline and its derivatives, oral β₂-mimetics, anticholinergics and inhaled cromoglycate.
For the treatment of uncontrolled rhinoconjunctivitis symptoms, only topical, nasal and ophthalmic preparations (excluding corticosteroids) were permitted.

For the treatment of uncontrolled asthma symptoms, only inhaled β₂-mimetics, on request, at the minimal required dose, were permitted. Patients whose symptoms required the use of forbidden drugs had to leave the study.

Any use of a concomitant medication was noted by the patient on his or her daily record card, and by the investigator in the case report form.

4. Measurement of efficacy

The following parameters were measured:

4.1 Visits

a) Symptoms of rhinoconjunctivitis (conjunctivitis, nasal obstruction, rhinorrhea, sneezing) in the 2 weeks preceding the visit were evaluated.

Each symptom was evaluated on a four-point scale:
* no symptom: score = 0
* mild symptom (present but not troublesome): score = 1
* moderate symptom (present and troublesome, but not disturbing daytime activity or sleep): score = 2
* severe symptom (present and disturbing daytime activity or sleep): score = 3

b) Symptoms of asthma (wheezing, dyspnea, cough) in the 2 weeks preceding the visit were evaluated. Each symptom was evaluated using the same scale used for the rhinoconjunctivitis symptoms.

c) Physical examination for the signs of rhinoconjunctivitis (conjunctivitis, nasal obstruction, rhinorrhea, sneezing) at each visit. Each sign was evaluated on a four-point scale:
* sign absent: score = 0
* sign present, mild: score = 1
* sign present, moderate: score = 2
* sign present, severe: score = 3

d) Physical examination for the signs of asthma (wheezing, dyspnea, cough) at the visit. Each sign was evaluated using the same scale used for the rhinoconjunctivitis signs.

e) Global evaluation by the patient of his or her rhino-conjunctivitis symptoms using a visual analogue scale from 0 ("very poor" condition) to 100 mm ("excellent" condition).
z) Global evaluation by the patient of his or her asthma symptoms using a visual analogue scale from 0 ("very poor" condition) to 100 mm ("excellent" condition).

g) At the end-of-study visit, global evaluation by the patient and investigator of the efficacy of treatment for rhinoconjunctivitis and asthma using a five-point scale:
   • marked deterioration: score = 0
   • mild deterioration: score = 1
   • unchanged condition: score = 2
   • mild improvement: score = 3
   • marked improvement: score = 4

4.2 Between visits

Between visits, the patients were given a card on which they noted, daily, the following information:

a) Symptoms of asthma during the previous day, evaluated according to a four-point scale:
   • no symptoms: score = 0
   • shortness of breath, but not incapacitated: score = 1
   • shortness of breath interfering with daily activities: score = 2
   • daily activities impossible: score = 3

b) Symptoms of asthma during the preceding night, evaluated according to a four-point scale:
   • normal sleep: score = 0
   • awakened once because of asthma symptoms: score = 1
   • awakened several times because of asthma symptoms: score = 2
   • awake during a large part of the night because of asthma symptoms: score = 3

c) The peak expiratory flow rate was recorded in the morning and evening. The measurements had to be conducted before consumption of β₂-mimetics. Each measurement was taken 3 times and the best of the 3 measurements was recorded on the daily record card.

d) Number of puffs of β₂-mimetics required during the previous day.

e) Number of puffs of β₂-mimetics required during the previous night.
5. Measurement of safety

5.1 Clinical adverse events

At each visit, the patients were questioned about adverse events. In addition, between visits, any adverse event could be noted by the patient on the daily record card. For each adverse event, the investigator was required to note: the dates of onset and disappearance, the frequency, the severity, the relationship to the study drug, whether or not treatment was required, whether or not the dose of the study drug had to be altered, and the outcome.

5.2 Laboratory tests

A sample of blood was drawn at the beginning of the study and another at the end of the study. The following parameters were measured: full blood count including a differential leukocyte count, total bilirubin, SGOT, SGPT, gamma-GT, alkaline phosphatase, urea and creatine.
8. **Statistical considerations**

8.1 **Number of patients**

The inclusion of 120 evaluable patients (60 patients per group) was planned, based on the following criteria:
- principal criterion of analysis: asthma index
  (for definition, see section 8.2)
- smallest clinically pertinent difference between the 2 groups: 1
- intra-group variance: 4 (data from study A117)
- \( \alpha \) error = 5%; \( \beta \) error = 20%

8.2 **Analysis of the principal criterion of efficacy**

The principal criterion of efficacy was the asthma index. This was defined as follows:

\[
\text{asthma index} = \frac{\text{score of } \beta_2\text{-mimetic consumption} + (\text{daytime asthma score} + \text{nocturnal asthma score})}{2}
\]

The daytime and nocturnal scores of asthma were obtained directly from the daily record cards; the \( \beta_2\)-mimetic consumption score was calculated according to the following scale:
- no consumption: score = 0
- 1 puff per day: score = 1
- between 2 and 6 puffs per day: score = 2
- > 6 puffs per day: score = 3

The asthma index, therefore, varied between a minimum of 0 and a maximum of 6. For those patients who were withdrawn from the study because of inefficacy, the maximal asthma index of 6 was attributed from the day of withdrawal from the study onwards.

A mean value for the index was calculated for the first 2 days of the study, and for each week. The 2 treatment groups were compared by the Wilcoxon test.

8.3 **Analysis of the other criteria of efficacy**

a) **Parameters on the daily record card**

For each parameter on the daily record card (daytime asthma symptoms, nocturnal asthma symptoms, \( \beta_2\)-mimetic consumption of the current day, \( \beta_2\)-mimetic consumption of the preceding night, \( \beta_2\)-mimetic consumption over the previous 24 hours, morning peak flow, evening peak flow), the mean was calculated for the first 2 days of treatment and for each week.

The peak flow data were compared using Student's t-test. For the other comparisons, the Wilcoxon test was used.
b) Presence of symptoms and signs of asthma and rhinoconjunctivitis

The symptoms and signs of asthma and rhinoconjunctivitis were evaluated by the investigator at each visit. The proportion of patients showing neither symptoms nor signs in the preceding 2 weeks was calculated, and a comparison was made between the CTZ 0.2 group and the CTZ 0.6 group.

In addition to individual symptoms of asthma and rhinoconjunctivitis, a global symptom for asthma and a global symptom for rhinoconjunctivitis were defined. These global symptoms were considered to be present if any of the individual symptom or sign was present.

Comparisons were made after the 1st, 2nd and final visits. The last visit was the 3rd visit in those patients who completed the study, and the 2nd visit in those who left the study after the 2nd visit.

The proportion of patients with symptoms on the 1st visit was calculated, and a comparison was made between the 2 groups using the Fisher test. The proportion of patients with symptoms at the 2nd visit and at the final visit were compared using the Cochran-Mantel-Haenszel test, with stratification by the criterion "presence/absence of symptoms at the 1st visit".

c) Severity of symptoms and signs of asthma and rhinoconjunctivitis

At each visit, the severity score for each sign of asthma was either the score for the 2 weeks preceding the visit or the score at the visit, whichever was higher. A global severity score for the asthma signs at each visit was defined as the highest score recorded among the individual signs at this visit.

The same method was used to analyse the severity of rhinoconjunctivitis signs. At each visit, the severity score for each rhinoconjunctivitis sign was either the score for the 2 weeks preceding the visit or the score at the visit, whichever was higher. The global severity score for rhinoconjunctivitis signs at each visit was the highest score recorded among the individual scores at this visit. The severity scores for the CTZ 0.2 and CTZ 0.6 groups were compared using the Wilcoxon test.

d) Visual analogue scales

Global evaluations for asthma and rhinoconjunctivitis symptoms by visual analogue scale were compared between the CTZ 0.2 and CTZ 0.6 groups using the Wilcoxon test.
e) Global evaluation of the treatment

Global evaluations (by the patient and the investigator) of the eficacy of treatment of asthma and rhinoconjunctivitis in the 2 treatment groups were compared using the Wilcoxon test.

All statistical tests were conducted using a two-side analysis with a 5% level of significance. They were adjusted to take into account any initial difference between the 2 groups CTZ 0.2 and CTZ 0.6, whether or not the difference was statistically significant.

8.4 Analysis of safety

Given the small number of adverse events, this data was not analysed statistically. For the same reasons, the laboratory test data was not analysed statistically.

8.5 Analysis of compliance

Compliance was calculated, for each 2 week period of treatment, as the ratio (expressed as a percentage) of the number of tablets actually consumed divided by the number of tablets which should have been consumed, according to the patient's body weight and the duration of treatment. The compliance of the CTZ 0.2 and CTZ 0.6 groups was compared using Student's t-test.
III. RESULTS

1. Demography

Sixty-three patients were included in the study. Patient 387/01 showed laboratory signs of hepatitis at inclusion and did not start treatment. This patient was not included in the analyses of efficacy and safety. The demographic data for the 62 remaining patients are summarized in Table I. The patients in the CTZ 0.2 group were significantly older (p = 0.015), heavier (p = 0.002) and taller (p = 0.003) than the patients in the CTZ 0.6 group. There was no significant sex difference.
Global evaluation of the rhinoconjunctivitis status at entry in the study by a visual analogue scale was 39.8 ± 19.3 mm (mean ± standard deviation) for the CTZ 0.2 group, and 47.5 ± 27.5 mm in the CTZ 0.6 group (difference not statistically significant). The corresponding values for the asthma status were 38.8 ± 21.2 and 38.9 ± 28.0 mm (difference not statistically significant).
4. Evaluability for efficacy
Overall, 42 patients (23 in the CTZ 0.2 group and 19 in the CTZ 0.6 group) were evaluable for efficacy for the 2 treatment periods; 49 patients (27 in the CTZ 0.2 group and 22 in the CTZ 0.6 group) were evaluable for efficacy for the 1st treatment period only.

5. Asthma Index

The asthma index improved in both treatment groups, but there was no statistically significant difference between them (Figure 3, Tables 4 and 5). There was a tendency in favor of the CTZ 0.6 group for the first 2 days of treatment \( (p = 0.07) \) and for the 1st week of treatment \( (p = 0.09) \), but this tendency was not observed during the remainder of the study.
6. Other parameters on the daily record card

The changes over time in other parameters on the daily record card are shown in Tables IV and V. These results are also shown graphically in Figures 4 to 8.

The daytime asthma score was significantly better in the CTZ 0.6 group for the first 2 days of treatment (p = 0.011) and the first week of treatment (p = 0.013).

The peak expiratory flow rates were better in the CTZ 0.2 group. The difference was statistically significant for the first 2 days, and for the 3rd and 4th weeks of treatment.

For all other parameters on the daily record card, there was no statistically significant difference between the 2 treatment groups.

7. Asthma and rhinoconjunctivitis symptoms at the visits

Changes at the 2nd and final visits in the proportion of patients with symptoms and/or signs of asthma and rhinoconjunctivitis are shown in Table VI. There was no statistically significant difference between the 2 treatment groups. For the proportion of patients with asthma symptoms, there were consistently higher values (= poorer therapeutic results) in the CTZ 0.6 group, even though the 2 groups were similar at inclusion in the study.

8. Severity of asthma and rhinoconjunctivitis signs at the visits

The scores for asthma and rhinoconjunctivitis signs at the 2nd and final visits are shown in Table VII. The scores for rhinoconjunctivitis signs were consistently better in the CTZ 0.6 group than in the CTZ 0.2 group. However, none of these differences was statistically significant.

A comparison of the severity of asthma signs revealed an inverse tendency. The scores were consistently higher (= poorer therapeutic results) in the CTZ 0.6 group. This tendency, though not statistically significant, is illustrated in Figures 9 to 12.

9. Visual analogue scales

The patients' self-assessments of asthma and rhinoconjunctivitis on the visual analogue scales are shown in Table VIII. There was no statistically significant difference between the 2 treatment groups. Self-assessments for rhinoconjunctivitis seemed to be better in the CTZ 0.6 group; however, the baseline evaluations were also better in the CTZ 0.6 group (see section 3). A comparison of the improvements between visits 1 and 2, and between visit 1 and the last visit, showed no difference between the CTZ 0.2 group and the CTZ 0.6 group.
There was no difference in the asthma status between the 2 groups at the 2nd visit; the CTZ 0.6 group tended to have a poorer result at the last visit, but the difference was not statistically significant.

10. Global evaluation of the efficacy of treatment

The global evaluations (by the patient and investigator) of the efficacy of treatment of asthma and rhinoconjunctivitis are shown in Table IX. The results tended to be slightly better in the CTZ 0.6 group for rhinoconjunctivitis, and slightly worse in the CTZ 0.6 group for asthma. However, these differences were not statistically significant. All evaluations were close to 3, corresponding to a "slight improvement".
There was no difference in the asthma status between the 2 groups at the 2nd visit; the CTZ 0.6 group tended to have a poorer result at the last visit, but the difference was not statistically significant.

10. Global evaluation of the efficacy of treatment

The global evaluations (by the patient and investigator) of the efficacy of treatment of asthma and rhinoconjunctivitis are shown in Table IX. The results tended to be slightly better in the CTZ 0.6 group for rhinoconjunctivitis, and slightly worse in the CTZ 0.6 group for asthma. However, these differences were not statistically significant. All evaluations were close to 3, corresponding to a "slight improvement".
12. **Adverse events**

Six adverse events were observed, in 5 patients (Table X). Only 2 of these 6 events were considered to be potentially related to the study drug:
13. **Serious adverse events**

   No serious adverse event was reported.

14. **Laboratory test results**

   At the end of the study, 9 patients had a hemoglobin concentration outside the normal limits. However, at entry in the study, a similar abnormality was observed in 10 patients and the deviations from the norms were small. The greatest difference from the norm was 6.7%. At the end of the study, 6 patients had a minor abnormality in the packed cell volume and 4 patients had a minor abnormality in the red blood cell count. Seven patients had a leukocyte count slightly higher than normal at the end of the study, versus 13 at the beginning of the study. All of these abnormalities were minor. A large number of patients had values outside the normal limits in their differential white cell counts, but these changes were of the same frequency and of the same magnitude at the beginning and end of the study.
IV. DISCUSSION

Only 63 patients, half the planned number, were recruited for the study. This low recruitment can be explained, in part, by the low pollen count (maximum 23 grains/m²/day) in the Perpignan region; this centre only recruited 3 patients. This low recruitment also illustrates the difficulty of conducting clinical trials in asthmatic children. Of those patients who were recruited for the study, 14 had to be entirely excluded from the analysis of efficacy, and 7 others had to be excluded from the analysis of efficacy for the 2nd part of the study. The most frequent cause of exclusion was poor patient compliance with the treatment or a mistake in the dose given (10 cases). Only 1 patient (2 %) withdrew from the study due to inefficacy, a result which contradicts the results of study All7 in which the withdrawal rate due to inefficacy was much higher (7 %). In that study, 6 cases out of 33 (18 %) withdrew; the withdrawal rate due to inefficacy was higher in the 0.2 mg/kg/day group (5/18 = 28 %) than in the 0.6 mg/kg/day group (1/15 = 7 %). In any event, the small number of subjects in the present study, considerably reduces its power. With the data from the 49 evaluable patients, the probability of detecting a difference of 1 unit in the asthma index is just 41 %; this probability increases only to 50 %, even when all recruited patients are considered.

Another problem with this study is the noncomparability between the demographic data of the 2 groups. At entry in the study, the patients in the CTZ 0.2 group were significantly older, heavier and taller than the patients in the CTZ 0.6 group. The difference in body weight remains statistically significant (p < 0.005) even when the group is limited to the 49 patients evaluable for efficacy. These demographic differences probably explain the more favorable expiratory peak flows observed consistently in the CTZ 0.2 group, but do not seem to have had an influence on asthma and rhinoconjunctivitis scores at entry in the study. The large differences between the body weights of the 2 groups increases the differences in the effective doses tested in the study. The ratio of the doses tested should, in theory, be 1 : 3; but the differences between the body weights of the 2 groups increases the actual dose ratio to 1 : 3.7. Hence, the differences between the body weights of the 2 groups cannot be incriminated if the analysis does not detect a dose-response effect.

At study entry, the 2 treatment groups were highly comparable for both the incidence and severity of rhinoconjunctivitis symptoms. Overall, the proportion of patients showing symptoms fell by 20 % to 40 % at the 2nd visit; this improvement was found to be maintained at the last visit. The improvement observed in nasal obstruction, however, seems more delayed. This may have been a reflection of the poorer efficacy of antihistamines on nasal congestion and nasal obstruction.
The analysis of the severity of rhinoconjunctivitis symptoms shows that the scores are consistently more favorable in the group treated with 0.6 mg/kg, even though the difference never reached statistical significance. The global evaluations (by the patient and investigator) of efficacy of treatment are also slightly in favor of the CTZ 0.6 group. The mean daily dose received by the CTZ 0.2 group is 7.5 mg, an amount very close to the recommended dose (10 mg) for the treatment of children suffering from allergic rhinoconjunctivitis (8).

One may therefore consider, that the CTZ 0.2 group received adequate treatment for allergic rhinoconjunctivitis. This fact, along with the small number of patients included in the study, probably explains the absence of a significant difference between the 2 groups.

The analysis of the efficacy of treatment for asthma is complex. The asthma index tends to be better in the CTZ 0.6 group during the first 2 days and 1st week of treatment; the daytime asthma score is significantly better in the CTZ 0.6 group during the first 2 days and 1st week of treatment. These findings seem to support the hypothesis that the 0.6 mg/kg dose is more effective than the 0.2 mg/kg dose at the beginning of treatment. However, this conclusion should be treated with caution because there was no baseline to ensure comparability of the 2 treatment groups for the parameters of the daily record card. Furthermore, there is a baseline for the presence and severity of asthma symptoms at the visits, and no significant difference between the 2 treatment groups was found for these parameters. Finally, there is no significant difference between the 2 treatment groups in the global evaluation of treatment by the patient and investigator. The overall conclusion which emerges from these data is that there is an improvement in the symptoms and signs of asthma in the 2 treatment groups, but that there are no clinically significant differences between the 2 doses tested.

The improvement in asthma symptoms in the 2 treatment groups cannot be taken as proof of the efficacy of the 2 doses of cetirizine. The improvement in both groups could have been due to a placebo effect (9), a spontaneous improvement in the illness or a fall in the pollen count. It seems likely that this latter factor would have played a role: 32 of the 63 patients were treated, at least in part, during the decreasing phase of the pollen count. It would be necessary to include a placebo group to demonstrate objectively the efficacy of the 2 doses of cetirizine. Unfortunately, previous experience has shown that many patients treated with placebo alone withdraw from the study due to uncontrolled rhinoconjunctivitis symptoms; a satisfactory solution to this problem has not yet been found.
V. CONCLUSION

The small population studied, the absence of a baseline for the parameters on the daily record card, and the absence of a placebo group make the results of this study difficult to interpret. The available data do not support the hypothesis that the 0.6 mg/kg/day dose is superior to the 0.2 mg/kg/day dose in the treatment of asthma.

The only definite conclusion that can be drawn from this study is that cetirizine has an excellent tolerance, even at the 0.6 mg/kg dose.
REFERENCES

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