STUDY OF CETIRIZINE 2HCl IN THE TREATMENT OF
THE ALLERGIC DISEASE WITH NASAL SYMPTOMATOLOGY
IN CHILDREN

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Tradename : Zyrtec R
Generic name : Cetirizine
Code number : ucb P071 (= cetirizine 2HCl)
Chemical name : (2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy)acetic acid, dihydrochloride.

ucb, Pharmaceutical Sector
DRD, Clinical Research & Development
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B-1420 BRAINE 1' ALLEUD
(Belgium).
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1. INTRODUCTION

In animal and human pharmacology, cetirizine 2HCl has proven to be a potent long-acting anti-H₁.

At a dose practically devoid of side effects, cetirizine significantly inhibits the reaction to nasal instillation of a specific allergen (rhinomanometry). It has shown a clinical activity on the symptoms of perennial rhinitis in adults.

The aim of the study reported here was to evaluate the efficacy of a single daily oral dose of cetirizine 2HCl on the symptoms of perennial rhinitis in children.
II. MATERIAL AND METHODS

Study design

Controlled, double-blind study comparing the activity of cetirizine to that of a placebo in two independent groups.

Patients

Forty children were to be selected, who complied with the following criteria:

Inclusion criteria

For entry to the study, the patients must be aged between 2-16 years and present since at least 3 weeks an allergic disease with nasal symptomatology. The allergic origin had to be evidenced and the use of an antihistamine had to be justified. The parents were expected to give their consent.

Exclusion criteria

Were to be excluded from the study children with asthma or with a severe renal or hepatic insufficiency, a Quicke edema or an infectious episode, cortico-dependent children or those who could not, throughout the study, remain off all generally or locally administered antihistamines other than cetirizine, or off cromoglicate, anticholinergic drugs, &-sympathico-mimetics, corticosteroids or antibiotics.

Particular conditions

A 15-day weaning period was to be observed for ketotifen and corticosteroids; the other drugs were to be cancelled at least 4 days before entry to the study.

Products

Cetirizine was presented in the form of a 10 mg/ml concentrated solution in a dropper bottle, each drop containing 0.5 mg cetirizine 2HCl.

Placebo was presented as a solution of identical aspect and taste, in dropper bottles too.
Dosage

The products were to be administered once a day over one week, dosage being adapted to body weight.

The daily dose, to be administered in the evening, diluted in water, milk or orange juice, was fixed to:

- 2.5 mg (5 drops) for less than 20 kg body weight
- 5 mg (10 drops) for 20-35 kg body weight
- 7.5 mg (15 drops) for 35-50 kg body weight
- 10 mg (20 drops) for more than 50 kg body weight.

Evaluation of treatment

At the end of the 1-week treatment period, the investigator had to evaluate the efficacy of the therapy in comparison with the first visit, using a 4-point symptomatic scale:

- 0 = absent
- 1 = slight
- 2 = moderate
- 3 = severe

This included measurement of the intensity of 4 symptoms:

nasal obstruction, rhinorrhea, conjunctivitis, sneezing.

The investigator also had recourse to a visual analog scale to evaluate the patient's condition, the extremes being 'very bad' and 'excellent'.

In addition, he had to evaluate the side effects and to appreciate the value of treatment, taking the achieved therapeutical effect and the observed untoward effects into account. Treatment was judged:

- excellent
- good
- moderate
- bad

Both the patient and the investigator were asked to compare the test treatment to one or the other previous treatment.

The patient was invited to come back earlier than foreseen to the investigator's in case of inefficacy; he was then considered as a 'dropout for inefficacy'. He also was allowed to have recourse to mequitazine, with the recommendation to avoid excessive use.
III. RESULTS

Compliance with the protocol

The protocol was complied with, though several values are missing in the case report forms:

weight: twice
height: 5 times
patient's global evaluation: 7 times.

No patient had recourse to mequitazine, no concomitant treatment was administered, no patient left the study.

Patients

Thirty-six patients were selected to take part in the study; 17 were given cetirizine, 19 a placebo. There were 14 girls and 22 boys aged between 4-16 years, weighing 15-75 kg and ranging in height from 96 to 172 cm. At the time of the first symptoms of allergic rhinitis, they ranged in age from 1 to 11 years.

Analysis of the patient identification variables (age, weight, height, age at onset of disease) using the Student t test reveals that both groups (active and placebo) were perfectly comparable.

TABLE I

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cetirizine group (6 girls + 11 boys)</th>
<th>Placebo group (8 girls + 11 boys)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean</td>
<td>sd</td>
</tr>
<tr>
<td>Age (years)</td>
<td>17</td>
<td>12.64</td>
<td>3.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>15</td>
<td>40.26</td>
<td>12.38</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>13</td>
<td>150.69</td>
<td>18.79</td>
</tr>
<tr>
<td>Age at onset of disease (years)</td>
<td>17</td>
<td>7.11</td>
<td>2.54</td>
</tr>
</tbody>
</table>
Clinical symptomatology

For the 4 studied symptoms (nasal obstruction, rhinorrhea, conjunctivitis and sneezing), evaluated from 0 = absent to 3 = severe, the condition of the patients did not differ from one to the other group at the onset of the study. The same applies when considering the condition of the patients as evaluated on the 0-100 mm visual analog scale.

**TABLE II**

Symptoms before treatment

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cetrizine group (6 girls + 11 boys)</th>
<th>Placebo group (8 girls + 11 boys)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n mean sd</td>
<td>n mean sd</td>
<td>value</td>
</tr>
<tr>
<td>Nasal obstruction</td>
<td>17 1.94 0.43</td>
<td>19 1.79 0.42</td>
<td>0.3</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>17 2.35 0.61</td>
<td>19 2.47 0.61</td>
<td>0.6</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>17 1.18 0.53</td>
<td>19 1.21 0.42</td>
<td>0.8</td>
</tr>
<tr>
<td>Sneezing</td>
<td>17 2.65 0.49</td>
<td>19 2.68 0.48</td>
<td>0.8</td>
</tr>
<tr>
<td>Patient's condition</td>
<td>17 31.88 5.7</td>
<td>19 30.74 5.28</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*: terfenadine
**: diphenamid iodomethylate, clorcinazine ZHCl, phenylaminopropanol HCl (tablets) or pholcodine (syrup).
Evolution under treatment

Subjected to analysis of covariance, evolution under treatment shows that nasal obstruction was significantly more improved in the cetirizine group than in the placebo group.

All other parameters improved in all patients and no difference could be shown between the two groups at the end of the 1-week treatment period.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cetirizine group</th>
<th>Placebo group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(6 girls + 11 boys)</td>
<td>(8 girls + 11 boys)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>mean</td>
<td>sd</td>
</tr>
<tr>
<td>Nasal obstruction</td>
<td>17</td>
<td>0.94</td>
<td>0.43</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>17</td>
<td>0.88</td>
<td>0.86</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>17</td>
<td>0.29</td>
<td>0.47</td>
</tr>
<tr>
<td>Sneezing</td>
<td>17</td>
<td>0.94</td>
<td>0.66</td>
</tr>
<tr>
<td>Patient's condition</td>
<td>17</td>
<td>55.53</td>
<td>15.1</td>
</tr>
</tbody>
</table>

No side effect was reported,

be it in the cetirizine group : 0/16  
or in the placebo group : 0/19

On the contrary, side effects were observed with the intake of other drugs:

under Primalan \( R \) \( ^R \) : 6/7 : somnolence  
under Teldane  : 6/17: headache : 3 times  
              : nausea : once  
              : gastroalgia : twice  
under Denoral  : 1/9 : somnolence
Global evaluation

Be it by the investigator or by the patient, global evaluation does not show any difference between the two groups of patients.

<table>
<thead>
<tr>
<th>Evaluation</th>
<th>by the investigator</th>
<th>by the patient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cetirizine group</td>
<td>placebo group</td>
</tr>
<tr>
<td>Excellent</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Good</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Moderate</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Bad</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

The two products are not significantly different from previous treatments.

<table>
<thead>
<tr>
<th>Compared to</th>
<th>Cetirizine is better as good</th>
<th>Cetirizine is less as good</th>
<th>Placebo is better as good</th>
<th>Placebo is less as good</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denoral (R)</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0.09</td>
</tr>
<tr>
<td>Teldane (R)</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0.36</td>
</tr>
<tr>
<td>Primalan (R)</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>


IV. Discussion

Except for nasal obstruction, placebo improves the symptomatology as well as cetirizine. After one week of treatment, it is not possible to differentiate the two products: improvement of the symptoms is important in nearly all cases, from the first to the second visit.

The following remarks should be made:

1. The equally favourable evolution of the cetirizine group and placebo group can be explained by the following circumstances:

   Spontaneously resolvent episode of viral or vasomotor rhinitis following perennial rhinitis, difficult to differentiate clinically from an exacerbation of perennial rhinitis.

   Highly placebo-reactive pathology.

   Uncontrolled intake of mequitazine or other treatments.

2. It might have been advisable to evaluate the activity from the second or third day, or to pursue the study beyond the one-week period.

3. It remains interesting to note that no side effect was reported throughout the study while side effects were rather frequently reported with previous treatments.

V. Conclusion

Compared to a placebo in the treatment of children with perennial rhinitis, cetirizine could not be differentiated from the comparison product. Both groups were significantly improved after one week of treatment. The efficacy of cetirizine could thus be neither confirmed nor invalidated.