CLINICAL EVALUATION OF A NEW ANTIHISTAMINE, BUCLIZINE HYDROCHLORIDE (VIBAZINE*)

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DURING the decade or so since the innovation of the first histamine-antagonizing agents, numerous compounds representing structural modifications of the original substances have been devised. The aim has been to produce compounds that (1) exhibit a greater degree of effectiveness in a higher percentage of the various allergic disorders, (2) are attended with a lower incidence of untoward reactions, and (3) have a longer duration of action and thus obviate the inconvenience of frequent administration.

Many of the effective compounds have an ethylenediamine group in their structure, and fairly recently one with a diethylenediamine (piperazine) group was introduced. This latter agent is chlorcyclizine and it is characterized by a relatively prolonged duration of action (eight to twenty-four hours).

A more recent and particularly promising piperazine derivative has become available for clinical trial and differs from chlorcyclizine by having three, rather than two, benzylic rings in its structure. The purpose of this article is to report a clinical trial of this new compound, buclizine hydrochloride, which has been named "Vibazine" by the manufacturer and is designated chemically as 1-p-chlorobenzhydryl-4-p-(tert-butyl)-benzylpiperazine. It is represented by the following structural formula:

Pharmacologic studies demonstrated that orally administered doses of Vibazine protected guinea pigs from nebulized or intravenously injected histamine for at least four days in all cases, a period of protection that was considerably longer than was provided by even larger doses of either tripelennamine or chlorcyclizine. The oral L.D. of Vibazine in mice was found to be 2,100 mg. per kilogram of body weight, while that of tripelennamine was 235 mg. per kilogram and that of chlorcyclizine was 500 mg. per kilogram. Chronic toxicity studies in rats and dogs receiving the drug over periods of six months revealed no morbid changes. These data indicate high effectiveness, low toxicity, and a prolonged duration of action for Vibazine.

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*Vibazine hydrochloride (brand of buclizine hydrochloride) was kindly supplied for this study by Dr. M. Carlucci of Chas. Pfizer & Company, Inc.
MATERIALS AND METHODS

In this study, Vibazine was used in the adjunctive treatment of fifty-nine patients with various allergic disorders, principally seasonal hay fever. The patients included twenty-three males and thirty-six females, ranging in age from 4 to 61 years; ten of them were children 12 years of age or younger. The individual dose found effective in most cases was 25 mg., but an individual dose of 50 mg. was found to give better results in six (10 per cent) of the fifty-nine patients. The effective dose was given one to six times daily, as determined by the response in the individual case (only once or twice daily in 50 per cent of the patients). The duration of therapy ranged from one day (five patients) to five weeks of continuous use (eight patients). The average duration was two weeks.

RESULTS

The therapeutic results achieved with Vibazine are tabulated in Table I. "Excellent" results represent 75 to 100 per cent relief; "fair" results represent partial, but less than 75 per cent, relief; and "poor" results represent little or no relief.

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>NUMBER OF CASES</th>
<th>EXCELLENT</th>
<th>FAIR</th>
<th>POOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hay fever</td>
<td>53</td>
<td>29</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Vasomotor rhinitis or non-seasonal coryza</td>
<td>10</td>
<td>6</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Bronchial asthma</td>
<td>6</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Urticaria</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vernal conjunctivitis</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td>72</td>
<td>41</td>
<td>16</td>
<td>15</td>
</tr>
</tbody>
</table>

*Some patients had more than one allergic condition.

It will be seen from these figures that 80 per cent of the patients were benefited, 60 per cent obtaining excellent relief. Only 20 per cent were not relieved. It is noteworthy that three of the fifteen patients not relieved had previously used other antihistamines without benefit.

One of the patients obtaining an excellent result stated that Vibazine was the most effective antihistamine of any that he had used, another stated that it was the only one that he had found effective at all, and nine patients (seven with excellent results and two with fair results) found it superior because it was the only one without side effects.

Onset of Action.—Relief appeared in one-quarter to one-half hour after administration in all fifteen patients in whom this factor was determined.

Duration of Action.—In the forty-six patients benefited by Vibazine, the duration of relief after a single dose was at least twelve hours in twenty-two (50 per cent) and as long as twenty-four hours in twelve. The duration of relief was no longer than eight hours in ten patients, no longer than six hours in
eight, and three or four hours in six. Thus, in the majority (70 per cent) the duration of action was sufficiently long to last through the night after a bedtime dose.

Side Effects.—Adverse reactions occurred in six (10 per cent) of the patients. The most frequent was drowsiness (four patients); headache was reported by one, and jitteriness by one. It was necessary to discontinue use of Vibazine in three cases (5 per cent of patients treated), because of drowsiness in one, jitteriness in one, and headache in one. The patient who discontinued Vibazine because of drowsiness had obtained an excellent therapeutic effect, but was unable to tolerate any antihistamine. The patient experiencing jitteriness also had excellent relief, but had a similar reaction to all antihistamines she had tried. One patient with drowsiness not severe enough to require discontinuance of Vibazine had excellent relief and had previously found other antihistamines valueless. Another with drowsiness not severe enough to require discontinuance of Vibazine had fair relief and reported having the same reaction to other antihistamines. The third with drowsiness not severe enough to require discontinuance of the drug had fair relief but required individual doses of 50 mg.

Ten patients who previously had been unable to tolerate other antihistamines because of the drowsiness they produced were able to use Vibazine without side effects. Of these, seven had excellent results (and in one Vibazine was the only antihistamine found effective), two had fair results, and one had a poor result (all other antihistamines had also proved ineffective).

SUMMARY AND CONCLUSIONS

A new antihistaminic drug, buclizine hydrochloride (Vibazine hydrochloride) was submitted to clinical trial in fifty-nine patients with various allergies, principally hay fever. A significant degree of relief was provided in 80 per cent of the cases treated, the results being excellent in 60 per cent. The following observations drawn from this study indicate that Vibazine represents a valuable addition to the list of histamine-antagonizing agents.

1. Vibazine compares favorably in effectiveness with the most potent of such agents in current use. In fact, several patients found it to be the only one that provided relief.

2. As regards side effects, Vibazine compares favorably with the best tolerated antihistamines. Untoward reactions severe enough to require discontinuance of its use occurred in only 5 per cent of the series reported, and nine patients unable to tolerate any other antihistamines were relieved by Vibazine without side effects.

3. Vibazine provides the advantages of prolonged action. In 70 per cent of the patients, relief was maintained for eight to twenty-four hours after a single dose. This means that the action of a bedtime dose will last through the night in most cases.
REFERENCES