CLINICAL EVALUATION OF A NEW ANTIHISTAMINE, BUCLIZINE HYDROCHLORIDE

By

Swaminandan Prasad, M.D., (PAT.)
Department of Medicine, P.W. Medical College, Patna

&

Amarjit Singh Chopra, M.B., B.S. (Hons.)

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Since the innovation of the first histamine-antagonizing agents, numerous compounds representing the structural modification 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 allergic patients (2) have low toxicity and (3) have a prolonged action and thus obviate the inconvenience of frequent administration.

Buclizine hydrochloride, I-p-chlorbenzhydryl 1-4-p-tertiary butylbenzyl piperazine dihydrochloride whose structural formula appears below has been recently marketed in India under the trade name of Longiphene by Unichem Laboratories. It belongs to a newer class of antihistamine in which in addition to diethylene diamidin (piperazine) there are three benzyl rings. (1)

![Chemical Structure of Buclizine Hydrochloride]

In animals buclizine hydrochloride has been shown to possess marked protracted activity against aerotized and intravenously injected histamine. Although the onset of action is unusually slow but the duration of action is much prolonged. For example it has been shown that the drug (1) per kilogram body weight given orally to guineapig protected the animal for about 16 days against lethal bronchoconstrictor effect of histamine aerosol (2) Clinical experience, however, does not bear this out as doses upto 75 mg. or more daily are well tolerated and there is no cumulative effect. It has been found to be comparatively non-toxic in dogs and rats. (3) In man also doses upto 25-75 mgm per day for an average of 4 months produced no significant abnormality in the formed elements of blood or in hepatic or renal function.

Materials and methods:

In this study Longiphene was used alone or in combination in the treatment of fifty-two patients with various allergic disorders principally Vasomotor rhinitis in the period between 1st September 1960-January 1961. The patients included 29 males (55.58%) and 23 females (44.42%) ranging in age from 4 years to 60 years with an average of 28 years. The individual dose found effective in most cases was 25 mg.—50 mg. This was given as 1 tablet (25 mg.) daily at bed time in 11 cases, 1 tablet morning and evening in 18 cases and as ½ tablet morning and evening in 23 cases. The duration of therapy ranged from 3 days to 10 days. The average duration was 5 days. Of the 52 cases, 15 had vasomotor rhinitis, 11 common cold, 11 eczema, 4 Post operative nausea and vomiting, 5 pruritus, 3 tropical eosinophilia, 2 bronchial asthma and one Urticaria. Most patients had moderate to severe symptoms and 9 of them had previous treatment with other antihistaminics. Much difficulty was experienced in
the follow up, as many patients failed to report for check-up for more than once. Blood count was done in cases but again it could not be repeated in all these cases. As the main object of this study was to determine the clinical response to Longiphene, no control was attempted.

**Result:**

The therapeutic results achieved with Longiphene are tabulated in Table I. "Excellent" result represent 75-100% relief, "Good" 50-75% necessary to prolong the treatment to 10 days in one case. Those cases who had tried other antihistaminics preferred it because it had no sedative effect. All these cases were kept on Longiphene alone without adjunctive treatment.

Of the 11 cases of common cold best results were obtained when it was instituted early right at the onset of the disease in the dose of 25 mg. at bed time. Two cases experienced immediate relief which lasted for 4 days. Therefore they developed severe mucopurulent discharge and fever which had to be treated with antimicrobial agents. With adjunctive treatment of Vit. C. 500 mg. daily orally and prophylactic sulphadiazine, a good response was noted and the attack was completely averted in 6 cases. Here Longiphene was administered in the dose of 25 mg. morning and evening.

In eczema though the skin lesions itself did not respond so well there was a marked relief of itching, in 63.6% of cases.

A girl aged 9 years who complained of breathlessness at night and had 31% Eosinophilia with 21,000/cm. total leucocytic count showed an excellent response with 1/2 tab. (25 mg. tab.) morning and evening, so much so, that she was completely asymptomatic after three days of treatment. On examination of stool Round worm ova was discovered for

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Cases</th>
<th>Result</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasomotor Rhinitis</td>
<td>15</td>
<td>Excellent</td>
<td>10</td>
</tr>
<tr>
<td>Common Cold</td>
<td>11</td>
<td>Good</td>
<td>3</td>
</tr>
<tr>
<td>Eczema</td>
<td>11</td>
<td>Fair</td>
<td>2</td>
</tr>
<tr>
<td>Pruritus</td>
<td>5</td>
<td>Poor</td>
<td></td>
</tr>
<tr>
<td>Post operative Nausea &amp; vomiting</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tropical Eosinophilia</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchial Asthma</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urticaria</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patient did not report
which she was treated with piperazine citrate preparations. Since then she is asymptomatic. Unfortunately she did not report for a re-examination of blood. A better response was obtained in one case who received simultaneously three tablets of Hetrazan a day.

In Bronchial asthma though both the patients said that they felt better with 1 tablet (25mg) morning and evening it was very difficult to gauge its actual efficacy as simultaneously they were being given bronchodilators (intravenous aminophylline) and antibiotics.

6% of the cases of pruritus responded well to longiphene while in 20% there was no response.

Onset of action-Relief of symptoms was usually experienced about ½ an hour after the dose particularly in cases having Vasomotor Rhinitis.

Duration of Action: In most of the cases it was 12 hours. Most of the patients of vasomotor rhinitis were relieved by the first dose though the drug was continued for at least five days.

Side Effect:

Adverse reaction occurred in only three cases (6%). One case reported experiencing a marked sedation and hangover the next morning after a single evening dose. There was also mild headache.

A second case reported experiencing weakness in the body. The 3rd one had gastrointestinal upset leading to loose motion, excessive wind formation. It is doubtful as to how much of this upset was due to longiphene itself.

However most of the patients who had previously tried other antihistamines preferred longiphene as it did not cause sedation.

Summary and Conclusion

A new antihistaminic drug, buclizine hydrochloride, “longiphene” has been introduced. It was submitted to clinical trail in fifty-two cases with various allergic disorders. A significant degree of relief was experienced in 80% of the cases treated. The following observations can be drawn from this study.

1. That longiphene compares favourably with most of the antihistaminic in current use and that it is the drug of choice in vasomotor rhinitis.

2. It causes minimum side effects and only in one case out of 52 it was necessary to discontinue the drug. Many patients described it as the only drug that relieved them.

3. It has relatively a long duration of action so that even a single bedtime dose covers the patient for 12-24 hours.

I am thankful to my friends and colleagues who not only submitted themselves for the study but helped me in collecting these cases.

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Longiphene (brand of buclizine hydrochloride) was kindly supplied for the study by M/s. Unichem Laboratories.)

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