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Clinical Trial

A CLINICAL TRIAL OF FLUPEROLONe:
A NEW TOPICAL STEROID

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For the evaluation of a new topical steroid, flupero-lone (P-1742: Methral; Pfizer) a clinical trial was planned in four phases. First, in order to obtain a clinical impression, ointments of both 0.25% and 1.0% and spray pack preparations, were used for the treatment of a variety of commonly occurring dermatoses. Secondly, following encouraging results from this pilot trial and favourable reports from another centre (Sneddon, 1962), a double blind comparative trial was undertaken with preparations containing either 0.25% flupero-lone or 1.0% hydrocortisone. Both were of identical appearance and consistency, and were dispensed in a water miscible base. In this phase of the trial, patients were given, in a blind, random manner, one of the two preparations, but at the first follow-up visit after one week, the preparation was changed. The randomization was such that approximately equal numbers of patients commenced therapy with both preparations. The third phase of this trial was also a double blind study, planned in an identical manner, but comparing 0.1% flupero-lone and 1.0% hydrocortisone. Lastly, in the fourth phase, patients with various types of eczema were treated with 0.1% flupero-lone but at the first follow-up visit the preparation was changed to 0.01% flupero-lone, to see whether this low concentration would be adequate to maintain the improvement observed during treatment with the 0.1% preparation. The patient was unaware that the second preparation was of a lower concentration than the original.

Chemically this compound is of interest both due to inclusion of a fluorine atom, and to the modification of one of the side chains by the introduction of a methyl grouping at position C21. The structure of flupero-lone can be described as 21-methyl-9α fluoro-prednisolone acetate (Fig. 1).

![Fig. 1.—Flupero-lone: note inclusion of fluorine atom at C9 and methyl group at position C21.](http://pmj.bmj.com/)
Animal studies (Llaurado and Schneider, 1960) had already demonstrated that this steroid possessed potent anti-inflammatory activity.

**Results**

A total of 66 patients were included in the four phases of these trials.

In the initial clinical evaluation there was a total of 38 patients treated as shown in Table 1.

<table>
<thead>
<tr>
<th>Fluperolone Preparation</th>
<th>No. of Patients Treated</th>
<th>Much Improved or Improved</th>
<th>No Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0% ointment</td>
<td>14</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>0.25% ointment</td>
<td>10</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>1.0% followed</td>
<td>4</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>by 0.25%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spray pack preparation</td>
<td>10</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>38</strong></td>
<td><strong>35</strong></td>
<td><strong>3</strong></td>
</tr>
</tbody>
</table>

The impression gained was that fluperolone showed obvious potent anti-inflammatory activity, and that pruritus was relieved more rapidly with fluperolone than would be expected with hydrocortisone. From previous clinical experience of trials with topical steroid ointment it was considered that the 0.25% preparation was at least as effective as, or possibly slightly superior to, 1.0% hydrocortisone.

The second phase of this trial, a blind comparative study of 0.25% fluperolone and 1.0% hydrocortisone, gave results as shown below (Table 2).

<table>
<thead>
<tr>
<th>Superior Preparation</th>
<th>No. of Cases</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25% fluperolone</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>1.0% hydrocortisone</td>
<td>5</td>
<td>10</td>
</tr>
</tbody>
</table>

Thus this phase shows both to be equally effective, in these cases.

Phase three of the trial, comparing 0.1% fluperolone and 1.0% hydrocortisone, gave the following results (Table 3).

<table>
<thead>
<tr>
<th>Superior Preparation</th>
<th>No. of Cases</th>
<th>Equal Response</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1% fluperolone</td>
<td>3</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>1.0% hydrocortisone</td>
<td>5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As a result of these various investigations it can be concluded that 0.1% fluperolone is as effective as 1.0% hydrocortisone in the treatment of a wide variety of dermatological conditions.

In particular throughout this trial, it was observed that pruritus was relieved more rapidly with fluperolone than with hydrocortisone.

**Summary**

A clinical trial, in four phases, demonstrates the efficacy of a new topical steroid preparation, fluperolone, in the treatment of various dermatoses. Fluperolone at 0.1% concentration is comparable in efficacy to 1.0% hydrocortisone, and clinical evidence demonstrates that the fluperolone relieves pruritus more rapidly than hydrocortisone, and has a quicker onset of action.

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A Clinical Trial of Fluperolone: A New Topical Steroid

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