TREATMENT OF NON-SPECIFIC URETHRITIS WITH TRI-ACETYL-OLEANDOMYCIN*†

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Recently, a new derivative of oleandomycin, tri-acetyl-oleandomycin, has been prepared and characterized (Celmer, Els, and Murai, 1958). It has a spectrum of activity similar to that of oleandomycin but is stated to be clinically more effective, possibly because of its better absorption from the gastro-intestinal tract. It has been shown to be effective against various Gram-negative and most Gram-positive pathogens (Shubin, Dumas, and Sokmensuer, 1958), and there is some evidence that it is active against large viruses such as that of lymphogranuloma venereum (Loughlin, Alcindor, and Mullin, 1959). On the other hand, Blyth (1958) found oleandomycin ineffective in vitro against pleuro-pneumonia-like organisms (PPLO) isolated from patients with non-specific urethritis (N.S.U.). As PPLO are believed by some to be of aetiological importance in N.S.U. (Dienes and Edsall, 1937; Klieneberger-Nobel, 1959), it was thought of interest to assess the clinical effect of tri-acetyl-oleandomycin in this condition.

Material and Methods

24 patients were selected from those attending the Special Clinic, St. Mary’s Hospital, Paddington. These were cases of well marked N.S.U. of under 8 days’ duration (mean: 3.3 days). The patients were of much the same age and social standing. The investigation was planned as a double-blind therapeutic trial, and the allocation of antibiotic and placebo† was made by the use of random sampling numbers. The key was not known until the clinical assessment of treatment and re-treatment had been concluded. The drug and placebo were dispensed in identical capsules, the dose of the antibiotic being 250 mg. four times daily for 4 days.

Patients were examined on the sixth and seventh day after the start of treatment and success or failure was judged by the presence or absence of urethral discharge. The assessment was made at this early stage to exclude some of the factors which commonly interfere later on with the evaluation of treatment in cases of N.S.U. These factors include a high incidence of defaulting, the unpredictable course of urethritis, and difficulties in distinguishing between failures of treatment and re-infections. The absence of urethral discharge so soon after treatment does not necessarily mean cure, but this form of examination at an early stage probably gives the least biased estimate in comparing the effect of drugs in cases of N.S.U.

The patients who showed little or no improvement at this examination were considered to be failures of treatment and were given a course of oxytetracycline. A brief note on the outcome of re-treatment is given.

Results

The results are shown in Table 1. Two patients who were accepted for the trial were later found to have gonorrhoea and have been excluded. Tri-acetyl-oleandomycin appeared to clear the urethral discharge rapidly in cases of N.S.U. The results are significant when compared with those of the group receiving the placebo (P < 5 per cent.). The only toxic effect due to tri-acetyl-oleandomycin was slight diarrhoea, which occurred in one case.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of Cases</th>
<th>Urethritis Present 6–7 Days after Onset of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tri-acetyl-oleandomycin</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Placebo</td>
<td>10</td>
<td>8</td>
</tr>
</tbody>
</table>

* Received for publication July 27, 1959.
† "Evramycin" is the trade mark of John Wyeth Limited.
‡ The placebo capsules contained lactose powder.
The eleven patients who showed little or no improvement by the seventh day after the start of the trial were re-treated with oxytetracycline 250 mg. orally four times daily for 4 days. Oxytetra
cycline was chosen because it is generally accepted as one of the most effective drugs in the treatment of this condition (Willcox, 1953). The results of re-
treatment are given in Table II. The response of the control group to oxytetracycline was similar to that in the group receiving tri-acetyl-oleandomycin. The immediate re-treatment results of the patients who had failed to respond to tri-acetyl-oleandomycin was less satisfactory.

<table>
<thead>
<tr>
<th>Original Treatment</th>
<th>Treatment Failures</th>
<th>Results of Re-treatment with Oxytetracycline (assessed at end of treatment)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Discharge Present</td>
</tr>
<tr>
<td>Tri-acetyl-oleandomycin</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Placebo</td>
<td>8</td>
<td>1</td>
</tr>
</tbody>
</table>

Cultural tests for the isolation of PPLO were made in all cases before treatment was begun and were repeated at the time of clinical assessment in those patients who still showed a urethral discharge (Table III).

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Tri-acetyl-oleandomycin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPLO</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Before Treatment</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Treatment Failures</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

The finding of PPLO appeared to be independent of the effect of tri-acetyl-oleandomycin on the urethritis. No clinical feature was found to dis-
tinguish PPLO positive cases from negative ones.

### Summary

Tri-acetyl-oleandomycin was compared with a placebo in a double-blind trial in 22 cases of N.S.U. selected to include only those with marked untreated N.S.U. of recent onset.

Clinical assessment was made soon after the end of treatment. Urethral discharge had ceased in 75 per cent. of the cases treated with the antibiotic and in 20 per cent. of the placebo group; the question of “cure” was not explored here. The presence or absence of PPLO was not related to the presence or absence of discharge.

This work was carried out under the aegis of the Medical Research Council Working Party on Non-
Specific Urethritis, with the aid of a grant from the U.S. Public Health Service. I wish to thank Dr. J. Jefferiss and Dr. R. R. Willcox for their help and for permission to use the cases under their care, and Mr. Ambrose King for his encouragement, help, and criticism in the preparation of this paper. I am indebted to Dr. Klieneberger-Nobel of the Lister Institute for the bacteriological investigations and to John Wyeth Ltd., for supplying tri-acetyl-oleandomycin (“Eevramycin”) and the placebo capsules.

### Table II

REASULTS OF RE-TREATMENT WITH OXYTETRACYCLINE

### Table III

INCIDENCE OF PPLO IN THE URETHRAL DISCHARGE BEFORE AND AFTER THE THERAPEUTIC TRIAL

### References


