Amoxicillin in the treatment of gonorrhea

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Single-dose antibiotic therapy for the treatment of acute uncomplicated gonorrhoea has been the subject of research in many countries, and many dose schedules of various antibiotics using single-dose oral therapy have been suggested. When treatment has been given under supervision this has resulted in the eradication of Neisseria gonorrhoeae, preventing long-term sequelae and chronic persistent infection. Using this method of treatment a bacteriological clearance rate of not less than 95 per cent. in male and female patients has come to be accepted as routine. Single-dose treatment is important from medical and economic aspects; if infection can be eradicated at once, morbidity and chronicity with the attendant loss of working time and expense of treatment will be minimized.

Since its introduction, penicillin G has maintained its unique position as the drug of choice for the treatment of gonorrhoea. In 1961, with the advent of ampicillin, a semi-synthetic penicillin, an oral therapy was introduced which proved of great value. Ampicillin is now recognized worldwide as a standard oral therapy for single-dose administration. It is recommended by the Atlanta Centre for the Treatment of Venereal Disease in the USA as the drug of choice (USPHS, 1974) and also by clinics in the United Kingdom, probenecid is often used concomitantly.

Various antibiotics have been investigated with the object of improving the bacteriological clearance rate. This paper reports the results obtained with a new semi-synthetic penicillin, amoxyclillin (Amoxil-Bencard), which was introduced in 1973.

In chemical structure and activity amoxyclillin is closely related to ampicillin (Sutherland and Rolinson, 1970). Its spectrum of activity is close to that of ampicillin against most susceptible organisms, but it shows greater activity than ampicillin against the gonococcus. Like ampicillin, it is not inactivated by gastric acid, but it has the added advantage of increased absorption after oral administration. Peak serum levels occur 2 hours after ingestion and are double those achieved by an equivalent dose of ampicillin (Croydon and Sutherland, 1971). In the presence of food the absorption rate is only slightly reduced.

Side-effects are very much fewer than with ampicillin.

Preliminary studies in vitro (Hunter, Rolinson, and Witting, 1973) showed that amoxyclillin was more active than penicillin G against the more resistant strains of gonococci, and only slightly less active against sensitive strains. For this reason a clinical trial was set up at the West London Hospital to investigate the efficacy of this semi-synthetic compound against gonococci.

Method

The patients admitted to the study were men and women with uncomplicated genital gonorrhoea attending the Department, of Genitourinary Medicine, West London Hospital. The patients were entered into the study without selection unless they were visitors who would not be able to attend for follow-up, were hypersensitive to penicillin, or were suspected of having concomitant syphilis.

In males diagnosis was made by identifying typical Gram-negative diplococci on a Gram-stained smear; vancomycin, colistin, nystatin, trimethoprim (VCNT) plates were inoculated for culture in all cases.

In females smears for Gram-staining were taken from the urethra and cervix in all instances. Material from both sites was inoculated on VCNT plates.

Amoxyclillin plate dilution sensitivity tests were carried out on all isolates.

A single oral dose of 3 g. amoxyclillin was given under supervision in the clinic. Patients were asked to return after 3 days, and then at weekly intervals for 4 weeks. They were asked to avoid sexual intercourse during the period of follow-up.

At each attendance the patient was questioned concerning symptoms and sexual exposure since the last visit; they were then examined and further smears and cultures were taken. In view of the difficulty of distinguishing between relapse and re-infection, patients
were regarded as cases of treatment failure when gonococci could be demonstrated within 14 days of treatment, provided that further sexual contact was emphatically denied.

**Results and comments**

Altogether 162 patients (97 men and 65 women) were treated with amoxycillin. All were suitable for assessment in that they had identifiable organisms in their smear and/or culture. Cultures were negative in twenty cases, although typical Gram-negative diplococci were seen in the clinic at the first visit.

At each follow-up period some patients defaulted and some were given further treatment contrary to the protocol, and in these instances they could no longer be assessed for further follow-up. We did not presume that those who lived locally and failed to attend for follow-up were cured. Although Evans (1966) showed that most patients did return to the same clinic if symptoms recurred after treatment, it was considered that this assumption could not be made in the present study.

When grouped together, the male and female cases do not take into consideration the anatomical differences between the sexes, and for this reason we have evaluated the bacteriological response rate in the two sexes separately (Table).

For simplification, all failures are classified as defaulters at subsequent follow-up.

At the first follow-up, 82 out of 97 males were assessable, thirteen had defaulted, and two admitted to a contact with a known infected female; 81 (99 per cent.) were cured, and at this stage only one patient was a true failure. Fifty cases were seen at the second follow-up, 10 days after therapy, and all who were assessable were cured (100 per cent.), but at this time 45 had defaulted.

In the 65 females, a significantly better attendance rate was achieved, for all 65 were assessable at the first follow-up (significance $\chi^2 = 7.68$; $P < .01$).

Of these patients, 62 (95 per cent.) were cured and three showed evidence of active disease. At the second follow-up, 51 were assessable, fifty were cured, and one still showed gonococci present, fourteen having defaulted.

The response to treatment was not significantly different between males and females ($\chi^2 = 1.58$).

The Figure shows that in the male patients a substantial default rate occurred after the second visit. The female patients attended more regularly during the follow-up period.

Of the 142 isolates studied, 9-3 per cent. had a minimum inhibitory concentration (MIC) of 0-03 to 0-25 $\mu$g./ml. and 3-6 per cent. had an MIC of 0-25 to 1 $\mu$g./ml. Only one of the patients with an MIC of 1 $\mu$g./ml. was a clinical failure.

In a previous series of 664 patients treated with procaine penicillin, 457 (69 per cent.) were sensitive to penicillin, with an MIC of 0-03 units/ml. (0-018 $\mu$g.); 207 (31 per cent.) were insensitive, 121 (18 per cent.) had an MIC between 0-03 and 0-25 units/ml. (0-018 to 0-15 $\mu$g.), 62 (9 per cent.) had an MIC of 0-25 to 1 unit/ml. (0-15 to 0-6 $\mu$g.), and 24 (4 per cent.) had an MIC of above 1 unit (Beck, 1973).

This is similar to findings published by the Medical Research Council (1961); 13-3 per cent. of gonococci showed an MIC ranging from 0-125 to 1 unit/ml. In London, at St. Thomas' Hospital, Gray, Phillips, and Nicol (1970) found that the percentage of strains showing partial sensitivity was 35 per cent., which was unchanged from the previous report in 1966.

**Conclusion**

Amoxycillin seems to be an acceptable treatment for gonorrhoea, although in areas where there is a sizeable proportion of insensitive strains of *Neisseria gonorrhoeae* it would be advisable to administer 1 g. probenecid in addition.

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**Table: Bacteriological response in 97 men and 65 women**

<table>
<thead>
<tr>
<th>Sex</th>
<th>1st follow-up</th>
<th>2nd follow-up</th>
<th>3rd follow-up</th>
<th>4th follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total assessable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Success</td>
<td>82 (84 per cent.)</td>
<td>50 (51-5 per cent.)</td>
<td>21 (22 per cent.)</td>
</tr>
<tr>
<td></td>
<td>Discharged</td>
<td>81 (99 per cent.)</td>
<td>50 (100 per cent.)</td>
<td>18 (85-5 per cent.)</td>
</tr>
<tr>
<td></td>
<td>Failure</td>
<td>1 (1 per cent.)</td>
<td>2</td>
<td>1 (4-5 per cent.)</td>
</tr>
<tr>
<td></td>
<td>Re-infection</td>
<td>2</td>
<td></td>
<td>2 (10 per cent.)</td>
</tr>
<tr>
<td></td>
<td>Default</td>
<td>13</td>
<td>45</td>
<td>76</td>
</tr>
<tr>
<td>Female</td>
<td>Total assessable</td>
<td>65 (100 per cent.)</td>
<td>51 (78 per cent.)</td>
<td>34 (52 per cent.)</td>
</tr>
<tr>
<td></td>
<td>Success</td>
<td>62 (95 per cent.)</td>
<td>50 (98 per cent.)</td>
<td>32 (94 per cent.)</td>
</tr>
<tr>
<td></td>
<td>Discharged</td>
<td>3 (5 per cent.)</td>
<td>1 (2 per cent.)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Failure</td>
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<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Re-infection</td>
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</tr>
<tr>
<td></td>
<td>Default</td>
<td>14</td>
<td>29</td>
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Summary
A series of 162 patients with uncomplicated genital gonorrhoea was assessed after single-dose treatment with 3 g. amoxycillin. This seems to be an acceptable method of treatment, resulting in clearance rates in both male and female patients of 99 and 95 per cent. respectively at the first follow-up. The default rates on follow-up over a 4-week period are also shown.

We should like to thank Miss M. Rees for the statistical evaluation of the results and Mrs V. Igglesden for typing the manuscript.

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Amoxycillin in the treatment of gonorrhoea.

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Br J Vener Dis 1975 51: 398-400
doi: 10.1136/sti.51.6.398

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