Spectinomycin hydrochloride in the treatment of gonorrhoea: Its effect on associated Chlamydia trachomatis infections

J. D. Oriel, G. L. Ridgway, S. Tchamouroff, and Jean Owen

From the Departments of Genito-Urinary Medicine and Clinical Microbiology, University College Hospital, London

SUMMARY Sixty-three heterosexual men were successfully treated with a single injection of spectinomycin hydrochloride 2 g for urethral infections with Neisseria gonorrhoeae. Chlamydia trachomatis was recovered from the urethra of 11 of these men both before and after treatment. In six men, the organism was isolated after but not before treatment. No isolates were obtained from the remaining men either before or after treatment. All 17 of the men who yielded C. trachomatis developed post-gonococcal urethritis. Eight of 46 men from whom no isolate was obtained in their cultures developed post-gonococcal urethritis. Seventeen of 50 women successfully treated with spectinomycin for cervical infections with N. gonorrhoeae yielded isolates of C. trachomatis both before and after treatment. The organism was isolated from five women before but not after treatment, and from four women after but not before treatment. In 24 women culture for C. trachomatis was negative both before and after treatment. Spectinomycin hydrochloride in the dosage used rarely eliminated C. trachomatis from the genital tract of either men or women; in this respect it resembled two other drugs commonly used for the treatment of gonorrhoea—penicillin and ampicillin.

Introduction

Patients with genital infections with Neisseria gonorrhoeae often have a concomitant infection with Chlamydia trachomatis. This organism, which is an important cause of non-gonococcal urethritis (Holmes, et al., 1975; Oriel et al., 1976a), has been isolated from 20 to 30% of men with gonococcal urethritis (Richmond et al., 1972; Oriel et al., 1976a) and from 30 to 60% of women with gonococcal cervicitis (Wentworth et al., 1973; Hilton et al., 1974; Oriel et al., 1974). Several antibacterial agents in dosages that are curative for N. gonorrhoeae infections are ineffective against co-existing C. trachomatis infections. Thus gentamicin completely fails to eliminate C. trachomatis (Oriel et al., 1975), and both penicillin and ampicillin show only weak antichlamydial activity (Richmond et al., 1972; Oriel et al., 1976b). Most men with infection of the urethra by C. trachomatis which persists after treatment for gonorrhoea develop post-gonococcal urethritis (PGU) (Richmond et al., 1972; Oriel et al., 1975).

Spectinomycin, an aminocyclitol antibiotic, has given good results in the treatment of gonorrhoea (Cornelius and Domescik, 1970; Schroeter et al., 1975), and has been recommended as the drug of choice for patients not cured by other antimicrobials (Venereal Disease Advisory Committee, 1974). Its clinical effect against C. trachomatis thus becomes important, although in vitro studies indicate only marginal activity (Ridgway et al., 1976). We are reporting the effect of a single intramuscular injection of spectinomycin hydrochloride 2 g on C. trachomatis associated with N. gonorrhoeae in both men and women. Cell culture for C. trachomatis was performed before and after treatment in all
cases and the development of PGU in both *Chlamydia*-positive and *Chlamydia*-negative men was noted.

**Materials and methods**

All patients were seen in the Department of Genito-Urinary Medicine, University College Hospital, London between August 1976 and February 1977, and informed consent was obtained before inclusion in the study. After local and general examination, specimens were collected as described below.

**SPECIMEN COLLECTION FROM MEN**

A specimen of urethral secretion was taken from each man with a disposable plastic loop and spread on a slide for Gram staining and microscopical examination. A second specimen was inoculated on to a selective culture medium for *N. gonorrhoeae*. A cotton-wool tipped wire endourethral swab was then inserted 4-5 cm into the urethra. On withdrawal, the swab was transferred to 2 ml of transport medium for *C. trachomatis*. A two-glass urine test was carried out at each visit, and serological tests for syphilis were also performed.

**SPECIMEN COLLECTION FROM WOMEN**

Women were examined in the lithotomy position. The cervix was exposed with a Cusco speculum. Urethral and cervical specimens for microscopical examination and culture for *N. gonorrhoeae* were taken using plastic disposable loops. A specimen from the posterior vaginal pool was also taken for microscopy and culture for *Trichomonas vaginalis*. The cervix was then cleaned with cotton-wool, and a cotton-wool tipped swab rotated in the cervical canal. On removal, the swab was transferred to 2 ml of transport medium for culture for *C. trachomatis*. Rectal specimens for culture for *N. gonorrhoeae* were taken from some patients, but cultures for *Chlamydia* were not performed on rectal specimens. Serological tests for syphilis were included for all patients.

In cases in which gonorrhoea was diagnosed, the patient (male or female) was given 2 g spectinomycin hydrochloride by intramuscular injection. Each patient was asked to return for re-examination after 3 days, 7 days, and 14 days. There was some individual variation in follow-up attendance, but in many cases it was possible to follow-up patients for longer periods. At each attendance the diagnostic tests described above were repeated. Patients were requested to refrain from sexual intercourse during the follow-up period.

**ASSESSMENT OF PGU**

PGU was defined as the presence of ≥20 polymorphonuclear leucocytes in at least three fields of a Gram-stained urethral smear examined at a magnification of ×900 (Oriel *et al.*, 1975).

**LABORATORY METHODS**

*N. gonorrhoeae* was cultured on a selective medium (Phillips *et al.*, 1972). Cell culture for *C. trachomatis* was by the method of Reeve *et al.* (1975), using McCoy cells pre-treated with idoxuridine.

**Results**

**MEN**

A group of 114 heterosexual men with gonococcal urethritis was treated. Of these men, 51 were excluded for the following reasons: default (38), initial contaminated *Chlamydia* culture (8), treatment failure at first follow-up examination (1), reinfection with *N. gonorrhoeae* during follow-up (4). Thus, full results were available for 63 men. Cultures for *C. trachomatis* were positive at the initial visit in 11 (17.5%) of these men. A further six men yielded isolates during follow-up, for an overall isolation rate of 27.0% (Table 1).

<p>| Table 1 Effect of a single dose of spectinomycin (2 g intramuscularly) on the frequency of isolations of Chlamydia trachomatis and on the development of post-gonococcal urethritis (PGU) in 63 heterosexual men with gonococcal urethritis |</p>
<table>
<thead>
<tr>
<th>Isolate of <em>C. trachomatis</em> in culture</th>
<th>No. of patients developing PGU</th>
<th>No. of isolations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td>After treatment</td>
<td>No. of isolation</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>11/11</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>0/0</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>6/6</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>8/46</td>
</tr>
</tbody>
</table>

Cultures for *C. trachomatis* were positive both before and after treatment in 11 patients. The intervals between isolations were one week or less for six men, two weeks for four men, and three weeks for one man. No patient who initially yielded *C. trachomatis* became isolation-negative after treatment. Six patients who were initially isolation-negative became isolation-positive after treatment, the intervals being one week for one man, two weeks for one man, and three weeks for four men. In 46 patients, isolates of *C. trachomatis* were not obtained before or after treatment; 13 of this group were follow-up for two weeks, 16 for three weeks, and 17 for four weeks.
After treatment with spectinomycin, 25 of the 63 patients with gonococcal urethritis (39.7%) developed PGU. All 17 men with positive cultures for C. trachomatis after treatment and eight of 46 men with negative cultures (17.4%) developed PGU.

WOMEN
A series of 55 women with confirmed gonococcal cervicitis was treated, but five were excluded (default (3), reinfection with N. gonorrhoeae during follow-up (1), initial contamination (1)). There were no treatment failures. Thus, results were available for 50 women (Table 2). Of these, 22 (44%) yielded C. trachomatis from the cervix on first examination and a further four during follow-up for an overall isolation rate of 52%. C. trachomatis was isolated from 17 women both before and after treatment. The intervals between examinations were one week or less for three women, two weeks for six women, three weeks for three women, and four weeks or more for five women. C. trachomatis was isolated from five patients before treatment but not subsequently, the intervals being two weeks (1 woman), three weeks (1 woman), and four weeks (3 women). C. trachomatis was not isolated from four patients before treatment but was isolated subsequently, the intervals being one week (1 woman), three weeks (2 women), and over four weeks (1 woman). Finally, C. trachomatis was not isolated from 24 women either before or after treatment, with intervals between examinations of two weeks (7 women), three weeks (3 women), and over four weeks (14 women).

Table 2  Effect of a single dose of spectinomycin (2 g intramuscularly) on the frequency of isolation of Chlamydia trachomatis from the cervix of 50 women with gonococcal cervicitis

<table>
<thead>
<tr>
<th>Isolate of C. trachomatis obtained</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>17</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>5</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>4</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>No</td>
<td>24</td>
</tr>
</tbody>
</table>

Discussion
Spectinomycin in the dosage used was an effective treatment for gonorrhoea in our patients and had a low failure rate. However, this antimicrobial had little effect on associated C. trachomatis infection in either men or women; in this respect it resembled penicillin and ampicillin.

The failure of the three agents which are the most widely used for the treatment of gonorrhoea to have a significant effect on associated C. trachomatis infection indicates an unsatisfactory situation. C. trachomatis is an important genital pathogen. It undoubtedly causes many infections of non-gonococcal urethritis, cervicitis, and neonatal eye disease (Dunlop et al., 1966; Rees et al., 1977); it may be implicated in the pathogenesis of salpingitis (Mardh et al., 1977), epididymitis (Har- nisch et al., 1977), and neonatal respiratory disease (Beem and Saxon, 1977). Its treatment appears to be desirable. Between 20 and 60% of patients with gonorrhoea are infected by C. trachomatis, but at present only a proportion of the men (those diagnosed as having PGU) and none of the women are likely to receive effective treatment.

Because of the appearance of β-lactamase producing strains of N. gonorrhoeae, the treatment of gonorrhoea is at present being reappraised. Whether one drug will be found which gives good results in the treatment of both N. gonorrhoeae and C. trachomatis infections remains to be seen, but the time is ripe for further trials of antimicrobials, single, combined, or perhaps sequential, in the treatment of these serious infections.

We are grateful to Dr E. Joan Stokes for kindly providing laboratory facilities and to Ms Lam Po Tang for technical assistance. This work was supported by the Medical Research Council and by Upjohn Ltd.

References


Spectinomycin hydrochloride in the treatment of gonorrhoea


