Comparison of Spiramycin and Doxycycline for Treatment of Chlamydia trachomatis Genital Infections

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We performed a single blind controlled multicenter study in which we compared the efficacy and safety of 100 mg of doxycycline versus those of 1 g (3 × 10⁶ IU) of spiramycin given orally twice daily for 14 days in the treatment of culture-positive Chlamydia trachomatis genital tract infections. A total of 367 patients were enrolled in the study, and 364 patients were evaluable for safety and 265 patients were evaluable for efficacy. The cure rate between treatment groups was not statistically significant, being 98% (125 of 128 patients) in the spiramycin group and 100% (133 of 133 patients) in the doxycycline group. Female patients who received spiramycin were more likely to report dysesthesias that resolved after the completion of therapy. The results of the study show that spiramycin is an effective drug for the treatment of C. trachomatis infection and warrants further assessment over a shorter treatment period (7 days) and during pregnancy.

Chlamydia trachomatis is a frequent cause of sexually transmitted disease and is associated with significant morbidity in women and neonates. The antibiotic of choice for the treatment of C. trachomatis infections is a tetracycline, with macrolides reserved for second-line treatment or during pregnancy (5). The success rate in eradicating genital tract infections with tetracyclines given for at least 7 days is greater than 90% (5). Spiramycin is a macrolide antibiotic with a range of MICs for C. trachomatis of 0.025 to 2.0 μg/ml (4). The drug is concentrated intracellularly (2) and has been used extensively in Europe for the treatment of toxoplasmosis during pregnancy (1). The purpose of the present study was to compare the efficacy and safety of spiramycin with those of doxycycline for the treatment of culture-proven C. trachomatis genital infections.

Patients of either sex over the age of 18 years were asked to participate in a single blind controlled multicenter study comparing oral doxycycline, 100 mg, versus spiramycin, 1 g (3 × 10⁶ IU) given twice daily for 14 days. For patients to be eligible for entry into the study, they had to have a positive rapid detection test result for C. trachomatis at the infection site (endocervix or urethra) with subsequent confirmation by cell culture techniques. Patients were excluded from the study if they had concomitant infections, recent antibiotic therapy, complicated genitourinary tract infections such as prostatitis or salpingitis, drug hypersensitivity, or significant hepatic or renal impairment.

Women of childbearing age were required to use a recognized contraceptive method during the study. All patients were asked to refrain from sexual activity until the first posttreatment follow-up visit and to use condoms until the end of the study. They were asked to avoid antacids in order not to reduce the absorption rate of doxycycline.

At the initial visit, the medical history was obtained and a physical examination was performed. Samples were taken for Chlamydia antigen detection and culture, and blood and urine specimens were taken for hematology, biochemistry, syphilis serology, and urinalysis. Patients could be entered into the study pending the Chlamydia culture result if they had a positive rapid antigen test result. Capsules and packaging were identical in appearance and were supplied in blister packs. Patients randomized to receive spiramycin were told to take their capsules 1 h before a meal, and those taking doxycycline were told to take them immediately after a meal. Other than these instructions patients were unaware of which treatment regimen they were on. Patients were asked to return 1 to 4 days after the completion of therapy, at which time they were questioned about adverse events and a medication count was performed. Examination was performed, and if signs or symptoms of infection persisted, the Chlamydia culture was repeated. The blood and urine tests were also repeated. A final visit was required at 14 to 28 days posttherapy, during which all patients were required to provide a sample for a test-of-cure Chlamydia culture. Data were submitted to the appropriate statistical analysis, and type I error was set at 5% (P < 0.05).

A total of 367 patients were enrolled in the study, and 265 (93 males, 172 females) were evaluated for efficacy. The most common reason for exclusion from the efficacy evaluation was a negative pretreatment Chlamydia culture (85 patients; 40 in the spiramycin group, 45 in the doxycycline group). A total of 131 patients were randomized to receive spiramycin (45 males, 86 females) and 134 (48 males, 86 females) were randomized to receive doxycycline. The cure rates were 98% (125 of 128 patients) in the spiramycin group and 100% (133 of 133 patients) in the doxycycline group. The three treatment failures in the spiramycin group were males. The difference in cure rates was not statistically significant either by sex or for the entire group. Three spiramycin- and one doxycycline-treated patients were considered to have been reinfected.

Three hundred sixty-four patients were analyzable for safety (180 in the spiramycin group, 184 in the doxycycline group). Comparisons between baseline and end-of-treatment laboratory data did not reveal clinically relevant changes in either treatment group. Spiramycin treatment produced a statistically significant higher number of side effects (Table

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TABLE 1. Type and incidence of side effects

<table>
<thead>
<tr>
<th>Treatment group (no. of patients)</th>
<th>No. of events with the following severity: Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Somatic sensation (no. of patients)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spiramycin (n = 180)</td>
<td>60</td>
<td>39</td>
<td>0</td>
<td>24bc</td>
</tr>
<tr>
<td>Doxycycline (n = 184)</td>
<td>42</td>
<td>17</td>
<td>7c</td>
<td>1</td>
</tr>
</tbody>
</table>

* Indicates paresthesia and/or hypoesthesia of the circumoral area, tongue, and/or extremities.
bc Twenty-one females and three males.
cP < 0.05 by the χ² test.

1). However, patients treated with doxycycline presented with a pattern of significantly more severe adverse events. Of interest was the development of dysesthesias in 13% (24 of 180) of patients treated with spiramycin. Women were more likely to experience this than men. The dysesthesias were self-limited and resolved after the discontinuation of therapy. Three patients receiving doxycycline and no patients in the spiramycin group discontinued their medication because of intolerance.

The results of the present study indicate that spiramycin and doxycycline are equally effective for the treatment of urethritis and endocervicitis caused by C. trachomatis. However, there were qualitative and quantitative differences in tolerance profiles between the treatment groups. Patients receiving spiramycin experienced a statistically significant greater number of adverse events primarily because of the higher incidence of mild to moderate peripheral sensory disturbances. These manifestations did not lead to the discontinuation of treatment and resolved after therapy had stopped. Apart from their more frequent distribution in females, no explanation for their presence can be given. This transient adverse event has been reported previously (3). The adverse events reported by doxycycline-treated patients were more severe, and three of these patients discontinued their medication because of gastrointestinal intolerance.

C. trachomatis infections can be successfully treated with a 7-day course of doxycycline, tetracycline, ofloxacin, or erythromycin (5). A single-dose treatment with 1 g of azithromycin is also effective therapy. Only erythromycin is recommended for the treatment of C. trachomatis infections during pregnancy. Spiramycin can be used during pregnancy and has now been shown to be an effective antichlamydial agent. Further studies with spiramycin should be performed by using a shorter treatment period (7 days), and there should be an evaluation of spiramycin as treatment for C. trachomatis infections during pregnancy.

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REFERENCES