Rosoxacin in the treatment of uncomplicated gonorrhoea in men

KANCHANA PANIKABUTRA, CHARAS ARIVARIT, ANUPONG CHITWARAKORN, AND CHOOSAK SAIENSNOH

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SUMMARY Between 3 January and 4 March 1983 we treated 200 male patients diagnosed as having uncomplicated gonococcal urethritis with one of two regimens. They were divided into two groups and randomly assigned to treatment with either 2 g spectinomycin administered intramuscularly (group A) or 300 mg rosoxacin by mouth (group B). Of 187 isolates tested for the production of β-lactamase, 101 (54%) were penicillinase producing Neisseria gonorrhoeae (PPNG) strains. All 81 cases followed in group A (spectinomycin) were cured, compared with 88.5% (77 out of 87) of the patients followed in group B (rosoxacin).

We concluded that rosoxacin at a dosage of 300 mg administered orally was fairly effective in the treatment of gonococcal urethritis in men caused by both PPNG and non-PPNG strains.

Introduction

Since the emergence of penicillinase producing Neisseria gonorrhoeae (PPNG) strains in 1976, penicillin is no longer the drug of choice in the treatment of gonorrhoea.1 After the first two cases of PPNG in Bangkok were reported in 1977, the failure rates in the treatment of uncomplicated gonorrhoea with penicillin increased until a failure rate of 30% was reached in 1979.2 3 PPNG strains account for a large proportion of all gonococcal isolates in Thailand. In 1981 42.9%-48.9% of strains of N gonorrhoeae isolated in Bangkok were reported to be PPNG.4 5

Although spectinomycin is the drug that produces acceptable cure rates in and is recommended in the treatment of gonorrhoea caused by PPNG strains, we need to find an alternative treatment.4 6-8 Since 1981 PPNG strains resistant to spectinomycin have been reported in many parts of the world.9-13 The in vitro activity of rosoxacin, a pyridyl quinolone derivative, against N gonorrhoeae has been studied and shown to be more active than penicillin, cefuroxime, and tetracycline. Its activity was not affected by the production of β-lactamase.14 We undertook this study to compare the efficacy of rosoxacin and spectinomycin in the treatment of uncomplicated gonorrhoea in men.

Patients and methods

STUDY DESIGN

Men attending this hospital between 3 January and 4 March 1983 who were diagnosed as having uncomplicated gonorrhoea with a positive smear on the initial visit were selected. The study comprised 200 men, all of whom were Thai. They were divided into two groups and randomly assigned to treatment with either 2 g spectinomycin administered intramuscularly (group A) or 300 mg rosoxacin by mouth (group B).

DIAGNOSTIC METHODS

The diagnosis was based on the finding of Gram negative intracellular diplococci in the Gram's stained smears and on the results of cultures of specimens taken from the urethra. Blood for routine serological tests for syphilis was taken in every case. The Gram's stained smears were examined in the clinic; the other specimens were inoculated direct on to Thayer-Martin medium and incubated at 35°C in an atmosphere of carbon dioxide. Cultures were examined after 24 and 48 hours, and a diagnosis of gonorrhoea was based on typical colonial morphology, Gram's stained smear microscopy showing Gram negative diplococci, and a positive oxidase test. Isolates were confirmed as gonococci by sugar fermentation reactions. The colonies were subcultured to identify PPNG by the cephalosporin test.15 The confirmed gonococcal isolates were tested for antibiotic sensitivity by agar plate dilution techniques.16

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FOLLOW UP
Follow up visits were arranged three, seven, and 14 days after treatment. Urethral specimens for Gram's stained smear microscopy and culture were taken on each occasion. Routine serological tests for syphilis were performed at monthly intervals for three months.

If gonococci persisted or reappeared within 14 days of treatment and further sexual intercourse was denied by the patient, then the treatment was considered to have failed. The reappearance of gonococci after 14 days, irrespective of the patient's history, was considered to be due to reinfection. Those who admitted sexual intercourse before the first follow up examination were excluded from the final assessment.

Patients with microscopical or culture evidence of gonococcal infection at the follow up visits were treated with spectinomycin 2 g administered intramuscularly. Those who at day 7 had signs of urethritis (>4 polymorphonuclear leucocytes/1000 × microscope field of Gram stained smear) but no evidence of N. gonorrhoeae were considered to have postgonococcal urethritis (PGU).17

STATISTICAL ANALYSIS
The unpaired t test and the χ² test were used.

Results
Of the 200 patients enrolled in the study, 32 were excluded; 11 because N. gonorrhoeae did not grow in the initial culture, four because the patients had sexual intercourse before the first follow up examination, and 17 because the patients defaulted after the treatment. Of 189 isolates, 187 were tested for β-lactamase production: 101 (54%) gave positive results. There were 81 patients in group A and 87 in group B. Table I shows the results of treatment.

**TABLE I** Results of treatment of gonorrhoea with spectinomycin or rosoxacin

<table>
<thead>
<tr>
<th></th>
<th>Group A (spectinomycin)</th>
<th>Group B (rosoxacin)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No assessed</td>
<td>No cured</td>
</tr>
<tr>
<td>PPNNG strains</td>
<td>46</td>
<td>46</td>
</tr>
<tr>
<td>Non-PPNG strains</td>
<td>34</td>
<td>34</td>
</tr>
<tr>
<td>Not tested</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>81</td>
</tr>
</tbody>
</table>

PPNG = penicillinase producing Neisseria gonorrhoeae.

SENSITIVITY OF N. GONORRHOEA TO ANTIBIOTICS
Table II shows the minimum inhibitory concentrations (MICs) of spectinomycin and rosoxacin for PPNNG and non-PPNG strains. The difference between the MICs of either drug for PPNNG and for non-PPNG strains was not significant. The mean MIC of spectinomycin was 8.04 mg/l for PPNNG strains and 8.23 mg/l for non-PPNG strains (t = 0.4917; p>0.05). The mean MIC of rosoxacin was 0.0133 mg/l for PPNNG strains and 0.0114 mg/l for non-PPNG strains (t = 0.5521; p>0.05).

Table III shows the correlation between the MICs and the results of treatment with rosoxacin. Of the 41 patients infected with PPNNG strains whose MICs ranged from 0.0002 mg/l to 0.03 mg/l, 37 (90%) of 20007; p>0.05).

**TABLE II** Sensitivity of N. gonorrhoeae to antibiotics

<table>
<thead>
<tr>
<th></th>
<th>Group A (spectinomycin)</th>
<th>Group B (rosoxacin)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PPNG</td>
<td>Non-PPNG</td>
</tr>
<tr>
<td>MICs (mg/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.00001</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>0.00002</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>0.00005</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>0.0001</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>0.001</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>0.005</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>0.008</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>0.01</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>0.03</td>
<td>31</td>
<td>31</td>
</tr>
<tr>
<td>&gt;0.06</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mean MIC</td>
<td>8.04</td>
<td>8.23</td>
</tr>
</tbody>
</table>

PPNG = penicillinase producing Neisseria gonorrhoeae.

**TABLE III** Correlation between the MICs and the results of treatment with rosoxacin (group B)

<table>
<thead>
<tr>
<th>MICs of rosoxacin (mg/l)</th>
<th>PPNG Cured</th>
<th>PPNG Not cured</th>
<th>Non-PPNG Cured</th>
<th>Non-PPNG Not Cured</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00001</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>0.00002</td>
<td>1</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>0.00005</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>0.001</td>
<td>2</td>
<td></td>
<td>2</td>
<td></td>
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<tr>
<td>0.005</td>
<td>2</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>0.008</td>
<td>2</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>0.01</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>0.03</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>&gt;0.06</td>
<td>3</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>41</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PPNG = penicillinase producing Neisseria gonorrhoeae.
were cured. Of the 38 patients infected with non-PPNG strains whose MICs ranged from 0-00001 mg/l to 0-03 mg/l, 34 (89-5%) were cured.

SIDE EFFECTS

Of the 93 patients who received rosoxacin and came for follow up examination, 18 (19-4%) reported side effects: 17 had mild dizziness and one had generalized itching, but no clinical signs were seen on examination.

POST GONOCOCCAL URETHRITIS (PGU)

Of the 80 patients in group A (spectinomycin) who had more than one follow up examination, 33 (41.3%) had PGU. Of the 72 patients in group B (rosoxacin), 33 (45.8%) had PGU. There was no difference between the two groups ($\chi^2 = 0-32; p>0-01$).

Discussion

In areas of the world where PPNG strains are highly prevalent the drugs that should be used in the treatment of gonococcal infections should be highly effective for both PPNG and non-PPNG strains. Apart from spectinomycin, many new cephalosporins (namely cefuroxime, cefotaxime, cefoxitine, and ceftriaxone) have been reported to be highly effective in the treatment of such infections.\(^{4-6}\) The administration of these drugs requires intramuscular injection which is often painful. Rosoxacin is a drug that can be given by mouth in only two 300 mg capsules. In this dosage the drug has been reported to be highly effective in the treatment of both PPNG and non-PPNG strains with cure rates from 94% to 100%.\(^{22-31}\) The results of treatment of gonococcal infections with the same dosage in Thailand were different. Polnikorn et al\(^23\) reported a cure rate of 87.5% and in our study we had a 88.5% cure rate. The prevalence of PPNG strains in the study population of Polnikorn et al was 52%, and in our patients it was 54%.

The difference between the cure rates in group A (spectinomycin) and group B (rosoxacin) was significant ($\chi^2 = 9-89; p<0-01$). In group B (rosoxacin) there was no difference between the results of treatment of the patients infected by PPNG and non-PPNG strains ($\chi^2 = 0-02; p>0-01$).

The side effects encountered among the patients who took rosoxacin in our study were considered to be mild, and all the patients recovered spontaneously. We conclude that the tolerance to this antimicrobial agent was good.

The authors thank Sterling Drug International Inc of Thailand for providing the rosoxacin used in this study.

References

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