Rosoxacin in the treatment of uncomplicated gonorrhoea in men

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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. 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 1979.23 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.45

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.468 Since 1981 PPNG strains resistant to spectinomycin have been reported in many parts of the world.913 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 of gonorrhoea was made 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
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 x microscope field of Gram stained smear) but no evidence of N gonorrhoeae were considered to have post-gonococcal urethritis (PGU). 17

STATISTICAL ANALYSIS

The unpaired t test and the $\chi^2$ 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 $\beta$-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>PPNG 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.

Table II shows the minimum inhibitory concentrations (MICs) of spectinomycin and rosoxacin for PPNG and non-PPNG strains. The difference between the MICs of either drug for PPNG and for non-PPNG strains was not significant. The mean MIC of spectinomycin was 8.04 mg/l for PPNG 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 PPNG 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 PPNG strains whose MICs ranged from 0.00002 mg/l to 0.03 mg/l, 37 (90%) cured of PPNG strains and 0 of non-PPNG strains.

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>Non-PPNG Cured</th>
<th>PPNG Not cured</th>
<th>Non-PPNG Not Cured</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00001</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0.00002</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0.00005</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0.001</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0.002</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0.005</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0.008</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0.01</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0.03</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0.06</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>&gt;0.06</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</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 general-
ized itching, but no clinical signs were seen on ex-
namination.

POST GONOCOCAL 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 dif-
fERENCE 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 treat-
ment of gonococcal infections should be highly effec-
tive 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.\(^4\,5\,18\,26\) 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%.\(^27\,31\) The results of treatment of gonococcal
infections with the same dosage in Thailand were
different. Polnikorn et al\(^25\) 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 popula-
tion of Polnikorn et al\(^25\) was 52%, and in our patients
it was 54%.

The difference between the cure rates in group A
(spectinomycin) and group B (rosoxacin) was signifi-
cant ($\chi^2 = 9·89$; p < 0·01). In group B (rosoxacin)
there was no difference between the results of treat-
ment 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 spontane-
ously. We conclude that the tolerance to this anti-
microbial agent was good.

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233