Ofloxacin in Treating Nongonococcal Urethritis

Somchai Tungphaaisal, M.D.*
Sonthit Sutthijumroon, M.D.*
Verapol Chandeying, M.D.*
Savanun Taravanit, M.D.**

A study of 49 men attending the Sexually Transmitted Diseases Clinic, VD Center, Region 12 between January 7, 1988 to March 31, 1988 was carried out with the objective of evaluating the efficacy of ofloxacin in the treatment of NGU. After excluding the cases of urethritis from Neisseria gonorrhoeae the cases of NGU formed the basis for this report. The clinical criteria for diagnosis was the presence of 10 or more polymorphonuclear (PMN) leukocytes in any five microscopic fields (at a magnification of 1,000) in the Gram-stained urethral smear. NGU was treated with ofloxacin 200 mg orally twice daily for 7 days, and also was prescribed to their wives or sexual partners. Follow-up visit was scheduled 1-2 weeks after the completion of the treatment. The clinical response was good in 81.6% (40 in 49 cases) and fair in 10.2% (5 in 49 cases) and unchanged in 8.2% (4 in 49 cases). There were no adverse drug reactions of ofloxacin. So ofloxacin seemed to be an effective and safe drug for NGU.

INTRODUCTION

Acute urethritis manifests itself as a combination of urethral discharge and discomfort. The discomfort frequently takes the form of dysuria (soreness or irritation noted during micturition). Irritation may be recognized at other times, and may appear as itching, tingling, or burning localized to the distal or proximal portion of the penis. Severity ranges from mild to extremely irritable. Dysuria may be noticed only on first morning voiding, when the urine stream is most concentrated. Urethral discharge also varies considerably in amount. There may be a purulent emission that heavily stains clothing. Conversely, discharge may be formed in such small amounts that it is apparent only on arising, as a small droplet at the meatus. Urethral discharge may be clear, white, yellow, green, or brown and is occasionally described as malodorous. Urethral discharge
may be considerably reduced or completely eliminated by recent urination.1

The pathognomonic confirmatory laboratory finding is an increased number of polymorphonuclear leukocytes (PMN) on gram stain of urethral discharge or in the sediment of the first-voided urine. Urethritis is called nongonococcal if Neisseria gonorrhoeae cannot be detected. The term nongonococcal urethritis (NGU) is preferable to the term nonspecific urethritis, because NGU has specific causes, and some of these have been explained.2 The organisms that are proven or possible causes of sexually transmitted NGU in heterosexual men are Chlamydia trachomatis (30-50%),3-7 Ureaplasma urealyticum (10-40%), and neither (20-30%); such as Trichomonas vaginalis, Yeasts, Herpes Simplex virus, and Corynebacterium.2

Ofloxacin is a potent, broad spectrum member of the carboxyquinolone class of antimicrobial agents. It has potent activity in vitro against a wide variety of gram-positive and gram-negative aerobic and anaerobic bacteria, including those associated with urinary tract infections and sexually transmitted diseases. Against C. trachomatis infecting cells grown in culture, ofloxacin demonstrates MIC₉₀ levels of about 1 ug/ml.8 It is 1/3 to 1/10 of tetracycline. Against Chlamydia, ofloxacin is more potent than ciprofloxacin, enoxacin and norfloxacin. MIC₉₀ levels of 2 to 8 ug/ml are exhibited by ofloxacin against U. urealyticum or Gardnerella vaginalis, about 1/2 of doxycycline versus the Ureaplasma.8

The prospective study was made to evaluate the efficacy of ofloxacin in the treatment of NGU in the heterosexual males.

MATERIALS AND METHODS

Study population

A study of 49 men attending the Sexually Transmitted Diseases Clinic, VD Center, Region 12 between January 7, 1988 to March 31, 1988 was carried out with the objective of evaluating the efficacy of ofloxacin in the treatment of nongonococcal urethritis, after excluding the cases of urethritis from N. gonorrhoeae by gram stain and urethral culture. The cases of NGU formed the basis for this report. The reasons for attending the clinic were listed in Table 1.

Exclusion criteria

1. Receiving antibiotics within 7 days prior to the study
2. Urethritis caused by N. gonorrhoeae

Inclusion criteria

1. Sexually active male age 15-45 years
2. Chief complaints of one of the followings
   2.1 Urethral discharge
   2.2 Dysuria

Table 1 The reasons for attending to STD Clinic of NGU

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Percent</td>
</tr>
<tr>
<td>Urethral discharge</td>
<td>47</td>
<td>95.9</td>
</tr>
<tr>
<td>Dysuria</td>
<td>33</td>
<td>67.3</td>
</tr>
</tbody>
</table>

*p value* < 0.001

Patient evaluation

The patients complaining of urethral discharge and/or dysuria were examined. The specimens were taken with a bacteriologic loop passed 2 cm. into the urethra. The first specimen was stained with gram stain and examined for the presence of intracellular gram-negative diplococci and polymorphonuclear leukocytes count. The slide was scanned at a magnification of 1000 to evaluate the presence and amount of mucus, to look for squamous cells and to identify areas of mucus that appeared to contain inflammatory cells. Most often, PMN leukocytes were distributed uniformly in urethral mucus, but in some cases they were distributed in a patchy fashion, representative areas containing the densest concentration of such leukocytes were selected. The number of polymorphonuclear leukocytes per microscopic field at a magnification of 1,000 in five nonadjacent fields was then established with the use of an oil-immersion lens. Therefore, specimen containing 10 or more polymorphonuclear leukocytes in any five microscopic fields was considered for significant leukocytes in urethral secretion.

If gonococci was not seen and ten PMN leukocytes or more per oil field were present, the patient was admitted to the trial. The other specimen was inoculated on modified Thayer-Martin medium and incubated at 37°C in an atmosphere of air plus 5% carbon dioxide.

Treatment

The patients who were diagnosed as NGU would be treated with ofloxacin 200 mg. twice daily for 7 days. Their wives or sexual partners would be treated with the regimen dose to prevent ping-pong phenomenon. After complete medication for one week, the patients were advised to return for test of cure and instructed to abstain from drinking alcohol and from having sexual contact until the next visit.

RESULTS

The urethral findings of the urethral secretions were shown in Table 2. The clinical response to treatment (Table 3) was classified as:

- Good both the clinical assessment and the laboratory testing were improved
Table 2 Urethral findings among NGU

<table>
<thead>
<tr>
<th>Findings</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Percent</td>
</tr>
<tr>
<td>PMN leukocytes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 or more</td>
<td>49</td>
<td>100</td>
</tr>
</tbody>
</table>

*by Z test

Table 3 The clinical response

<table>
<thead>
<tr>
<th>Level</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>40</td>
<td>81.6</td>
</tr>
<tr>
<td>Fair</td>
<td>5</td>
<td>10.2</td>
</tr>
<tr>
<td>Stable</td>
<td>4</td>
<td>8.2</td>
</tr>
</tbody>
</table>

Fair — the clinical assessment was improved but the laboratory testing was unimproved
Stable — both the clinical assessment and the laboratory testing were unimproved

As shown in Table 3, the disappearance of the symptoms and signs was significantly achieved by ofloxacin therapy. There were no adverse drug reactions.

DISCUSSION

For research purposes the criteria used for diagnosis of urethritis have usually included presence of urethral discharge and of 20 or more PMN in two or more of five random X 400 fields of the sediment of the first 10-15 ml of urine collected when the patient has not voided for four hours or longer. This criteria is undoubtedly too restrictive. In a study of men with minimal or no discharge, there was a definite bimodal distribution of the numbers of PMN in gram-stained urethral specimens and in the first-voided urine; the presence of 15 or more PMN in any five random X 400 fields of the sediment of the first voided-urine, was correlated with a mean of more than four PMN in five X 1,000 oil-immersion fields in gram-stained specimens of urethral exudate, and either finding was regarded as abnormal. Swartz et al independently concluded that a mean of more than four PMN per oil-immersion field on urethral smear correlated with urethritis.

Thus, uses of smears or urines to provide objective evidence of urethritis is only a rough guide to the presence of urethral pathogens. Just as with gonorrhea, the unescapable conclusion is that culture is necessary to identify the organisms. In this study we used the criteria for diagnosis of NGU of 10 or more PMN in any five microscopic fields, the similar criteria as mucopurulent cervicitis which was the counterpart of urethritis.

Results of treatment for NGU are not good as with gonorrhea, even though almost every antimicrobial in clinical usage has been tried. Tetracycline, erythromycin and a combination of sulfonamides and aminocyclitols were recognized as being most effective therapy in the 1950s. The basis for these observations has been clarified by more recent research, because all three regimens are capable of eradicating C. trachomatis and U. urealyticum, while spectinomycin eradicates U. urealyticum from the urethras of 60 to 70 per cent of men. Although many studies of treatment of NGU have been performed, the optimal drug, dosage and duration of therapy have not been determined. The assessment of the reported efficacy of various antimicrobial regimens is often difficult because:

1. Until recently, most studies have not employed cultures for both C. trachomatis and U. urealyticum.
2. C. trachomatis-positive NGU responses differently from C. trachomatis-negative NGU.
3. Manifestations may spontaneously disappear in some cases even without specific therapy.
4. Patients frequently remain sexually active so that relapse cannot be distinguished from reinfection.
5. Patients frequently default.
6. The appropriate duration of follow-up for assessment of results is debatable.
7. Eradication of C. trachomatis and U. urealyticum does not ensure a lasting clinical cure.

The treatment should not be delayed awaiting the confirmatory evidence of a negative gonorrhea culture but should be commenced on the basis of a provisional diagnosis as it is established that there is urethral inflammation.

Under this study, ofloxacin 200 mg. was orally used twice daily for 7 days, and also was prescribed to their wives or sexual partners. Follow-up visit was scheduled 1-2 weeks after the completion of the treatment. The result was good in 81.6% (40 in 49 cases), fair in 10.2% (5 in 49 cases) and unchanged in 8.2% (4 in 49 cases). There were no adverse drug reactions of ofloxacin. So ofloxacin seemed to be an effective and safe drug for NGU.

As a part of the management of urethritis, every attempt should be made to treat the patient’s sexual partner(s). This procedure is widely accepted for partners of men with gonorrhea, and is equally appropriate for partners of men with NGU, although a number of studies have been shown that this does not reduce the overall incidence of recurrence.
ACKNOWLEDGEMENT

The authors wish to thank Daiichi Seiyaku Co., Ltd., for providing ofloxacin used in this study.

REFERENCES