Treatment of Gonococcal Infection:
An Analysis of Cases Treated Over Ten Years
at Tokai University Hospital

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(Received August 5, 1987)

The results of gonococcal infection treatment at Tokai University Hospital during the past decade were summarized. Symptoms and signs of gonococcal urethritis and their therapeutic responses were essentially the same as in other series previously reported. Among drug regimens employed, penicillins were found most effective while cephalosporins proved to be relatively less effective. One-shot therapy with cephalosporins also proved less satisfactory.

(Key Words: Urethritis; N. gonorrhoeae, STD, GU.)

INTRODUCTION

The Department of Urology, Tokai University Hospital, dealt with approximately 130 men with gonococcal infection during the period from 1975 to 1985. Most of these cases were of acute gonococcal urethritis. No definite or preferred drug therapies were used. The dosage as well as the duration of administration were quite variable. Although the therapeutic data from these cases were difficult and awkward to analyze and evaluate by well standardized criteria, they appeared at least to permit us to obtain a rough estimate of the duration of treatment required for disappearance or eradication of the infecting organism and also to distinguish between effective and less effective drugs. Work to formulate criteria for evaluation of drug effectiveness in gonorrheal and nongonorrheal urethritis by the UTI (Urinary Tract Infection) Study Group is now under way. Since the criteria is expected to dictate the standardization of the time and method of evaluation of therapeutic response as well as of the duration of medication and observation, their establishment will certainly preclude obtainment of such data as are to be presented here. These circumstances prompted us to conduct the present analytical study.

MATERIALS AND METHODS

Patients with gonococcal infection who were seen at the Department of Urology, Tokai University Hospital during a period from February 1974 through 1985 were considered for inclusion in the study. An overwhelming majority of the patients had acute gonococcal urethritis and some were not free of the infecting organism after receiving several treatments. Of these patients, those from whom positive cultures for gonococcus were obtained were chosen for the study. Patients who failed to reattend or were missing before term of treatment as well as those from whom adequate data were not obtained were excluded from the study. Thus, approximately 130 cases were subjected to final analysis. Time (in days) elapsing from exposure to onset and from onset to visiting the hospital and the number of treatment days required for obliteration of symptoms were determined on the

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basis of patient’s personal report. Those whose report was considered incredible were excluded from the analysis.

RESULTS

Concerning the time elapsing from exposure to onset, reliable data were obtained from 115 cases, indicating that the time interval ranged from 1 to 21 days, averaging 6.34 days.

The time interval between onset and visiting hospital averaged 6.66 days for 122 cases. One case in which the patient previously received treatment from a certain doctor for more than a month was excluded from the calculation.

Data regarding the occurrence or nonoccurrence of relapse were obtained from 35 cases. In this study, when symptoms returned more than one month after being labelled as cured patients were considered as having a recurrence. By this criterion, 2 out of the 35 cases had a recurrence, while the remaining 33 cases were recurrence-free for at least 12.8 months, on average, after cure was achieved. The data on recurrence were based on those patients who visited the hospital to undergo a reexamination or revisited the hospital for some other reason other than the disease in question and this accounts for the small number of relevant cases.

For the entire cases in this survey the numbers of days required for the disappearance of symptoms (as alleged by the patients) averaged 2.32 days. Disappearance of gonococci and leukocytes from the urethral discharge was confirmed in 63 cases after an average of 5.51 days’ treatment. This means that eradication of the organism was achieved within 5.51 days of treatment since many patients paid a revisit for examination some time after they became symptom-free.

Therapeutic effects by drug families are summarized in Table 1. Judgement of drug effectiveness was based only on evaluations made at Days 3 and 7 of treatment. Patients who were evaluated for drug effectiveness at other days of treatment were deliberately excluded. A drug regimen was evaluated as effective (successful) when it brought about disappearance of gonococci and symptoms and a reduction of urinary leukocytes to the level of less than one cell seen per microscopic field on examination of an initial urine specimen (first urine), while otherwise it was regarded as ineffective (failure).

By these criteria, penicillins (PCs) were evaluated as effective in 76.5% of cases at Day 3 and in 83.9% at Day 7 of treatment. The corresponding figures for Quinolones were 50% and 62.5%, respectively. Tetracyclines (TCs) proved to be effective in 81.8% of cases at Day 7, while cephalosporins (CEPs) were effective in 33.3% at Day 7.

Cases in which drug effectiveness was evaluated at Day 3 were not included in those assessed at Day 7. One-shot therapy was mostly with the CEP; these drugs used by this mode of administration proved to be least effective, the effectiveness rate being 45.5% at Day 3 and 33.3% at Day 7, respectively (Table 2). Two cases had a recurrence, which occurred one month after therapy in one of them, although the possibility of an intercurrent reinfection was not completely ruled out. In the other case, the disease recurred 7 days after one-shot therapy after having been transitorily cured.

Among cases in which initial therapy had

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Days</th>
<th>Cases</th>
<th>Effective</th>
<th>Noneffective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillins</td>
<td>3</td>
<td>17</td>
<td>13(76.5%)</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>31</td>
<td>26(83.9%)</td>
<td>5</td>
</tr>
<tr>
<td>Quinolones</td>
<td>3</td>
<td>4</td>
<td>2(50.0%)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>8</td>
<td>5(62.5%)</td>
<td>3</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>3</td>
<td>2</td>
<td>0(0%)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>11</td>
<td>9(81.8%)</td>
<td>2</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>3</td>
<td>7</td>
<td>4(57.1%)</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>6</td>
<td>2(33.3%)</td>
<td>4</td>
</tr>
</tbody>
</table>
failed, there were 24 where data concerning drug susceptibility of gonococcal strains isolated at that time were available, according to which all strains were sensitive to the drugs administered with the exception of one which was recorded as insensitive to Ampicillin (ABPC).

DISCUSSION

The length of time elapsing from exposure to the onset of gonorrhea in our present series was 6.34 days on the average as mentioned earlier, which is somewhat longer than hitherto reported figures of 2-4 days. The value might be reasonably acceptable, being slightly smaller than a corresponding figure for non-gonococcal urethritis of 12.8 days (10, 11, 13, 14, 24, 26, 27).

On the other hand, the present survey disclosed that the patients visited the hospital a little less than one week after the onset of disease. This delay is accounted for partly by the patient’s reluctance to be seen in a large hospital with symptoms of a shameful disease and may also be due partly to the current decrease in knowledge of venereal diseases.

The number of treatment days required for obliteration of symptoms averaged 2.32 for 48 cases responding favorably to medication. The UTI Study Group recommends the evaluation of drug efficacy at Day 3 of medication. The number of treatment days elapsed until cure (based on bacteriological examination and not on the patient’s allegation) was 5.51 on the average and it seems likely that the disease actually was already cured before the patient became aware of his being cured of the disease and reported so (7, 18, 19).

Among various drugs used in the present series, PCs were prescribed in the largest proportion of cases. It seems probable that in some of the cases in which the therapeutic response was evaluated at Day 7, the drug regimen might have proven effective already at Day 3 although there is no evidence confirmative of this. Therefore, the actual number of days of treatment with PC required till disappearance of symptoms should be considerably different from the calculated mean, 2.32 days.

At the present time, ABPC and spectinomycin appear to be the drugs of first choice for the treatment of gonococcal infection (5, 9, 20, 21, 28). The results of this analytical study indicate that the rate of effectiveness was highest for PCs among all drug regimens employed. Second to them were TCs; drugs in the Quinolone (3, 4, 12, 17, 22, 23) and CEP series (15, 16) proved less effective than the former two families.

All these drugs were administered q.i.d orally. Their dosage being varied, it is impossible to determine the optimal dosage and best drug. However, it can at least be said that they were

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Table 2  Therapeutic effects by one-shot therapy with cephalosporins

<table>
<thead>
<tr>
<th>Days after administration</th>
<th>Cases</th>
<th>Effective</th>
<th>Noneffective</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>11</td>
<td>5(45.5%)</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>1(33.3%)</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 3  Disc Susceptibility of drugs used for initial therapy and failed to cure gonococcal infection. (n = 24)

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Disc susceptibility</th>
<th>over (+ +)</th>
<th>(-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalosporins</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>9</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Penicillins</td>
<td>9</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Quinolones</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

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more useful when administered by mouth than when given as one-shot therapy. Most of the drugs administered by one-shot injection were CEPs (25), which, despite their proven antibacterial activity against gonococci and of being given by one-shot injection in a maximum daily dose, were proven effective in less than half of the cases so treated. It may therefore be concluded that one-shot therapy at least with CEPs is not recommendable.

A careful scrutiny of therapeutic failures disclosed that in all these cases but one the infecting organism was sensitive to administered drugs (which, theoretically, should have therefore produced a more or less beneficial effect); drug dosages were by no means inadequate and insofar as the patients questioned about self-medication many had been taking oral doses regularly as instructed.

Of all gonococcal strains isolated in our hospital, a large majority were susceptible to drugs used, none were found resistant to TCs, and few had acquired resistance to PC and ABPC. As data from other medical institutions indicate more frequent occurrence of resistant strains, the methods and means of bacteriological study, e.g., discs and culture medium, employed in our present study were reexamined for eventual differences from those in other reported studies, but no meaningful variations could be detected. The reasons for the bacteriological features of gonococci as distinct from those of strains isolated in other institutions remain thus unclear (6, 8). It may be that the gonococci detected in our hospital really contained a smaller proportion of drug-resistant strains.

Treatment of gonococcal urethritis may result in so-called postgonorrhoeal urethritis, i.e., persistence of urethral inflammation after eradication of gonococci. Many such instances are accounted for by transition to nongonococcal urethritis due to persistent chlamydia trachomatis (1, 2). When mixed infection of the urethra with gonococcus and chlamydia trachomatis is treated with a drug to which chlamydia is susceptible, the urethritis remains in the absence of gonococci. The statistics in our present study encompass such cases indiscriminately labelled as gonococcal infection in disregard to the type of the organism causative of urethritis. In this connection, it should be noted that it was not until about 4 years ago that reliable methods of examination for chlamydia trachomatis, ureaplasma urealyticum and so forth were rendered available and put to clinical usage. This lack of knowledge and technique led us to label some cases as therapeutic failure merely for reasons of the persistence of leukocytes and pus in urethral discharge after treatment. The UTI Study Group, being fully aware of such confusion, is inclined to stipulate, in its forthcoming criteria for evaluation of drug efficacy, that judgement on cure of gonorrhea should be based not only on eradication of the specific organism from the sites of infection but also on disappearance of any other conjoined related symptoms. However, insofar as gonococcal urethritis is concerned, our criteria for evaluation of drug effectiveness mentioned earlier may reasonably be regarded as acceptable standard ones.

REFERENCES


