Trimethoprim-sulphamethoxazole in urinary tract infection due to *Streptococcus faecalis*

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**Synopsis** In-vitro sensitivities were performed on 140 specimens of urine which grew *Streptococcus faecalis* of more than 100 000 organisms/ml between March 1970 and February 1971. Although the combination of trimethoprim and sulphamethoxazole definitely appeared to be more effective than sulphonamide alone and as effective as ampicillin, its use for more than two weeks in 14 cases of uncomplicated urinary tract infection due to *Streptococcus faecalis* led to development of resistance. As in these cases organisms were resistant to sulphonamide to start with, it is suggested that the combination should be used in prolonged treatment only where the organisms are sensitive to both the individual antibiotics. Ampicillin is still the drug of choice in urinary tract infection due to *Streptococcus faecalis*. The alternative appears to be rotational therapy with other potent antibiotics.

The combination of trimethoprim and sulphamethoxazole has shown considerable promise in recent years in the treatment of urinary (Reeves, Faiers, Pursell, and Brumfitt, 1969; Gröneberg and Kolbe, 1969), respiratory (Hughes, 1969), and gastrointestinal (Brodie, MacQueen, and Livingstone, 1970; Kamat, 1970; Farid, Hassan, Wahab, Sanborn, Kent, Yassa, and Hathout, 1970) tract infections. It is effective against practically all the routinely encountered pathogens except *Pseudomonas aeruginosa* (Darrell, Garrod, and Waterworth, 1968). Trimethoprim and sulphamethoxazole exert a strongly synergic action, and the action is bactericidal, whereas that of a sulphonamide alone is only bacteriostatic (Bushby, 1969). Resistance to trimethoprim is fairly uncommon and the combination is often effective despite resistance to sulphonamide (*British Medical Journal*, 1969).

**Materials and Methods**

Out of a total of 140 strains, 96 were from inpatients at the hospital, 15 from outpatients, and 29 from local general practitioners. The specimens were collected from patients of all age groups and from both sexes. In-vitro sensitivities were performed on 5% lysed horse blood agar plates and they always included ampicillin (25 µg), sulphamethoxazole (200 µg), trimethoprim (2.5 µg), and trimethoprim-sulphamethoxazole (25 µg) discs (Waterworth, 1969).

The plates were inoculated with the help of sterile cotton wool swab sticks which were dipped into urine and the excess drained off in order to get a uniform growth. The results were read after overnight incubation at 37°C, the control strain used being *E. coli* (NCTC 10418). The sensitivity tests were repeated from pure culture whenever the inoculum appeared to be either too heavy or too light the next day.

The minimum inhibitory concentrations (MICs) of ampicillin, sulphonamide, and trimethoprim were determined against all the strains. The tube dilution technique was used for ampicillin. The MICs of sulphamethoxazole and trimethoprim were estimated by the plate dilution technique with the use of 5% lysed horse blood agar plates (Darrell *et al*, 1968).

**Criterion of infection**

The criterion of infection was a count exceeding 100 000 organisms/ml in two consecutive urine specimens showing the same bacterial species.

**Criterion of cure**

Examination of a specimen of urine from patient was carried out at one, two, and four weeks after starting treatment. Eradication of the organism was taken to be a cure.

**Results**

Before treatment the MICs of trimethoprim ranged...
between 0.25 and 1.0 µg/ml, that of sulphonamide between 80 and 200 µg/ml, and of ampicillin 1 and 2 µg/ml for all 23 isolates which later became resistant.

After treatment the MICs of trimethoprim and sulphonamide ranged between 8 and 16 µg/ml, and more than 200 µg/ml respectively for the 14 resistant strains. Of the nine strains which became resistant to ampicillin, the MICs were between 10 and 18 µg/ml.

Out of a total of 140 patients, 111 cases were followed up. The particular antibiotic used for each patient was decided by the clinicians concerned. It was found that 68 patients were treated with ampicillin 500 mg eight hourly orally for seven days with nine failures, whereas 43 patients treated with trimethoprim-sulphamethoxazole, two tablets twice daily orally for five days with 14 failures. There was no significant difference between the two groups so treated. Out of a total of 68 patients, six had rash presumably due to ampicillin therapy, and the treatment was discontinued. They were subsequently treated with nitrofurantoin with good results.

<table>
<thead>
<tr>
<th>Result</th>
<th>Ampicillin</th>
<th>Trimethoprim-sulphamethoxazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number treated</td>
<td>68</td>
<td>43</td>
</tr>
<tr>
<td>Cured</td>
<td>59</td>
<td>29</td>
</tr>
<tr>
<td>Failed treatment</td>
<td>9</td>
<td>14</td>
</tr>
<tr>
<td>Rash</td>
<td>6</td>
<td>1</td>
</tr>
</tbody>
</table>

Table  Results of treatment

Out of 14 failures with trimethoprim-sulphamethoxazole, 11 cases were followed up and treated with ampicillin with excellent results, whereas out of nine failures with ampicillin, six cases were followed up and treated with trimethoprim-sulphamethoxazole with only two cases cured.

Discussion

From Figure 1 it becomes quite apparent that insofar as in-vitro sensitivity is concerned, the combination of trimethoprim-sulphamethoxazole appears to be more effective than sulphonamide alone and as effective as ampicillin in urinary tract infections. In the comparative study between these three antibiotics in the treatment of urinary tract infections, the combination was shown to be the best (Reeves et al, 1969). It has also been claimed that this combination was effective even when the strains were resistant to sulphonamide (Grüneberg and Kolbe, 1969). From Figure 2 it appears that this assumption is not true in cases of Streptococcus faecalis infections. In this series, 14 strains of Streptococcus faecalis became resistant to this potent combination, possibly due to two reasons. First, they were resistant to sulphonamide to start with and, second, the treatment had to be continued for more than two weeks. These factors may have helped sulphonamide-resistant strains to multiply selectively even with the combination of trimethoprim. It is suggested that ampicillin is still the drug of choice in urinary tract infection due to Streptococcus faecalis, and trimethoprim-sulphamethoxazole should not be used in these cases for more than two weeks. Rotational therapy with other antibiotics to which the organisms are sensitive might be worthwhile.
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References


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