Antibiotic resistance in community-acquired urinary tract infections

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We studied the antibiotic susceptibility of midstream urine isolates from patients with community-acquired urinary tract infections at Groote Schuur Hospital from 1986 to 1991.

The majority of the isolates was resistant to amoxycillin and co-trimoxazole, and the proportion of resistant *Escherichia coli* isolates increased during the study period. In a prospective 4-month study in 1991 we found that the vast majority of isolates was susceptible to aminoglycosides, amoxycillin/clavulanate, second-generation cephalosporins and the new fluoroquinolones. Based on these findings amoxycillin and co-trimoxazole should no longer be prescribed for urinary tract infections unless a susceptible isolate has been cultured. Appropriate empirical oral agents are expensive and not generally available in the public sector. There is an urgent need to make these agents available in the public sector, but their use should be restricted as widespread use for the treatment of other infections would inevitably lead to the development of resistance.

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Antibiotic resistance is a major problem in developing countries.[1] There are many reasons for this, including antibiotic use in animal feeds, inappropriate prescribing and poor sanitation. Resistance rates in *Escherichia coli* from normal bowel flora and clinical isolates are much higher in developing than in developed countries.[2]

We have noted that most of the isolates from urine samples at our laboratory are resistant to co-trimoxazole and amoxycillin (or ampicillin). Both are affordable antibiotics which are commonly prescribed for urinary tract infections (UTIs). We were uncertain whether nosocomial infection was responsible for the high prevalence of resistance, and thus undertook a study of antibiotic susceptibility in isolates from patients with community-acquired UTIs.

Methods

The study was carried out at Groote Schuur Hospital. UTI was defined as the culture of a single organism from a

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midstream urine specimen (specimens from catheterised patients were excluded) at a concentration of $>10^5$ colony-forming units/ml. Samples were cultured on cystine-lactose electrolyte deficient (CLED) medium with a standard loop for semi-quantitative counts. Antibiotic susceptibility was assessed according to the Kirby-Bauer method. Infections were considered community-acquired if the specimens were submitted from outpatients or within 48 hours of admission.

A retrospective study from 1985 to 1990 of the sensitivity of community-acquired UTI organisms to amoxycillin and co-trimoxazole was performed by means of a search of computerised records. From May to August 1991, the antibiotic susceptibility of community-acquired UTI isolates against a range of agents was prospectively assessed.

Results

The proportion of all isolates resistant to amoxycillin or co-trimoxazole for the years 1985-1990 is shown in Fig. 1, and that of *E. coli* in both study periods in Fig. 2. From May to August 1991 the antibiotic susceptibility of 264 isolates (63% *E. coli* and 18% other Enterobacteriaceae) was examined (Fig. 3). The mean age of patients in the latter period was 46 years, and 68% were women.

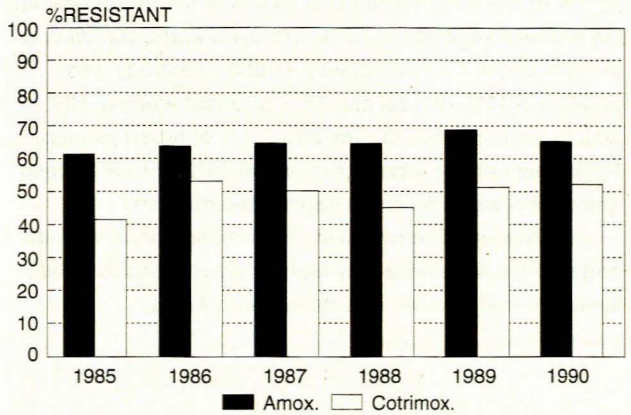
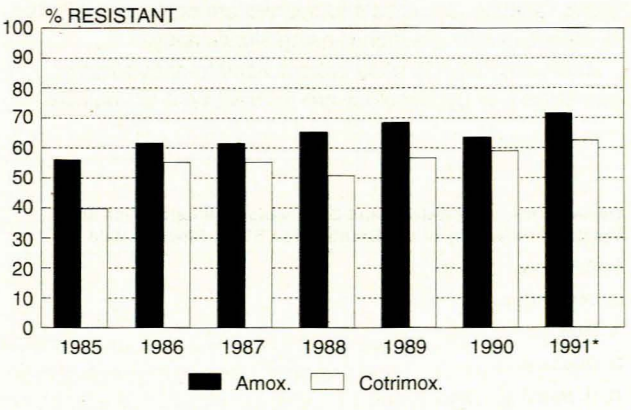
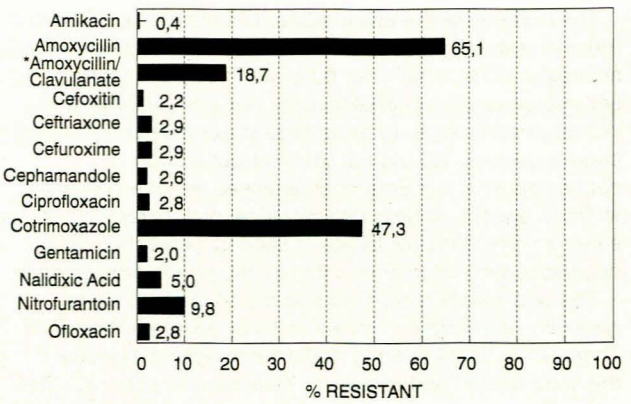


Fig. 1. Resistance to amoxycillin and co-trimoxazole in isolates from patients with community-acquired UTIs, 1985-1990.



*For the 4 months May – August only

Fig. 2. Resistance to amoxycillin and co-trimoxazole in *E. coli* isolates from community-acquired UTIs, 1985-1991.



*During the study unused antibiotic susceptibility discs were returned to the refrigerator, and the unstable clavulanate could have degraded. Subsequently unused discs were discarded and resistance levels were found to be < 5%.

Fig. 3. Antibiotic resistance of isolates from patients with community-acquired UTI, May to August 1991.

Discussion

We have shown that a high proportion of community-acquired UTI isolates are resistant to amoxycillin and co-trimoxazole. The resistance in *E. coli*, the commonest UTI pathogen, is similar to that found in other centres in South Africa (A. A. Forder — personal communication).

Successful treatment of UTI, despite the *in vitro* demonstration of resistance to the antibiotic used, is not infrequent. However, spontaneous cure of UTI has been reported in as many as 50 - 70% of cases.[3,4] Furthermore, selection of an inappropriate antibiotic in bacteraemic patients (40% of patients with pyelonephritis[5]) adversely affects survival.[6] Therefore amoxycillin/ampicillin and co-trimoxazole should no longer be prescribed for UTI unless susceptibility has been demonstrated.

The type and duration of treatment of UTI depend on the site of infection and the presence of complicating factors. Lower UTI, or cystitis, is characterised by dysuria together with either haematuria, pyuria or bacteriuria (detected microscopically or by means of dipsticks). Upper UTI is easily recognised when it appears clinically as pyelonephritis, but occult renal infection is present in about one-third of patients whose infection seems limited to the bladder.[7] Significant fever generally indicates renal infection. 'Complicated' UTI is defined as infection in men, pregnant women, or patients with abnormal urinary tracts. These patients should be treated for 7 - 14 days.[7]

Urine cultures are an unnecessary expense in uncomplicated lower UTI.[7,8] Patients respond well to single-dose or short-course (3 days) antibiotic therapy.[7] Single-dose therapy, although marginally less effective than conventional therapy, is cost-effective and well tolerated.[9] The new fluoroquinolone antibiotics (ciprofloxacin, norfloxacin and ofloxacin) are effective agents for single-dose therapy.[10] Beta-lactam antibiotics in general, and cephalosporins particularly, are not very effective when given in a single dose.[9] Patients who relapse after single-dose therapy generally have occult upper UTI[7] and can be treated accordingly.

The duration of therapy in upper UTI should be 14 days.[7] Patients requiring parenteral therapy should be given an aminoglycoside, which can be given once daily,[11] or a second-generation cephalosporin. Our susceptibility data indicate that there is no advantage in using third-generation cephalosporins. We did not test first-generation cephalosporins, but Enterobacteriaceae are often resistant to these agents. Appropriate empirical oral therapy would be either amoxycillin/clavulanate, a second-generation oral cephalosporin (cefaclor or cefuroxime), or a fluoroquinolone.

The oral agents recommended are all expensive and generally unavailable in state clinics or peripheral hospitals. There is an urgent need to make these agents available in the state sector, particularly for patients with upper UTI, for whom the consequences of prescribing an antibiotic to which the isolate is resistant could be severe or even fatal. Lower UTIs should respond to the urinary antiseptics (nalidixic acid, nitrofurantoin), but the multiple dosing required will lead to poor compliance, and these agents are not as cost-effective as single-dose therapy.

The use of these antibiotics in the public sector will need to be restricted in order to prevent the development of increasing resistance. Resistance is less likely to arise with single-dose therapy.[9] We appeal to those in the private sector to prescribe these agents sparingly — they should not be used as first-line therapy for other common community-acquired infections.

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