

PRACTICE OBSERVED

Practice Research

Treatment of urinary tract infection with a single dose of amoxicillin, co-trimoxazole, or trimethoprim

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Most episodes of urinary tract infection respond to short courses of antimicrobial agents. A single dose of sulphamonomethoxime, co-trimoxazole, streptomycin, or ampicillin/amoxycillin* have all been effective. We present the findings of a trial giving single doses of amoxicillin, co-trimoxazole, or trimethoprim to treat patients with acute symptomatic urinary tract infection in general practice.

Patients and methods

Patients of both sexes who were seen in general practice over one year with symptoms suggestive of urinary tract infection were randomly allocated to treatment groups to receive a single dose of 400 mg of trimethoprim, or four tablets of co-trimoxazole (320 mg of trimethoprim with 1600 mg of sulphamethoxazole), or a suspension of 3 g of amoxicillin to be taken last thing before bed at night. Patients under 15 years, pregnant women, those who had taken antibiotics for any reason in the previous seven days, and those who had side effects of any of the trial drugs were excluded from the trial. Two midstream specimens of urine were collected from each patient before the trial. Only those patients with two samples showing a pure growth of more than 100 000 organisms/ml were evaluated. Sixty-four patients with significant bacteriuria were studied over 206 candidates for inclusion in the trial. A third urine sample was examined seven days after treatment. If the original organism was still present in numbers exceeding 100 000/ml treatment was regarded as having failed. A negative screening culture (less than 10⁵ organisms/ml) was taken as evidence of cure. Any side effects that patients said they had were noted. Some characteristics of the patients allocated to each treatment group are shown in the table.

Results

The table shows that a similar number of patients was allocated to each treatment group and that the age and sex distributions were similar, as were the pathogens found in their urine samples. The cure rates for one week were 95% for trimethoprim, 87.5% for co-trimoxazole, and 90% for amoxicillin. The failures were scarcely contributed to by antibiotic resistance in the urinary pathogens: all

Characteristics of treatment groups

	Treatment with a single dose of		
	Trimethoprim 400 mg	Co-trimoxazole 1600 mg sulphamonomethoxime + 320 mg trimethoprim	Amoxicillin 3 g
No. of patients	20	21	20
No. of women	11	11	10
Age (years)	31.5	34.1	31.0
Urinary pathogens:			
<i>E. coli</i>	17	20	15
<i>St. faecalis</i>	2	1	1
<i>St. pneumoniae</i>	1	1	1
<i>M. luteus</i>	1	1	1
<i>C. parvulus</i>	1	1	1
No. of organisms resistant to treatment drug	0	8*	18 (90.5%)
Cured	19 (95%)	21 (87.5%)	18 (90.5%)
Failed treatment	1	2	2

*Eight strains resistant to sulphamonomethoxime, sensitive to trimethoprim.

three urinary pathogens in patients failing on co-trimoxazole treatment were sensitive to sulphamonomethoxime and trimethoprim, and only one of the two organisms not eradicated by amoxicillin was resistant to amoxicillin. Only two of the 64 patients complained of side effects: one with an allergic rash and the other with swelling of the upper lip and facial redness. Both patients had been treated with co-trimoxazole.

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(Oxoid) with 0.2% lysed horse blood were determined for most of the strains. Strains were identified to genus level by standard biochemical tests. Patients were randomly allocated to conventional or abbreviated treatment: either a seven-day course of trimethoprim 150 mg taken usually used in the practice, or co-trimoxazole two tablets at night for three days—that is, six tablets. The number of patients receiving drugs for seven days were as follows: co-trimoxazole 17; sulphamethoxazole 4; sulphadiazine 4; amoxicillin 6; mecillinam 2; nalidixic acid 2; and nitrofurantoin 2. The treatment was started immediately, and when the results of the culture were known was modified if necessary. Follow-up mid-stream urine samples were taken 10 to 14 days after the first visit when the patient returned to the surgery. A clinical cure was defined as complete resolution of symptoms, and a bacteriological cure as a negative mid-stream specimen on follow-up.

Results

One hundred and eighty-seven patients presented with frequency-dysuria and were entered into the trial. Ninety were treated with bactericure and of these 75 were followed up after treatment. The organisms isolated are shown in table 1. One of the two patients in each group who suffered bacteriological failure was infected with an organism resistant to the agent used: an enterococcus in the three-day

TABLE 1—Organisms isolated from patients in the two groups

Regimen	3 days		7 days	
	No.	%	No.	%
<i>E. coli</i>	31	26	31	26
<i>Klebsiella</i>	2	1	2	1
<i>Staphylococcus saprophyticus</i>	1	1	1	1
<i>Proteus</i>	1	1	1	1
<i>Enterococcus</i>	1	1	1	1
Total	41	34	41	34

TABLE 2—Results of treatment

Regimen	No. followed	No. of women	Mean age (range)	No. with bacteriological failure (%)	No. with clinical failure (%)
Three doses of co-trimoxazole	41	37	44 (18-72)	2 (5)	4 (10)
Seven-day course	1	1	46 (18-72)	1 (100)	1 (100)

ONE HUNDRED YEARS AGO Sir—Many will agree with the gentleman who says in your last week's issue that the failure of so many young men, at the College of Surgeons, is caused by the miserably imperfect manner in which students of the present day are educated in our metropolitan medical schools. In the first place, many of our hospitals are overcrowded with students, who cannot possibly have the attention and facilities due to them which they require during their anatomical and surgical education. In many hospitals, students are allowed to be surgeons' dressers before they have passed their primary examination, which, I think most will agree with me, ought not to be allowed, especially in a hospital with a limited number of beds, as it detours most students who have passed their anatomical examination from dressing and most men prefer waiting for a dressup at their own hospital to going elsewhere. Again, the regulations, I believe, at all hospitals, require all first and second year students to attend the hospital surgical wards daily; also the post mortem and out-patient courses. Now, in justice to the more advanced students who are reading for their final examination, it would be better to refer to our hospital regulations if the first and second year's students were deferred from these several departments until they have passed their primary examination, thereby giving more room for the advanced ones

and an ampicillin-resistant *E. coli* in the seven-day group. The overall results are shown in table II. Bacteriological failure occurred in 5% of the patients treated for three days and in 6% of the patients treated for seven days, and 2.5% of the patients treated with inappropriate drugs were excluded from the trial. Failure was observed in 10% and 9% of the three and seven-day groups respectively.

Discussion

Despite the many studies on the treatment of acute urinary tract infection, the optimum dose or duration of treatment has not been defined. What has emerged clearly is that most patients seen in general practice will respond to minimal treatment, and failure to respond identifies those who require more intensive treatment or possibly investigation. The precise nature of the abbreviated treatment appears to be unimportant. The results of 10-day or three-day courses with single large three-nightly doses are indistinguishable. The preference of patients must be allowed to play a part, and some may welcome treatment with a single dose; some may prefer to continue treatment for a day or two while symptoms linger. In our study a conventional dose of co-trimoxazole repeated on two successive nights (a total of six tablets) was as effective as a conventional treatment (14 or more tablets) in eliminating acute uncomplicated urinary infection in patients treated at home.

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Discussion

High cure rates were achieved in this trial, with all three single-dose treatments producing similar results. In most of the episodes of symptomatic urinary tract infection in general practice the usual five to seven day course of chemotherapy seems excessive. Patients whose infection is not cleared by a single dose may require fuller investigation and more carefully selected treatment.^{1,2} Some patients were cured with amoxicillin despite the *in vitro* amoxicillin-resistance of the pathogen, presumably because of the very high urinary concentrations of the drug after a dose of 3 g.

Side effects were not a major problem in this or most other series,¹⁻³ though Leigh *et al.*³ reported more side effects with single large doses of amoxicillin than with a standard treatment regimen. It may be expected that single-dose treatment of urinary tract infection will cause fewer side effects, and it should certainly be cheaper than multiple dose regimens. Whether treatment with a single dose is less likely to lead to bacterial resistance than treatment with multiple doses is something that should be studied.

Conclusions

Sixty-four patients with acute symptomatic urinary tract infection in general practice were treated with a single dose of trimethoprim (400 mg), co-trimoxazole (320 mg of trimethoprim/1600 mg of sulphamethoxazole), or amoxicillin (3 g). The cure rates after one week were 95%, 87.5%, and 90%. Side effects were not a problem. Since compliance is likely to be good, cure rates are high, side effects are uncommon, and costs are low single-dose treatment of urinary tract infection should be tried more widely.

Treatment of acute urinary tract infection with three doses of co-trimoxazole

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Gould *et al.*¹ showed that bacteria disappear from infected urine within hours after treatment is started. Cattell *et al.*² showed that after a single dose of a drug to which the organism was sensitive the concentration of bacteria in urine quickly fell below concentrations detectable by conventional laboratory techniques and remained so for several days. These findings suggested that treatment of urinary infection with several daily doses of antibiotics for a week or more results in patients receiving substantially more of a drug than is necessary to eliminate the infection.

Evidence exists that patients will respond to less treatment: in patients with acute uncomplicated infection treatment for three days was as effective as treatment for 10 days³ and most

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patients will respond to a single dose of a drug⁴—for example, a single large dose of amoxicillin⁵ or co-trimoxazole.⁶ On theoretical grounds⁷ and from the response to treatment of a model simulating conditions of bacterial growth in the infected urinary bladder⁸ we argue that a single large dose may not be the most economical and effective use of a drug. Cure is most likely after a small dose nightly for a few successive nights.

This study compares the efficacy of prescribing three nightly doses of co-trimoxazole with conventional treatment for acute urinary tract infection.

Patients and methods

Adult patients attending a surgery with frequency-dysuria syndrome between March and October 1979 who were not known to have renal or urinary tract abnormalities or to be pregnant were admitted to the trial. Mid-stream urine samples were collected after the procedure had been explained and the patient given simple written instructions to prevent contamination of the specimen. The urine was used to inoculate a dip-slide (Oxoid) or equivalent CLED slope in a sterile universal bottle. After inoculation definite growth was defined by the usual criteria (>10⁵ organisms/ml in pure culture). Antimicrobial sensitivities were determined by standards for a few representative methods, and plate minimum inhibitory concentrations on DTS

Women in General Practice

C B CHALLACOMBE

About 10 years ago, while still working as a house officer in a district general hospital, I was fortunate enough to be offered a chance to join two other doctors, both men, in a busy urban practice. I had been married for just over a year and had by then realised the practical difficulties of combining hospital medicine with the sort of family life that I wanted. It was my intention to have children and to be able to join my husband, who was working in dental research, in any foreign travel if the opportunity arose. I could also see the problems of combining these wishes with a full-time partnership in general practice.

Before joining the practice I discussed these plans with my prospective partners. I told them that it was my husband's intention to take a sabbatical year abroad at some time. We also discussed the possibility that my husband might move to a different hospital, in which case I might have to leave the practice.

My partners and I decided to have a clause regarding maternity leave in the partnership agreement. This stipulated that I was allowed three months' maternity leave with a reduced percentage of the practice profits. The maternity allowance from the family practitioner committee, together with the remaining profits, would provide the locum's salary while I was away.

I worked for two and a half years in the practice before having my first child. I continued to work full-time until a month before the baby was due. At the time I felt that I could have worked for longer. I would have preferred to decrease my work load gradually over the last few weeks. But because my partners thought that it would be difficult to organise arrangements for part-time sessions, they asked me to stop work completely and have a full-time locum.

There were difficulties in obtaining a suitable locum for the three months' sabbatical, but eventually, my partners insisted upon the locum being acceptable to them both. They also felt strongly that it was preferable to have one full-time locum than a series of part-time locums which might have been easier for me to organise. Eventually, with the help of my partners, a locum was found who met all the requirements.

Fortunately my son was only a week late in arriving, and I returned to work when he was eight weeks old. The first few months were difficult for me emotionally, since it took some time to adjust to leaving my baby with someone else while I went out to work. Luckily I found an excellent full-time nanny and managed to arrange my surgery hours around feeding times. I found night duties most taxing but was able to employ a hospital colleague to help me out with late night calls during the first few months.

During my second pregnancy three years later the extra family commitments that I now had made me realise that I would appreciate more than the three months' maternity leave which had been agreed. After discussions with my partners an extra month was agreed, which was taken partly as unpaid leave and partly as two weeks of my annual holiday. Even with this extra month I did not feel ready to return to full-time practice, but I was under pressure from my partners to do so.

The following months were the least enjoyable of my life. It was a joy to my practice career—so far. It required an enormous

effort to combine full-time practice with family life with two young children and a husband working hard at his own career. It was unfortunate that my return to work also coincided with one of my partner's annual summer holidays. It would have been impossible to meet my commitments if my husband had also been on call. Fortunately he was able to adapt his working day so that he could be at home if one of the children fell ill, and he also looked after them during the evenings.

Making the arrangements to leave the practice for one year to accompany my husband on sabbatical in the USA was much more complicated. Although I had mentioned this possibility when I joined the practice, no formal plans had been drawn up, and I think my partners had hoped that it would never happen. It would have been easier if we had agreed in principle to each of us taking a year's leave of absence. As it was, neither of my partners showed any real enthusiasm in arranging sabbaticals of their own.

The family practitioner committee readily granted me a year's leave of absence, provided my partners agreed and on condition that I employed a full-time locum for the whole time and did not take any employment myself. The main problems were again finding someone suitable and then making the financial arrangements. Somewhat surprisingly I managed to find a locum without too much difficulty. The financial problems were less easy to resolve. My partners thought that since they would have to work for a year with a locum who would inevitably take less than a third of the work load there should be some financial advantage to them. I, however, felt it was appropriate for me to retain a share of my profits, bearing in mind my contribution for seven years to the practice and my commitment to return. After lengthy discussions I reluctantly agreed that they should share all my remaining profits after the locum had been paid while I received nothing.

Later, when it became necessary for my husband to extend his sabbatical year by six weeks, the problem of making arrangements for the practice while resident in America, but these were eventually overcome.

It was difficult to settle back into full-time practice after a year's absence, but I certainly had no regrets about the time spent in America. Life became much easier once both my children were at school, and I now enjoy a very good working relationship with my partners.

There are many problems facing women in general practice, and flexibility in making arrangements is essential in order to combine work with looking after a home and children. Although the work load is equal, the work does not necessarily have to be done at the same time as one's partners do their work. Pregnancy is often said to be a disincentive for men to accept women partners in general practice, but with co-operation with one's partners the maternity leave can be organised. A request for a leave of absence for a year is not likely to be commonly met, but the problems of making arrangements are not insurmountable, especially if partners can be persuaded to consider sabbaticals for themselves.

General practice is a very rewarding occupation for me, and in retrospect I am glad that I managed to continue to be a full partner during times when it seemed easier to resign. But combining home and family life with full-time practice does require the co-operation of partners, husband, and occasionally children.

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