ANTIMICROBIAL SENSITIVITIES AND CAUSATIVE ORGANISMS OF URINARY TRACT INFECTIONS IN A RURAL FAMILY PRACTICE

Abstract

Objectives: To describe the antimicrobial sensitivities and the causative organisms of uncomplicated urinary tract infections (UTIs) in a rural family practice.

Setting: A family practice in the rural Port St Johns district.

Design: Descriptive and prospective.

Methods: Urine samples from consecutive patients with symptoms of UTI and pyuria on urine microscopy underwent bacterial culture. Sensitivity testing to antibiotics was performed on cultures yielding $\geq 10^5$ colony-forming units per millilitre (cfu/ml) of a single pathogenic organism.

Results: UTI was diagnosed in 53 patients, 46 females and 7 males. *Escherichia coli* (37) was the commonest organism isolated. Of all organisms isolated, only 15 (28%) were sensitive to ampicillin and 22 (42%) to cotrimoxazole. All organisms tested were sensitive to fosfomycin, ofloxacin, norfloxacin and ciprofloxacin and more than 80% of organisms were sensitive to cefaclor, nalidixic acid and pipemidic acid. Organisms were significantly less sensitive to ampicillin, co-trimoxazole, cefadroxil, nitrofurantoin and co-amoxiclav.

Conclusions: Ampicillin and cotrimoxazole can no longer be recommended for empirical treatment of UTI. Recommendations are made for antimicrobial treatment of uncomplicated UTIs in primary care in the Port St Johns district.

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Rational prescribing for urinary tract infections (UTIs) requires a knowledge of the causative organisms prevailing in the local community and their antimicrobial sensitivity.

World-wide, a narrow spectrum of organisms is responsible for infection in young women with acute uncomplicated cystitis: *Escherichia coli* in 80 percent, *Staphylococcus saprophyticus* in 5 to 15 percent, and occasionally klebsiella species, *Proteus mirabilis*, or other microorganisms[1]. South African studies have also shown a similar distribution of organisms in cystitis, the most common category of UTI in family practice[2,3].

However, organisms vary widely in their susceptibility to antimicrobial agents. Recent hospital and primary care based studies of UTI in South Africa have shown widespread resistance to amoxycillin and cotrimoxazole. At Groote Schuur Hospital, 65% of organisms isolated from community-acquired UTIs were resistant to amoxycillin and 47% to cotrimoxazole[4]. In an urban Cape Town family practice[2], 57% of isolates were resistant to amoxycillin and 49% to cotrimoxazole; and in a community health centre in Durban[3], 66% of isolates were resistant to ampicillin and 60% to cotrimoxazole. Despite these findings, the two antimicrobials are still recommended as empirical treatment for uncomplicated UTIs[5,6,7].

The above studies were from urban centres and there is an absence of studies from rural family practice. The objectives of this study were to document, in the Port St Johns district, the causative organisms of UTIs and their antibiotic sensitivities, and then make recommendations about the empirical choice of antibiotics for treating UTIs.

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Methodology

This study was undertaken in a solo family practice serving a predominantly rural, low income population. Any patient with an uncomplicated UTI was enrolled in the study, conducted between July 1995 and January 1998. A complicated UTI was defined as one occurring in a patient who has a functionally, metabolically, or anatomically abnormal urinary tract or caused by pathogens that are resistant to antibiotics[1].

Diagnosis of UTI: A UTI was diagnosed in an adult or a child 12 years of age or older with:

a) one or more urinary tract symptoms;
b) pyuria - at least 10 leukocytes per cubic millilitre (ml^3) of unspun urine[8]; and
c) a urine culture yielding $\geq 10^5$ colony forming units per millilitre (cfu/ml) of a single pathogenic organism.

Pyelonephritis was diagnosed if there was loin tenderness and criteria b) and c).

Pyuria is present in almost all symptomatic UTIs and its absence should strongly suggest another diagnosis[8]. A haemocytometer can accurately measure pyuria. It is easier to perform and more accurate than microscopic urinary sediment examination[8].

A UTI was diagnosed in a child less than 12 years of age with:

a) clinical signs consistent with UTI (more non-specific than in adults, e.g. lethargy, fever and failure to thrive); and
b) bacteriuria of $\geq 10^5$ cfu/ml of urine.

While the finding of pyuria is strong supportive evidence of UTI, approximately 30-50% of children with bacteriuria and UTI will not have a significant number of white cells (>5 leukocytes per high powered field) in the centrifuged urinary sediment[9]. Thus, demonstration of bacteria by culture is the mainstay of diagnosis.

Taking of urine specimens: The clean-catch midstream technique is usually recommended when urine samples are required from women. It is performed by holding the labia apart, cleaning the perineum and then obtaining a midstream sample. However, despite its widespread use, its clinical documentation is sparse[10] and it is difficult to understand and perform[11]. Studies from family practice have shown that holding the labia apart is the only technique necessary to reduce the risk of obtaining a contaminated urinary sample[12,13]. The actions of cleaning the perineum or using the midstream technique are superfluous.

In this study, the urine specimen was collected in the practice, with the woman instructed only to keep the labia apart and to pass urine directly into a sterile container. Men were instructed to retract the foreskin, if present, and then pass urine directly into the sterile container. In infants, a catheter specimen was obtained.

Processing of specimens: Uncentrifuged urine was examined microscopically immediately after being passed using an improved Neubauer counting chamber. If pyuria was present, it was inoculated onto MacConkey and blood agar media using a 1µ calibrated platinum wire loop and incubated overnight in the practice. If growth was present, the media were forwarded to the laboratory for organism identification, and antibiotic susceptibility according to the Kirby-Bauer method using Muller-Hinton medium.

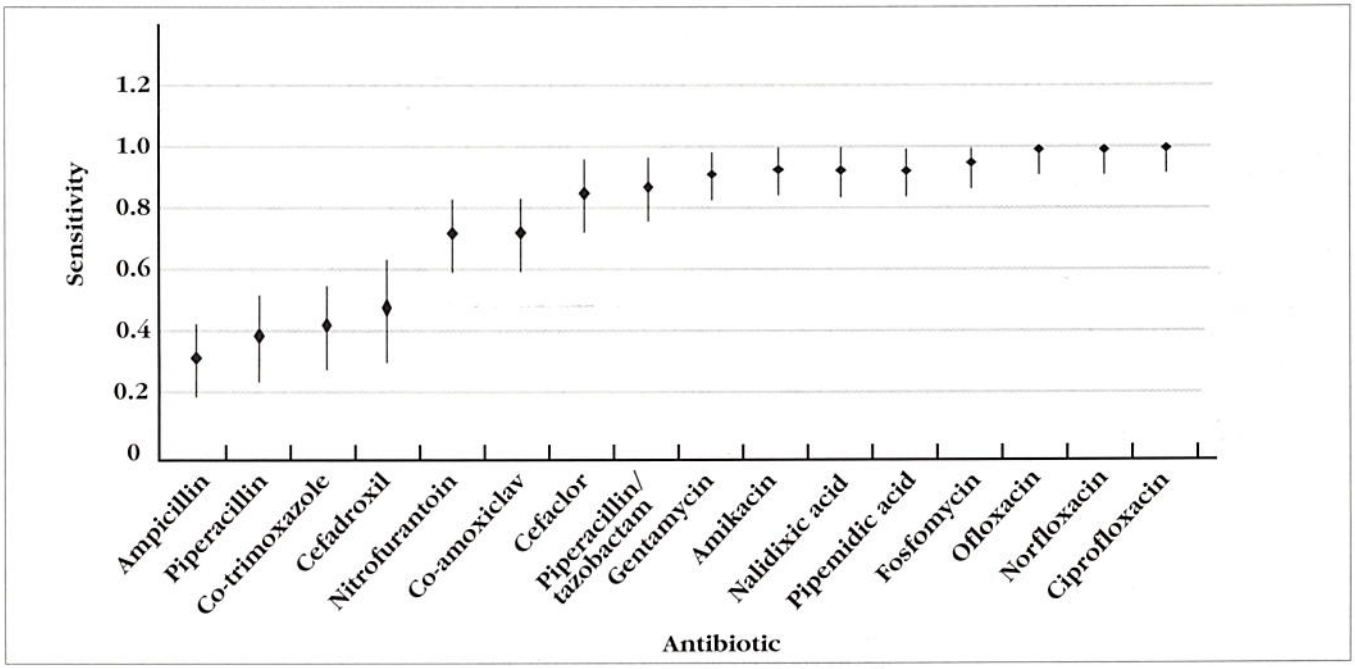
Results

UTIs were diagnosed in 53 patients; 31 had uncomplicated cystitis and 22 had pyelonephritis. Of the UTIs, 46 (87%) were in females, of whom four were pregnant, and 7 (13%) in males. The age range was 2 to 76 years. Table I shows the number of patients with UTI per age group.

Table II lists the organisms isolated.

Table III lists the susceptibility of isolates to antibiotics and the 95% confidence intervals around the sensitivity estimate for each antibiotic. Over the study period, the laboratory changed its antibiotics for susceptibility testing and thus the number tested per antibiotic varied. Only those antibiotics (16) are listed to which 50% or more of the isolates had susceptibility test-

Figure 1: Sensitivity and 95% confidence intervals of isolates



ing. The laboratory did report a category of intermediate sensitivity to antibiotics but only those isolates which were fully sensitive are listed. Figure 1 plots the sensitivity estimates and the confidence intervals for each antibiotic, allowing the comparison of any two antibiotics. If the confidence intervals of the two antibiotics do not overlap, then the sensitivities of the two antibiotics are considered to be significantly different from one another.

The plots in Figure 1 show that ampicillin, co-trimoxazole, cefadroxil, nitrofurantoin and co-amoxiclav have significantly lower sensitivities than the most effective antibiotics, i.e. fosfomycin, ciprofloxacin, norfloxacin or ofloxacin. However, the sensitivities of cefaclor, piperacillin/tazobactam, gentamycin, amikacin, nalidixic acid and pipemidic acid to not differ significantly from the most effective group.

Discussion

The urinary pathogens isolated in this study are similar to other studies of community-acquired UTIs in that *E. Coli* was the commonest pathogen[2,3,4]. The isolation of *salmonella typhimurium* and shigella are indicative of the study's rural location where typhoid and dysentery are endemic due to poor sanitation. Most UTIs occurred in females (86%), the group most commonly affected in community-acquired UTIs. Many patients presented with pyelonephritis and this may reflect the low socio-economic status of the rural practice population where, due to a lack of education, transport and money, illness is presented to the family doctor later in its course, when it is more advanced.

The majority of urinary tract pathogens were resistant to two drugs commonly used to treat UTIs, namely ampicillin (72%) and cotrimoxazole (58%). These results are similar to recent studies of uncomplicated UTIs in urban primary care settings[2,3,4], implying that urinary pathogens in urban and rural South Africa have similar antibiotic resistance patterns. This study supports the recommendation of the 1997 edition of the South African Medicines Formulary that ampicillin/amoxicillin, co-trimoxazole and trimethoprim are no longer suitable for empirical therapy of UTIs[14].

Age Group	Number (%)
0 - 9	7 (13)
10 - 19	9 (17)
20 - 29	10 (19)
30 - 39	6 (11)
40 - 49	7 (13)
50 - 59	4 (8)
60+	10 (19)

Table I: Number (%) of patients with UTI per age group (n=53)

Organism	Number (%)
Escherichia coli	37 (70)
Klebsiella oxytoca	4 (8)
Klebsiella pneumoniae	1 (2)
Staphylococcus saprophyticus	3 (5)
Proteus mirabilis	3 (5)
Salmonella species	2 (4)
Salmonella typhimurium	1 (2)
Citrobacter diversus	1 (2)
Shigella species	1 (2)

Table II: Microorganisms isolated from patients with UTI (n=53)

There was marked resistance to cefadroxil, where only 44% of isolates were fully sensitive. This reflects the widespread resistance in Gram-negative species to first generation chepalosporins[14]. For cefaclor, 82% of isolates were susceptible and this reflects the wider activity of second generation cephalosporins against community-acquired Gram-negative organisms[14]. All organisms were susceptible to the fluoroquinolones and the phosphonic acid derivative, fosfomycin, and more than 80% were sensitive to the quinolone derivatives, nalidixic acid and pipemidic acid.

The antimicrobials currently recommended by the South African Medicines Formulary for uncomplicated cystitis and pyelonephritis are co-amoxiclav or an oral cephalosporin or a quinolone, based on local sensitivity patterns[14]. Urinary antiseptics are an alternative (e.g. nitrofurantoin and methanime) for cystitis. Based on this study, the antibiotics recommended for empirical treatment of UTI in this area are listed in Table IV. This is a simplified list and more comprehensive guidelines should be consulted as necessary[1]. For acute uncomplicated cystitis, a three-day course of antibiotics is more effective than single dose therapy[1]. Oral generic quinolones, e.g. nalidixic acid, enoxacin and norfloxacin, are now available at a reasonable cost. While a urine culture is unnecessary in typical acute uncomplicated cystitis, it should ideally be done to guide therapy in pyelonephritis or in complicated urinary tract infections[1].

In pregnant women with cystitis, fluoroquinolones and fosfomycin are not recommended. Cefaclor is preferred for cystitis. Nalidixic acid can be used in pregnancy but only after the first trimester, according to the manufacturers' instructions. Hospitalisation is usually recommended for pyelonephritis in pregnancy[1] but many clinicians would still treat a mild illness with oral agents at home. Although susceptibility testing to third-generation cephalosporins was not done in this study, they are recommended for parenteral therapy in severe illness in pregnancy[1].

Some authorities state that ampicillin and co-trimoxazole can cure UTIs despite *in-vitro* laboratory resistance, as these antibiotics may reach concentrations in urine in excess of the minimum inhibitory concentrations of resistant strains[7]. However, a study in Durban suggests that *in-vitro* laboratory sensitivity testing can accurately predict the *in-vivo* response to therapy with these antibiotics; 8 (80%) of

Antibiotic	Number Sensitive	Total Tested	Proportion Sensitive	95% Confidence Interval Lower	Upper
Ampicillin	15	53	0.3	0.168	0.424
Piperacillin	16	46	0.3	0.214	0.503
Co-trimoxazole	22	53	0.4	0.281	0.559
Cefadroxil	16	36	0.4	0.279	0.619
Nitrofurantoin	36	50	0.7	0.575	0.838
Co-amoxiclav	35	48	0.7	0.582	0.847
Cefaclor	30	36	0.8	0.672	0.936
Piperacillin/tazobactam	40	46	0.9	0.737	0.951
Gentamycin	47	51	0.9	0.811	0.978
Amikacin	45	48	0.9	0.828	0.987
Nalidixic acid	47	50	0.9	0.835	0.987
Pipemidic acid	34	36	0.9	0.813	0.993
Fosfomycin	32	32	1	0.891	1
Ofloxacin	49	49	1	0.927	1
Norfloxacin	50	50	1	0.929	1
Ciprofloxacin	51	51	1	0.93	1

Table III: Antimicrobial susceptibility of isolates (n=53)

Condition	Empirical Antibiotic Treatment
Acute uncomplicated cystitis	3-day regimen: oral nalidixic acid, pipemidic acid, cefaclor, fosfomycin, ciprofloxacin, ofloxacin, or norfloxacin
- pregnancy	Consider 7-day regimen: oral cefaclor or nalidixic acid
Acute uncomplicated pyelonephritis	
- mild to moderate illness	10-day regimen: oral ciprofloxacin, ofloxacin, norfloxacin or cefaclor
- severe illness	Parenteral: gentamycin, amikacin, ciprofloxacin, ofloxacin in norfloxacin, until fever abates: then oral agent for 10 days
- pregnancy - mild illness	10-day regime: oral cefaclor
- moderate to severe illness	Parenteral gentamycin, amikacin, ceftriaxone or cefotaxime until fever abates; then oral agent for 10 days

Table IV: Treatment regimens for Urinary Tract Infection

10 patients with proven UTI, whose organisms were sensitive to either ampicillin or co-trimoxazole, had eradication of infection, as compared to 5 (23%) of 22 whose organisms were not sensitive[5].

The antibiotics recommended above for empirical treatment of UTIs are more expensive than the former first-line antibiotics, ampicillin and co-trimoxazole. Amongst patients with symptoms of UTI, it is important to treat those who truly have UTIs. A study in a community health centre reports that only 51 (23%) of 218 women with symptoms of UTI had a confirmed urinary tract infection[3]. In low-income primary care settings, it is impractical to do urine culture on all patients with symptoms. The leukocyte esterase dipstick has a sensitivity of 75-96% in detecting pyuria associated with infection and should be used to screen those with symptoms[1]. For patients with a negative test, microscopic evaluation for pyuria on unspun urine is easy and quick to perform, and will reduce the number of patients treated unnecessarily for suspected UTIs.

Summary

This study shows that in the Port St Johns district, the causative organisms of uncomplicated UTIs have low sensitivity to ampicillin and co-trimoxazole, a pattern similar to that of urban areas in South Africa. Ampicillin and co-trimoxazole should no longer be used in the empirical treatment of UTI.

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