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 210 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 (57) 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, oloxacan, norfloxacin and ciprofloxacin and more than 80% of organisms were sensitive to cefadroxil, nalidixic acid and papenamic 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.

Rational prescribing for urinary tract infections (UTIs) requires 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. South African studies have also shown a similar distribution of organisms in cystitis, the most common category of UTI in family practice.

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. In an urban Cape Town family practice, 57% of isolates were resistant to amoxycillin and 49% to cotrimoxazole; and in a community health centre in Durban, 66% of isolates were resistant to ampicillin and 60% to co-trimoxazole. Despite these findings, the two antimicrobials are still recommended as empirical treatment for uncomplicated UTIs.

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.

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.

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 leucocytes per cubic millilitre (ml) of unspun urine;
c) a urine culture yielding ≥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. A haemocytometer can accurately measure pyuria. It is easier to perform and more accurate than microscopic urinary sediment examination.

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 ≥10^4 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 leucocytes per high powered field) in the centrifuged urinary sediment. Thus, demonstration of bacteria by culture is the mainstay of diagnosis.

Taking of urine specimen: 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 and it is difficult to understand and perform. 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. 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 specimens examined immediately after being passed using an improved Neubauer counting chamber. If pyuria was present, it was inculated onto MacConkey and blood agar media using a 1µl 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, 86 (68%) 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 (10) are listed to which 50% or more of the isolates had susceptibility test-

O'Mahony D, MBChB, DCH, MRCPG,
DTM&H, DPH, Dip MID COG (SA)
Family Practitioner, Bridge Street,
Port St Johns

106 JANUARY 1999 — SAPF Vol 20 No 1
The laboratory did report a category of intermediate sensitivities 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-amoxyclav have significantly lower sensitivities than the most effective antibiotics, i.e., fosfomycin, ciprofloxacin, norfloxacin or ofloxacin. However, the sensitivities of cefadroxil, piperacillin/tazobactam, gentamicin, amikacin, nalidixic acid and pipemidic acid do not differ significantly from the most effective group.

**Discussion**

The urinary pathogen isolated in this study are similar to other studies of community-acquired UTIs in that *E. coli* was the commonest pathogen. 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 co-trimoxazole (58%). These results are similar to recent studies of uncomplicated UTIs in urban primary care settings, implying that urinary pathogens in urban populations are resistant to these antibiotics.

The antimicrobials currently recommended by the South African Medicines Formulary for uncomplicated cystitis and pyelonephritis are co-amoxyclav or an oral cephalosporin or a quinolone, based on local sensitivity patterns. Urinary antiseptics are an alternative (e.g., nitrofurantoin and methenamine) 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. For acute uncomplicated cystitis, a three-day course of antibiotics is more effective than single dose therapy. Oral generic quinolones, e.g., nalidixic acid, enoxacin and norfloxacin, are now available at a reasonable cost. While a urine culture is usually unnecessary, in typical acute uncomplicated cystitis, it should ideally be done to guide therapy in pyelonephritis or in complicated urinary tract infections.

In pregnant women with cystitis, fluoroquinolones and fosfomycin are not recommended. Cefadroxil 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 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.

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. 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
Antimicrobial sensitivities and causative organisms of urinary tract infections

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Number Sensitive</th>
<th>Total Tested</th>
<th>Proportion Sensitive</th>
<th>95% Confidence Interval Lower</th>
<th>95% Confidence Interval Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>15</td>
<td>53</td>
<td>0.3</td>
<td>0.168</td>
<td>0.242</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>16</td>
<td>46</td>
<td>0.3</td>
<td>0.214</td>
<td>0.303</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>22</td>
<td>53</td>
<td>0.4</td>
<td>0.281</td>
<td>0.359</td>
</tr>
<tr>
<td>Cefadroxil</td>
<td>16</td>
<td>36</td>
<td>0.4</td>
<td>0.279</td>
<td>0.381</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>36</td>
<td>50</td>
<td>0.7</td>
<td>0.575</td>
<td>0.698</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>55</td>
<td>48</td>
<td>0.8</td>
<td>0.582</td>
<td>0.667</td>
</tr>
<tr>
<td>Cefaclor</td>
<td>30</td>
<td>36</td>
<td>0.9</td>
<td>0.672</td>
<td>0.793</td>
</tr>
<tr>
<td>Piperacillin/azobactam</td>
<td>40</td>
<td>46</td>
<td>0.9</td>
<td>0.737</td>
<td>0.891</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>47</td>
<td>51</td>
<td>0.9</td>
<td>0.811</td>
<td>0.978</td>
</tr>
<tr>
<td>Amikacin</td>
<td>45</td>
<td>48</td>
<td>0.9</td>
<td>0.828</td>
<td>0.987</td>
</tr>
<tr>
<td>Nalidixic acid</td>
<td>47</td>
<td>50</td>
<td>0.9</td>
<td>0.835</td>
<td>0.987</td>
</tr>
<tr>
<td>Pipemidic acid</td>
<td>34</td>
<td>36</td>
<td>0.9</td>
<td>0.813</td>
<td>0.993</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>32</td>
<td>32</td>
<td>1</td>
<td>0.891</td>
<td>0.991</td>
</tr>
<tr>
<td>Oxytetracycline</td>
<td>49</td>
<td>49</td>
<td>1</td>
<td>0.927</td>
<td>0.992</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>50</td>
<td>50</td>
<td>1</td>
<td>0.927</td>
<td>0.992</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>51</td>
<td>51</td>
<td>1</td>
<td>0.931</td>
<td>0.992</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Condition</th>
<th>Empirical Antibiotic Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute uncomplicated cystitis</td>
<td>5-day regimen: oral nalidixic acid, pipemidic acid, cefaclor, ciprofloxacin, ofloxacin, or norfloxacin</td>
</tr>
<tr>
<td>- pregnancy</td>
<td>Consider 7-day regimen: oral cefaclor or nalidixic acid</td>
</tr>
<tr>
<td>Acute uncomplicated pyelonephritis</td>
<td>10-day regimen: oral ciprofloxacin, ofloxacin, or cefaclor</td>
</tr>
<tr>
<td>- mild to moderate illness</td>
<td>Parenteral: gentamicin, amikacin, ciprofloxacin, ofloxacin in norfloxacin, until fever abates. Then oral agent for 10 days</td>
</tr>
<tr>
<td>- severe illness</td>
<td>Parenteral: gentamicin, amikacin, ciprofloxacin, ofloxacin in norfloxacin, until fever abates. Then oral agent for 10 days</td>
</tr>
<tr>
<td>- pregnancy - mild illness</td>
<td>10-day regimen: oral cefaclor</td>
</tr>
<tr>
<td>- moderate to severe illness</td>
<td>Parenteral: gentamicin, amikacin, ceftriaxone or cefotaxime until fever abates. Then oral agent for 10 days</td>
</tr>
</tbody>
</table>

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 (25%) of 22 whose organisms were not sensitive.

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. 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. 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.

Acknowledgments
The author thanks Professor Keith Klugman for reviewing the protocol and Farzana Sui for her assistance in the statistical analysis.

References

A conference for everyone concerned with rural health
THE 3RD WORLD CONFERENCE ON RURAL HEALTH
under the auspices of WONCA, the World Organisation of Family Doctors
1st – 4th July 1999
at Crowne Plaza Riverside Hotel,
Kuching Sarawak, Malaysia
and 4th – 7th July 1999
Satellite Meetings at resorts
Organised by The Academy of Family Physicians of Malaysia in collaboration with the Ministry of Health and the State Government of Sarawak.