

SHORT REPORT

Increasing antibiotic resistance among urinary tract isolates

S Ladhani, W Gransden

Arch Dis Child 2003;88:444-445

A five year retrospective study was performed to identify organisms isolated from the urinary tract of 2815 children in the community and 1314 children with underlying renal problems and their antimicrobial susceptibilities. Isolates from children in the latter group were generally more resistant to commonly used antibiotics. In particular, up to a third of *E coli* isolates from children in the community and almost two thirds of *E coli* isolates from children with underlying renal disease may be resistant to trimethoprim.

At least 8% of girls and 2% of boys will have a urinary tract infection (UTI) in childhood, and between 30% and 40% will have another episode within two years.¹ A significant proportion of children investigated after a proven UTI will have an underlying renal tract anomaly, including obstructive lesions in 0-4% and vesicoureteric reflux in 8-40% of children.^{1,2} Current guidelines recommend that empiric treatment with a "best guess" antibiotic should be started in all cases of suspected UTI after an appropriate urine specimen is obtained.³ The use of an inappropriate antibiotic will delay effective treatment and increase the risk of renal scarring, which is associated with poor renal growth, impaired renal function, early hypertension, and chronic renal failure later in life.^{1,4} Unfortunately, little has been published on the range and antimicrobial susceptibilities of urinary tract pathogens in the United Kingdom. We present the results of a five year retrospective study of organisms isolated from the urinary tracts of children in southeast London and their antimicrobial profiles. We hope that this information will encourage other units to examine their data and develop local recommendations for empiric treatment of UTI in children.

METHODS

We compared two groups of children under the age of 15 years: those whose samples were obtained in general practice (community) and those under the care of tertiary paediatric nephrologists (renal) at Guy's Hospital, London. The latter group includes children with renal tract abnormalities, chronic renal failure, renal transplantation, and those receiving peritoneal and haemodialysis. Approximately 10% of these children receive antimicrobial prophylaxis against UTI, most often trimethoprim (80%), followed by nitrofurantoin (18%). The remainder receive another antibiotic, such as nalidixic acid, cefadroxil, co-amoxiclav, or ciprofloxacin. Children with renal transplants receive co-trimoxazole prophylaxis. Information on the method of urine collection from the children was not available. A bacterial culture of 10⁵ colony forming units of a single species per ml isolated from a urine specimen was considered to be significant.¹ The bacteria were identified by standard methods and the antimicrobial susceptibility determined by disk diffusion.⁵

RESULTS AND DISCUSSION

Between January 1996 and December 2000, 2815 urine isolates were obtained from children in the community and 1314 from children with renal problems. In keeping with other studies, Gram negative organisms accounted for over 90% of the isolates, with *Escherichia coli* predominating.¹⁻⁴ Enterococci accounted for around 20% of all isolates, which is higher than found in other studies.^{1-4,6} They were, however, isolated as a single species and formed at least 10⁵ colony forming units per ml, and were, therefore, considered to be significant pathogens.¹ *Klebsiella* spp., *Staphylococcus aureus*, other staphylococci, *Pseudomonas* spp., *Enterobacter* spp., and *S maltophilia* were more prevalent among urine isolates of children with renal problems, while *Escherichia coli* and *Proteus* spp. were more prevalent among isolates from children in the community ($p < 0.05$) (table 1).

Table 1 Organisms isolated from the urinary tracts of children in the community and those with an underlying renal problem (1996-2000)

Organism	Isolates from children in the community						Isolates from children with underlying problems					
	1996 n=634 (22.5%)	1997 n=551 (19.6%)	1998 n=501 (17.8%)	1999 n=564 (20.0)	2000 n=575 (20.4%)	Total n=2815 (100%)	1996 n=241 (18.3%)	1997 n=244 (18.6%)	1998 n=309 (23.5%)	1999 n=274 (20.9%)	2000 n=246 (18.7%)	Total n=1314
<i>Escherichia coli</i>	348	321	339	377	389	1774 (63.0%)**	99	101	114	120	96	530 (40.3%)
<i>Proteus</i> spp.	52	33	22	23	33	163 (5.8%)*	8	8	14	7	12	49 (3.7%)
<i>Klebsiella</i> spp.	26	19	16	17	16	94 (3.3%)	16	18	25	21	20	100 (7.6%)**
<i>Enterobacter</i> spp.	6	6	8	7	6	33 (1.2%)	15	11	8	5	11	50 (3.8%)**
<i>Morganella morganii</i>	7	3	7	3	5	25 (0.9%)	3	5	4	0	5	17 (1.3%)
<i>Pseudomonas</i> spp.	13	15	11	10	10	59 (2.1%)	33	24	38	23	24	142 (10.8%)**
<i>Stenotrophomonas maltophilia</i>	0	0	0	0	0	0 (0%)	0	0	2	4	3	9 (0.7%)**
Other Gram negative bacilli	10	7	6	5	1	29 (1.0%)	8	6	6	6	2	28 (2.1%)*
<i>Staphylococcus aureus</i>	3	4	3	5	10	25 (0.9%)	8	8	12	6	4	38 (2.9%)**
Other staphylococci	3	4	5	4	2	18 (0.6%)	8	11	9	9	11	48 (3.7%)**
<i>Enterococcus</i> spp.	143	129	74	101	95	542 (19.3%)	39	50	65	59	53	266 (20.2%)
Non-faecal streptococci	13	10	10	12	8	53 (1.9%)	4	2	12	14	5	37 (2.8%)

Asterisks indicate that the organism is relatively more frequently isolated in that group at a significance level of 0.05* and 0.001** respectively.

Table 2 Antimicrobial resistance of urinary tract isolates and percentage of the total

Antibiotic	<i>E coli</i> (% resistant)		<i>Proteus</i> spp. (% resistant)		<i>Klebsiella</i> spp. (% resistant)		<i>Enterococcus</i> spp. (% resistant)		<i>Enterobacter</i> spp. (% resistant)	
	Community (n=1774)	Renal (n=530)	Community (n=164)	Renal (n=50)	Community (n=94)	Renal (n=100)	Community (n=480)	Renal (n=258)	Community (n=33)	Renal (n=50)
Ampicillin	51.1	59.2**	15.2	20.0	100.0	100.0	1.0	31.5**	97.0	100.0
Cefadroxil	1.5	6.7**	1.3	4.0*	2.1	5.0*	100.0	98.4	93.9	98.0
Cefuroxime	0.9	5.9**	1.9	10.0*	1.1	11.0*	99.2	98.8	100.0	88.0
Co-amoxiclav	3.6	10.6**	4.3	10.0*	3.2	10.0	1.0	32.4**	100.0	98.0
Gentamicin	0.1	1.5**	0.6	36.0	11.7	42.0**	99.6	98.5	3.0	10.0
Ciprofloxacin	0.6	5.9**	0.6	20.0**	0.0	8.0*	99.6	99.2	0.0	14.0*
Nitrofurantoin	5.9	16.7**	100.0	100.0	0.0	10.0**	3.0	8.5*	57.6	76.0
Trimethoprim	27.6	50.4**	22.0	36.0*	25.5	51.1**	9.2	57.8**	3.0	32.0*
Vancomycin							0.0	6.2**		

Asterisks indicate statistical significance between the two groups at a significance level of 0.05* and 0.001**.

The main focus of this study lies in the antimicrobial profile of the organisms isolated. Two different populations were selected for this study because we observed that the antibiotic resistance for organisms isolated from the urinary tract of children under the care of paediatric nephrologists was high, and this was confirmed in our study (table 2); overall, they were significantly more resistant to most antibiotics tested. Among isolates of *E coli* from patients with renal problems, for each antimicrobial tested, resistance was more common compared to community isolates ($p < 0.001$). In particular, trimethoprim resistance was significantly higher for the five most prevalent organisms ($p < 0.05$) (table 2). Vancomycin resistant enterococci were not isolated from urine cultures of community patients. However, among urine isolates from children with renal problems, resistance to vancomycin first emerged in 1997 and gradually increased to 10.7% in 2000 (χ^2 for trend = 5.6, $p = 0.018$). This higher antibiotic resistance in the renal group of children may reflect increased exposure to antibiotics and hospital admissions compared to children in the community; the former group is also more prone to UTI.^{3,4}

E coli remains the predominant urinary pathogen in both groups of children—so awareness of trends in its susceptibility is important. Over the five year study period, trimethoprim resistance increased steadily from 24.1% (84/348 isolates) to 31.6% (123/389 isolates) in the community group (χ^2 for trend = 4.1, $p = 0.04$). The increase in trimethoprim resistance was much greater in children with renal problems, from 37.4% (37/99 isolates) to 62.5% (85/136 isolates) by 2000 (χ^2 for trend = 17.9, $p < 0.0001$). In the latter group, resistance to cefuroxime (χ^2 for trend = 13.4, $p < 0.001$) and gentamicin (χ^2 for trend = 5.4, $p = 0.02$), two intravenous antibiotics that are predominantly restricted to hospital use, also increased gradually over five years, in contrast to isolates from children in the community, which remained <1.9% and <0.5% resistant, respectively, for the same period. Finally, although ciprofloxacin is not recommended in children, it is occasionally used by nephrologists as a short term third line prophylactic antibiotic because of the complexity of many of the patients' underlying conditions and the prevalence of otherwise resistant urinary pathogens. Ciprofloxacin resistance among community *E coli* isolates emerged in 1997 and,

although still infrequent, it occurred in 1.0% of 389 isolates by 2000. In comparison, around 5% of *E coli* isolates from children with renal problems were resistant to ciprofloxacin in the same year.

CONCLUSIONS

Paediatric urinary tract isolates are becoming increasingly resistant to commonly used antibiotics. In particular, up to a third of *E coli* isolates from the community and almost two thirds of *E coli* isolates from children with underlying renal problems may be resistant to trimethoprim, currently the first line empiric antibiotic treatment for UTI. Furthermore, organisms isolated from children with underlying renal problems are significantly more resistant to most antibiotics tested—this should be taken into account when selecting empiric treatment for UTI in children with underlying renal problems. Based on the results of our study, nitrofurantoin should be considered for first line empiric treatment and/or prophylaxis of UTI in children.

Authors' affiliations

S Ladhani, W Gransden, Department of Paediatrics and Microbiology, Guy's Hospital, St Thomas's Street, London Bridge SE1 9RT, UK

Correspondence to: Dr S Ladhani, Department of Paediatrics and Microbiology, Guy's Hospital, St Thomas's Street, London Bridge SE1 9RT, UK; drshamez@aol.com

Accepted 8 October 2002

REFERENCES

- Larcombe J. Urinary tract infection in children. *BMJ* 1999;**319**:1173–5.
- Le Saux N, Pham B, Moher D. Evaluating the benefits of antimicrobial prophylaxis to prevent urinary tract infections in children: a systematic review. *Can Med Assoc J* 2000;**163**:523–9.
- Royal College of Physicians. Report of a Working Group of the Research Unit, Royal College of Physicians. Guidelines for the management of acute urinary tract infection in childhood. *J R Coll Phys Lond* 1991;**25**:36–42.
- Smellie JM, Prescod NP, Shaw PJ, et al. Childhood reflux and urinary infection: a follow-up of 10–41 years in 226 adults. *Pediatr Nephrol* 1996;**12**:727–36.
- Andrews JM. The development of the BSAC standardized method of disc diffusion testing. *J Antimicrob Chemother* 2001;**48**(suppl):S1, 29–42.
- Mangioarotti P, Pizzini C, Fanos V. Antibiotic prophylaxis in children with relapsing urinary tract infections. *J Chemother* 2000;**12**:115–23.