대한임상미생물학회지 : 제8권 제2호 2005
Korean J Clin Microbiol 2005 ; 8(2):142-147

3차 병원에 내원한 환자에서 지역사회 요로감염의 원인 균종과 항균제 감수성

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서 론 : 지역사회 감염에서 항균제 내성 균주의 빈도는 점점 증가하고 있다. 하지만 3차 병원에 내원한 환자의 지역사회 요로감염의 원인 균종 및 항균제 감수성에 대한 보고는 많지 않다.

방 법 : 2001년부터 2003년까지 3년간 3차 병원에 내원한 지역사회 요로감염증 환자의 원인 균종 및 항균제 감수성 결과를 조사하였다.

결 과 : 본 연구에서 임상적으로 의의 있다고 판단된 총 1,753 주가 검출되었다. *Escherichia coli* (38.3%)가 가장 많았고 그 다음으로는 *Pseudomonas aeruginosa* (10.8%), *Enterococcus faecalis* (7.3%), *Klebsiella pneumoniae* (6.4%), coagulase negative staphylococci (CoNS) (5.4%) 및 *Staphylococcus aureus* (5.2%)의 순으로 검출되었다. 성별에 따라 균종의 검출빈도에 차이를 보였는데, 남자에서 *E. coli*는 유의하게 낮은 빈도로 검출된 반면($P < 0.001$), *P. aeruginosa, E. faecalis*, 및 *S. aureus*가 더 높은 빈도로 검출되었다($P < 0.001$). Ampicillin, gentamicin, co-trimoxazole, ciprofloxacin에 대한 *E. coli*의 감수성 비율은 각각 26.0%, 65.8%, 51.3%, 62.5%이었다. *E. coli*와 *K. pneumoniae*의 extended spectrum beta-lactamase 생성빈도는 각각 7.9%와 15.6%이었다.

결 론 : 3차 병원에 내원하는 지역사회 요로감염 환자는 일반적인 지역사회 요로감염과 비교하여 원인 균종의 빈도에 큰 차이를 보이고, 균종의 분포가 다양하며 항균제 내성율이 높은 특성을 나타내었다.

INTRODUCTION

Urinary tract infection (UTI) is one of the most common infections described in the outpatient clinic[1, 2]. Over the past decade, antimicrobial resistance has increased substantially worldwide and resistant organisms are now a growing and frequent problems in community-acquired infections[3, 4]. In almost all cases of urinary tract infection, antimicrobial therapy is initiated empirically, so international guidelines for the management of UTI have been published in order to optimize the antibiotic treatment of UTI[2]. Because these data can vary according to geographical and regional differences[5-7], a surveillance of local antimicrobial susceptibility patterns is essential. Several studies reported on the etiology and antibiotic susceptibility patterns for bacteria isolated from UTI in Korea[8-12]. However, in most of these studies the bacterial isolates were mainly recovered among inpatients and there is very little information on the etiology and antimicrobial susceptibility patterns of community-acquired urinary tract infection (CA-UTI).

The aims of this study were to determine the etiology and their antimicrobial susceptibility patterns of CA-UTI patients visiting a tertiary-care hospital for 3 years (2001-2003).

MATERIALS AND METHODS

Sample Preparation

This study was conducted on patients attending outpatient clinics and patients within the first 72 hours of hospitalization at Inje University Busan Paik Hospital, a 820-bed tertiary care teaching hospital between January 2001 and December 2003. Freshly voided midstream specimens of urine were submitted to the clinical microbiology laboratory of our hospital for processing. Semiquantitative urine culture using a calibrated loop was used to inoculate sheep blood agar and

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MacConkey agar plates. Significant bacteriuria was defined as culture of bacteria at a concentration of more than 10^5 CFU/ml. Urine specimens containing less than 10^5 CFU/ml or multiple (three or more) species were considered contaminated and were excluded from this study. Additional patient information was collected from the patient's medical records.

Microbiological methods

Species identification was performed using conventional biochemical tests and Vitek system (bioMérieux Vitek Inc., Hazelwood, MO., USA). Antimicrobial susceptibility tests were performed using the microdilution method by Vitek system (bioMérieux Vitek Inc., Hazelwood., MO., USA). Intermediate and resistant results were grouped together for data analysis. All controls required by the manufacturer were carried out. Interpretations were done according to the guidelines of the National Committee for Clinical Laboratory Standards[13].

Statistical analysis

Chi-squared test was used to assess the statistical significance of differences. A statistically significant difference was defined as a P value of <0.05. Data analysis was performed using MedCalc software Version 8.0 for Windows (MedCalc Inc., Mariakerke, Belgium).

RESULTS

In total, 1,753 bacterial isolates yielded a significant growth of pathogens of CA-UTI in this study. The overall female to male ratio in this study was 1.36 : 1. Higher rates of CA-UTIs were recorded among old age patients (>50 years, 60.0 %). The rest was comprised of pediatric patients (<20 years, 17.5%) and middle age patients (20-50 years, 22.5%).

The frequency and distribution of the different microorganisms as the causes of CA-UTI is summarized in the Table 1. The most common pathogen was *Escherichia coli* (38.3%), followed by *Pseudomonas aeruginosa* (10.8%), *Enterococcus faecalis* (7.3%), *Klebsiella pneumoniae* (6.4%), coagulase negative staphylococci (CoNS) (5.4%) and *Staphylococ-*

Table 1. Frequency and distribution of CA-UTI isolates at a tertiary-care hospital.

Micororganisms	Isolates, N (%)						P value
	Male	(43%)	Female	(57%)	Total		
Escherichia coli	142	(18.8)	529	(53.0)	671	(38.3)	< 0.001
Pseudomonas aeruginosa	130	(17.2)	59	(5.9)	189	(10.8)	< 0.001
Enterococcus faecalis	70	(9.3)	58	(5.8)	128	(7.3)	0.007
Klebsiella pneumoniae	49	(6.5)	63	(6.3)	112	(6.4)	NS
CoNS	42	(5.6)	53	(5.3)	95	(5.4)	NS
Staphylococcus aureus	57	(7.6)	35	(3.5)	92	(5.2)	< 0.001
Enterobacter cloacae	34	(4.5)	19	(1.9)	53	(3.0)	0.003
Streptococcus agalactiae	9	(1.2)	38	(3.8)	47	(2.7)	< 0.001
Enterococcus faecium	24	(3.2)	19	(1.9)	43	(2.5)	NS
Serratia marcescens	28	(3.7)	12	(1.2)	40	(2.3)	< 0.001
Proteus mirabilis	18	(2.4)	20	(2.0)	38	(2.2)	NS
Morganella morganii	26	(3.4)	6	(0.6)	32	(1.8)	< 0.001
Citrobacter freundii	20	(2.7)	11	(1.1)	31	(1.8)	NS
Acinetobacter baumanii	14	(1.9)	11	(1.1)	25	(1.4)	NS
Burkholderia cepacia	20	(2.7)	4	(0.4)	24	(1.4)	< 0.001
Alcaligenes xyloxidans	5	(0.7)	13	(1.3)	18	(1.0)	NS
Enterobacter aerogenes	3	(0.4)	15	(1.5)	18	(1.0)	0.042
Proteus vulgaris	9	(1.2)	3	(0.3)	12	(0.7)	NS
Klebsiella oxytoca	5	(0.7)	5	(0.5)	10	(0.6)	NS
Enterococcus avium	4	(0.5)	4	(0.4)	8	(0.5)	NS
Others	45	(6.0)	22	(2.2)	67	(3.8)	
Total	754	(100.0)	999	(100.0)	1753	(100.0)	

Abbreviations: CoNS, coagulase negative staphylococci ; NS, not significant.

Table 2. Percent susceptibility of gram-negative bacilli to antimicrobial agents

Antibiotics	Susceptible (%)								
	CFR	EAE	ECL	ECO	KPN	MMO	PMI	SMA	PAE
Amikacin	93.3	94.4	98.1	95.9	85.7	100.0	94.7	65.0	41.6
Ampicillin	10.3	11.1	3.8	26.0	1.8	6.3	63.2	20.0	
Ampicillin- Sulbactam	26.7	16.7	3.8	31.7	53.6	34.4	94.7	17.5	
Aztreonam	62.5	66.7	56.3	90.8	73.2	100.0	100.0	64.7	46.2
Cefazolin	6.7	5.6	5.7	69.0	62.5	9.4	81.6	0.0	
Cefepime	100.0	94.4	86.7	93.5	78.8	100.0	100.0	63.2	40.0
Ceftazidime									47.5
Ceftriaxone	57.7	60.0	47.6	91.3	74.7	93.5	96.8	64.9	10.1
Ciprofloxacin	82.8	88.2	94.3	62.5	92.9	96.9	86.5	65.0	23.0
Gentamicin	76.7	94.4	75.5	65.8	67.6	75.0	89.5	57.5	24.6
Imipenem	100.0	100.0	100.0	100.0	100.0	93.8	100.0	87.5	52.9
Piperacillin-Tazobactam	60.0	66.7	50.9	88.7	72.3	96.8	97.4	62.5	52.7
Tobramycin	73.3	83.3	49.1	68.4	67.9	96.9	81.6	32.5	33.0
Co-trimoxazole	73.3	82.4	62.3	51.3	67.0	62.5	54.1	90.0	
Ticarcillin-Clavulanic acid									40.8
Piperacillin									41.6
ESBL(+)				7.9	15.6				

Abbreviations: CFR, *C. freundii*; EAE, *E. aerogenes*; ECL, *E. cloacae*; ECO, *E. coli*; KPN, *K. pneumoniae*; MMO, *M. morganii*; PMI, *P. mirabilis*; SMA, *S. marcescens*; PAE, *P. aeruginosa*.

Table 3. Percent susceptibility of gram-positive isolates to antimicrobial agents.

Antibiotics	Susceptible (%)			
	CoNS	SAU	EFA	EFM
Ampicillin			87.5	26.2
Ciprofloxacin	63.0	48.4	53.1	19.5
Gentamicin	35.2	25.0		
Nitrofurantoin	98.9	100.0	92.1	54.8
Oxacillin	22.8	39.1		
Teicoplanin	100.0	100.0	99.2	92.9
Co-trimoxazole	67.4	80.4		
Vancomycin	100.0	100.0	99.2	92.9
Gentamicin(HLR)			38.9	19.5
Streptomycin(HLR)			65.1	31.7
Penicillin	4.3	5.4	78.1	23.8
Tetracycline	52.2	39.1		
Rifampin	94.6	95.7		

Abbreviations: CoNS, coagulase negative staphylococci; SAU, *S. aureus*; EFA, *E. faecalis*; EFM, *E. faecium*; HLR, high-level resistance.

cus aureus (5.2%). There are significant differences in the distribution of CA-UTI pathogen according to patient gender. In female, the most common pathogen was *E. coli* (53.0 %) followed by *K. pneumoniae* (6.3%), *P. aeruginosa* (5.9 %) and *E. faecalis* (5.8%). In male, the most common pathogen was *E. coli* (18.8%) followed by *P. aeruginosa* (17.2%), *E. faecalis* (9.3%) and *S. aureus* (7.6%). Infection with *E. coli* was significantly lower in male and infections with *P. aeruginosa, E. faecalis*, and *S. aureus* were significantly more common in male patients ($P < 0.001$). There was no significant shift in the types of organisms causing CA-UTI for the three years (data not shown).

The antibiotic susceptibility patterns of the common CA-UTI pathogens are presented in Table 2 and 3. The susceptible rates of *E. coli* to ampicillin were 26.0%, 65.8% with gentamicn, 51.3% with co-trimoxazole, 62.5% with ciprofloxacin. The susceptibilities of *E. coli* to amikacin (95.9%), aztreonam (90.8%), cefepime (93.5), ceftriaxone (91.3), imipenem (100%) were significantly higher than those to ampicillin (26.0%), ampicillin-sulbactam (31.7%), cefazolin (69.0 %) ciprofloxacin (62.5%), gentamicin (65.8%), co-trimoxazole (51.3%). The susceptible rates to amikacin, cefepime, and imipenem were high in all *Enterobacteriaceae*. *S. marcescens* showed the highest resistance among *Enterobacteriaceae* to the most of antimicrobial agents. Susceptible rates to *Enterobacteriaceae* other than *E. coli* were different from those of *E. coli*. Aztreonam and ceftriaxone were very active against *E. coli* but not against *K. pneumoniae*, *Citrobacter* species or *Enterobacter* species. On the contrary, susceptible rates to co-trimoxazole and ciprofloxacin in *E. coli* were lower than those in other *Enterobacteriaceae*. Extended spectrum beta-lactamase (ESBL) was detected in 7.9% of *E. coli* and 15.6% of *K. pneumoniae. P. aeruginosa* and *A. baumanii* had the highest resistance for all antibiotics. The highest susceptible rates were to imipenem (52.7%) and piperacillin-tazobactam (52.7%). Among the gram-positive cocci, susceptible rates of *S. aureus* and CoNS to penicillin were 5.4 % and 4.3% and those to oxacillin were 39.1 and 22.8% respectively.

DISCUSSION

CA-UTI commonly occurs in patients more complicated than indicated by the UTI drug trials frequently published [14]. Moreover, its epidemiology, particularly related to causative organisms and resistance to antimicrobial drugs, has changed significantly in the recent years. However, little information exists on the epidemiology of CA-UTI in a tertiary -care hospital setting in Korea. This study investigated the distribution of organisms and their susceptibility of CA-UTI in patients visiting a tertiary-care hospital. The frequency of *E. coli* in CA-UTI varied in different studies from 50% to 85% [15-19]. But these studies were principally limited to uncomplicated CA-UTI, gram-negative bacilli, or female group. Therefore, since our results are based on different standpoint, it should not be directly compared with other data. Our study showed that E. coli was also the main uropathogen in CA-UTI. The proportion of uropathogens including *E. coli* in female was similar to other reports, however, it was quite different in male. The prevalence of *E. coli* in male was lower than that in female, while *P. aeruginosa* and *S. aureus* were higher. This may be due to the high prevalence of complicated UTIs in this study.

The guidelines of the Infectious Disease Society of America (IDSA) published in 1999 for the treatment of UTI recommend avoiding empirical treatment with a specific antibiotic when the local level of resistance among *E. coli* strains exceeds 20%. The IDSA also emphasized that physicians should obtain information about local resistance rates[2]. There is widespread concern about the rising antimicrobial resistance among urinary tract pathogens in the community. In a Korean study[8], 21.6% of *E. coli* in outpatient were susceptible to ampicillin and the susceptibilities of *E. coli* to co-trimoxazole and ciprofloxacin were 42.3 and 74.7% - this is comparable to our results, indicating that ampicillin is currently not a suitable agent for the empiric treatment of UTI in our region and co-trimoxazole might not be a reasonable choice in the treatment of CA-UTI. The most alarming finding in our study was the exceedingly high resistance rates among *E. coli* to quinolones isolates in CA-UTI (37.5%). These rates are higher than those reported in other studies[8, 20]. These results imply that quinolones, which are commonly used in the management of UTI, might gradually lose their utility in the empiric treatment of UTI. Given the low prevalence of resistance to amikacin, aztreonam, cefepime, and ceftriaxone, these agents might be considered as recommendations for initial empirical treatment in CA-UTI patients visiting tertiary hospital. The *P. aeruginosa* was highly resistant to all antibiotics even though the resistant rates were lower than in the hospital environments. It is worth noting the considerable isolation of *P. aeruginosa* in the community, because this organism shows high resistance in many antibiotics. Lee et al [9] reported that the incidence of ESBL producing *E. coli* in the community was 10.8% in childhood. We also observed that the rate of ESBL producing *E. coli* and *K. pneumoniae* exhibited significantly high (7.9 and 15.6%). It would be necessary to lookout of the spreading the ESBL producing *E. coli* to community society.

There were various organisms causing CA-UTI and the susceptibilities of isolates other than *E. coli* to many antibiotics showed also quite different patterns to those of *E. coli*. These data suggest that urine cultures cannot be neglected and the susceptibility results must be confirmed.

Because our hospital is a tertiary-care center, patients with CA-UTI referred for hospital evaluation have severe infections and complex problems which is confirmed by findings of the present study, such as the mean age of the population (50.7 years), the high admission rate (47.7%). So, urine culture results of our hospital are highly inclusive of patients with complicated UTI, such as recurrent UTI, treatment failure, urinary tract abnormalities. Thus, we must keep the difference between a physician's office and tertiary hospitals and it is important to understand the etiology and susceptibility results of CA-UTI patients visiting a tertiary-care hospital for the proper treatment.

Our results will serve as an indicator of empirical therapy of CA-UTI visiting tertiary-care hospitals and it is also necessary to continue monitoring the resistance of strains isolated in CA-UTI.

REFERENCES

1. Stamm WE and Hooton TM. Management of urinary tract infections in adults. N Engl J Med 1993;329:1328-34.
2. Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America (IDSA). Clin Infect Dis 1999;29:745-58.
3. Steinman MA, Gonzales R, Linder JA, Landefeld CS. Changing use of antibiotics in community-based outpatient practice, 1991-1999. Ann Intern Med 2003;138:525-33.
4. Tambic Andrasevic A, Tambic T, Kalenic S, Jankovic V. Surveillance for antimicrobial resistance in Croatia. Emerg Infect Dis 2002;8:14-8.
5. Colodner R, Keness Y, Chazan B, Raz R. Antimicrobial susceptibility of community-acquired uropathogens in northern Israel. Int J Antimicrob Agents 2001;18:189-92.
6. Mathai D, Jones RN, Pfaller MA. Epidemiology and frequency of resistance among pathogens causing urinary tract infections in 1,510 hospitalized patients: a report from the SENTRY Antimicrobial Surveillance Program (North America). Diagn Microbiol Infect Dis 2001;40:129-36.
7. Karlowsky JA, Jones ME, Thornsberry C, Critchley I, Kelly LJ, Sahm DF. Prevalence of antimicrobial resistance among urinary tract pathogens isolated from female outpatients across the US in 1999. Int J Antimicrob Agents 2001;18:121-7.
8. Ko YH, Oh JS, Cho DY, Bea JH, Koh SK. Changes of Causative Organisms and Antimicrobial Sensitivity of Urinary Tract Infection between 1979 and 2001. Korean J Urol 2003;44:342-50.
9. Lee JW, Shin JS, Seo JW, Lee MA, Lee SJ. Incidence and Risk Factors for Extended-Spectrum β-lactamase-Producing *Escherichia coli* in Community-acquired Childhood Urinary Tract Infection. J Korean Soc Pediatr Nephrol 2004;8:214-22.
10. Maeng KY. Study on the Ordinary Bacteria among Urinary Tract Pathogens Isolated during Recent 2 Years. Korean J Clin Pathol 1989;9:153-9.
11. Moon H and Lee M. Urinary Tract Infection Due to coagulase-negative Staphylococci: Species Identification, antimicrobial Resistance and Clinical Characteristics. Korean J Clin Microbiol 2003;6:23-8.
12. Ko HS, Choi DY, Han YT. A Study of the Changes of Antibiotic Sensitivity to the Causative Organisms of Urinary Tract Infection for Recent 5 Years. Korean J Urol 1999;40:809-16.
13. National Committee for Clinical Laboratory Standards. Performance standards for antimicrobial susceptibility testing; tenth informational supplement M100-S10. Wayne, PA: National Committee for Clinical Laboratory Standards.
14. Ferry S, Burman LG, Mattsson B. Urinary tract infection in primary health care in northern Sweden. I. Epidemiology. Scand J Prim Health Care 1987;5:123-8.
15. Ti TY, Kumarasinghe G, Taylor MB, Tan SL, Ee A, Chua C, et al. What is true community-acquired urinary tract infection? Comparison of pathogens identified in urine from routine outpatient specimens and from community clinics in a prospective study. Eur J Clin Microbiol Infect Dis 2003;22:242-5.
16. Farrell DJ, Morrissey I, De Rubeis D, Robbins M, Felmingham D. A UK multicentre study of the antimicrobial susceptibility of bacterial pathogens causing urinary tract infection. J Infect 2003;46:94-100.
17. Kahlmeter G. An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO.SENS Project. J Antimicrob Chemother 2003;51:69-76.
18. Chazan B, Sakran W, Raz R, Colodner R. Improved antimicrobial susceptibility of community-acquired uropathogens in northern Israel (1995-1999-2002). Int J Antimicrob Agents 2004;24:89-92.
19. Gupta K, Scholes D, Stamm WE. Increasing prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in women. JAMA 1999;281:736-8.
20. Jones RN, Kugler KC, Pfaller MA, Winokur PL. Characteristics of pathogens causing urinary tract infections in hospitals in North America: results from the SENTRY Antimicrobial Surveillance Program, 1997. Diagn Microbiol Infect Dis 1999;35:55-63.

Etiology and Antimicrobial Susceptibility of Bacterial Pathogens Causing Community-Acquired Urinary Tract Infection at a Tertiary-care Hospital

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Background: Resistant organisms are now a growing and frequent problem in community-acquired infections. There is little information on the etiology and antimicrobial susceptibility patterns of community-acquired urinary tract infection (CA-UTI) at a tertiary-care hospital.

Methods: We evaluated the distribution of etiological organisms with their antimicrobial susceptibility patterns of CA-UTI in the patients visiting a tertiary-care hospital during the period of three years from 2001 through 2003.

Results: In total, 1,753 bacterial isolates yielded a significant growth as pathogens of CA-UTI in this study. The most common pathogen was *Escherichia coli* (38.3%), followed by *Pseudomonas aeruginosa* (10.8%), *Enterococcus faecalis* (7.3%), *Klebsiella pneumoniae* (6.4%), coagulase negative staphylococci (CoNS) (5.4%) and *Staphylococcus aureus* (5.2%). The prevalence of *E. coli* was significantly higher in females ($P < 0.001$), whereas *P. aeruginosa, E. faecalis,* and *S. aureus* were significantly more common in male group ($P < 0.001$). The susceptibility rate of *E. coli* was 26.0% to ampicillin, 65.8% to gentamicin, 51.3% to co-trimoxazole, and 62.5% to ciprofloxacin. The susceptibility patterns of *Enterobacteriaceae* other than *E. coli* were different from those of *E. coli*. Extended spectrum beta-lactamase was detected in 7.9% of *E. coli* and 15.6% of *K. pneumoniae*.

Conclusion: This study demonstrates a diversity of etiological organisms and a high rate of resistance to commonly used antimicrobials of CA-UTI in patients visiting a tertiary-care hospital.

(Korean J Clin Microbiol 2005;8(2):142-147)

Keywords: Community-acquired infection, Urinary tract infection, Etiology, Antibiotic resistance

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