

Infection/Inflammation

Results of Urine Culture and Antimicrobial Sensitivity Tests According to the Voiding Method Over 10 Years in Patients with Spinal Cord Injury

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Purpose: We studied the results of urine cultures and antimicrobial sensitivity tests according to the voiding method used by spinal cord injury (SCI) patients over a recent 10-year period.

Materials and Methods: We retrospectively analyzed 1,236 urine samples and their antimicrobial sensitivity tests for 112 patients who had used only one voiding method between January 2000 and December 2009. The voiding methods were classified into four groups: clean intermittent catheterization (CIC), suprapubic catheterization, urethral Foley catheter, and spontaneous voiding.

Results: Of the 1,236 urine samples, 925 (74.8%) were positive and 279 (30.2%) had more than one bacteria. The CIC group showed the lowest rate of bacteriuria, colony counts, and polymicrobial infection ($p < 0.001$). Causative organisms were mostly Gram-negative bacteria (84%), including *Pseudomonas aeruginosa* (22.9%), *Escherichia coli* (21.1%), *Klebsiella* species (6.7%), and *Citrobacter* species (6.3%). The rate of Gram-positive bacterial infection was 13.6%, and major pathogenic organisms were *Streptococcus* species (8.6%) and *Staphylococcus* species (2.6%). Major pathogenic organisms and the results of antimicrobial sensitivity tests differed according to the voiding method.

Conclusions: Although the patient's condition and preferences are important when choosing the method of bladder management, CIC is the best voiding method for reducing urinary tract infections in SCI patients. When immediate use of antibiotics is needed for treatment of urinary tract infections, an appropriate antibiotic can be chosen according to the voiding method on the basis of our study and can be administered before the results of an antimicrobial sensitivity test are available.

Key Words: Bacteriuria; Microbial sensitivity tests; Spinal cord injuries; Urinary tract infections

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INTRODUCTION

Spinal cord injury (SCI) patients have many urological complications, including urinary tract infection (UTI), bladder stone, renal stone, hydronephrosis, and vesicoureteral reflux [1,2]. Of these complications, recurrent UTI is a major cause of morbidity, such as upper urinary tract deterioration [3]. Therefore, prevention and proper manage-

ment of UTIs in SCI patients are very important.

Voiding methods for SCI patients with neurogenic bladder include clean intermittent catheterization (CIC), suprapubic catheterization (SPC), urethral Foley catheter (UF), and condom drainage. However, these voiding methods increase the risk of catheter-related recurrent UTIs that require multiple courses of antibiotic therapy. Eventually, the risk of antibiotic-resistant organisms is increased.

Therefore, preventing the occurrence of antibiotic-resistant organisms through the use of suitable antibiotics is a major issue.

There are many studies about urologic complications and UTIs of SCI patients, but studies about UTIs according to the method of bladder drainage are rare. In the present study, therefore, we investigated the results of urine cultures and antimicrobial sensitivity tests according to the method of bladder drainage used by SCI patients over a recent 10-year period.

MATERIALS AND METHODS

From January 2000 to December 2009, 112 SCI patients were included in this study. We retrospectively reviewed the medical records of the patients to analyze the results of urine cultures and antimicrobial sensitivity tests. The age distribution was comparable for all four groups and ranged from 25 to 80 years with a mean age of 55.9 years. The male:female ratio was 111:1 (99.1%:0.9%). All patients had used only one voiding method (no change in voiding method) during the study period. The patients were classified into four groups as follows: CIC (n=41), SPC (n=34), UF (n=9), and spontaneous voiding (SV; n=28).

Of a total of 1,353 urine samples, we excluded 117 urine samples that were considered unresolved bacteriuria. A total of 1,236 urine samples were finally analyzed in our study. Of these 1,236 urine samples, 898 (72.7%) were obtained from patients with symptoms such as fever, flank pain, suprapubic discomfort, cloudy urine, and foul odor, and 338 (27.3%) were collected in the case of regular periodic follow-up.

Urine samples were collected by catheterization or by using the clean-catch technique for patients able to void spontaneously. Urine specimens collected by catheterization were obtained by aseptically aspirating the clamped and disinfected catheter with a sterile syringe after the catheter change or at the time of intermittent catheterization.

All specimens were cultured and isolates were identified in the routine laboratory. The minimum viable count for diagnosis of bacteriuria was 10^3 CFU/ml.

Antimicrobial sensitivity tests were performed on bacteria considered significant, and the results were stratified by voiding method group. The antibiotics included in our study were penicillin, ampicillin, Augmentin, cefazolin, ce-

foxitin, cefotetan, cefuroxime, ceftazidime, ceftriaxone, cefepime, ofloxacin, ciprofloxacin, levofloxacin, gentamicin, tobramycin, amikacin, piperacillin, piperacillin/tazobactam, imipenem, meropenem, vancomycin, trimethoprim-sulfamethoxazole, and tetracycline.

The method of statistical analysis used was the chi-square test (with Fisher's exact test) using SPSS ver. 15.0 (SPSS Inc., Chicago, IL, USA). A p-value of < 0.05 was considered to be statistically significant.

RESULTS

1. Results of urine cultures

1) Positive urine culture: Of the 1,236 samples, 925 (74.8%) were positive. In the CIC group, 366 (69.8%) urine samples were positive and this result was significantly lower than in the other groups ($p < 0.001$) (Table 1).

2) Colony counts: Colony counts of isolated bacteria are presented in Table 2. The CIC group showed lower colony counts than did the other groups ($p < 0.001$).

3) Polymicrobial infection: Polymicrobial infection was common. Among all (925) positive urine samples, multiple species were identified in 279 (30.2%) urine samples. In the CIC group, 2 species were isolated in 53 (14.5%) urine samples and 3 species were isolated in 2 (0.5%) urine samples. These results were significantly lower than in the other groups ($p < 0.001$) (Table 3).

4) The major organisms in the urine samples: The vast majority of cases of bacteriuria were caused by gram-negative bacteria (84%). Major pathogenic gram-negative bacteria included *Pseudomonas aeruginosa* (22.9%) and *Escherichia coli* (*E. coli*, 21.1%), followed by *Klebsiella* spe-

TABLE 1. Positive urine cultures according to voiding method

	Sterile cultures (%)	Positive cultures (%)	Total (%)	p-value ^a
CIC	158 (30.2)	366 (69.8)	524 (100)	< 0.001
SPC	74 (17.7)	343 (82.3)	417 (100)	
UF	22 (22.4)	76 (77.6)	98 (100)	
SV	57 (28.9)	140 (71.1)	197 (100)	

CIC: clean intermittent catheterization, SPC: suprapubic catheterization, UF: urethral Foley catheter, SV: spontaneous voiding, ^a: analyzed by chi-square test

TABLE 2. Colony counts of the positive urine cultures

Colony counts (CFU/ml)	10^3 (%)	10^4 (%)	10^5 (%)	$10^6 \leq$ (%)	Total (%)	p-value ^a
CIC	2 (0.5)	182 (49.7)	129 (35.2)	53 (14.5)	366 (100)	< 0.001
SPC	2 (0.6)	126 (36.7)	116 (33.8)	99 (28.9)	343 (100)	
UF	0 (0.0)	25 (32.9)	27 (35.5)	24 (31.6)	76 (100)	
SV	0 (0.0)	51 (36.4)	51 (36.4)	38 (27.1)	140 (100)	

CIC: clean intermittent catheterization, SPC: suprapubic catheterization, UF: urethral Foley catheter, SV: spontaneous voiding, ^a: analyzed by chi-square test

TABLE 3. Isolates of urine cultures according to voiding method

Isolates	1 (%)	2 (%)	3 (%)	Total (%)	p-value ^a
CIC	311 (85.0)	53 (14.5)	2 (0.5)	366 (100)	< 0.001
SPC	190 (55.4)	148 (43.1)	5 (1.5)	343 (100)	
UF	45 (59.2)	30 (39.5)	1 (1.3)	76 (100)	
SV	100 (71.4)	40 (28.6)	0 (0.0)	140 (100)	

CIC: clean intermittent catheterization, SPC: suprapubic catheterization, UF: urethral Foley catheter, SV: spontaneous voiding, ^a: analyzed by chi-square test

TABLE 4. Major causative organisms (Top 1-10)

	CIC (%)	SPC (%)	UF (%)	SV (%)
<i>Pseudomonas aeruginosa</i>	56 (14.0)	158 (34.6)	21 (21.2)	49 (27.5)
<i>Escherichia coli</i>	137 (34.3)	54 (11.8)	27 (27.3)	43 (24.2)
<i>Streptococcus species</i>	36 (9.0)	52 (11.4)	3 (3.0)	16 (9.0)
<i>Klebsiella species</i>	47 (11.8)	15 (3.3)	13 (13.1)	8 (4.5)
<i>Citrobacter species</i>	38 (9.5)	28 (6.1)	6 (6.1)	6 (3.4)
<i>Providencia species</i>	10 (2.5)	55 (12.1)	2 (2.0)	11 (6.2)
<i>Serratia marcescens</i>	22 (5.5)	25 (5.5)	7 (7.1)	5 (2.8)
<i>Acinetobacter species</i>	18 (4.5)	16 (3.5)	4 (4.0)	12 (6.7)
<i>Morganella morganii</i>	7 (1.8)	25 (5.5)	9 (9.1)	6 (3.4)
<i>Proteus species</i>	5 (1.3)	14 (3.1)	5 (5.1)	10 (5.6)
<i>Staphylococcus species</i>	24 (6.0)	14 (3.1)	2 (2.0)	12 (6.7)
Total	400 (100)	510 (100)	130 (100)	178 (100)

CIC: clean intermittent catheterization, SPC: suprapubic catheterization, UF: urethral Foley catheter, SV: spontaneous voiding

cies (6.7%), *Citrobacter species* (6.3%), *Providencia species* (6.3%), *Serratia marcescens* (4.8%), *Acinetobacter species* (4.0%), *Morganella morganii* (3.8%), and *Proteus species* (2.7%). Of the isolates, 13.6% were gram-positive bacteria, mainly *Streptococcus species* (8.6%) and *Staphylococcus species* (2.6%).

The most commonly isolated pathogens in each group were *E. coli* in the CIC and UF groups and *Pseudomonas aeruginosa* in the SPC and SV groups, respectively (Table 4).

2. Results of antimicrobial sensitivity tests

In the antimicrobial sensitivity tests, vancomycin, meropenem, and imipenem showed very high (more than 90%) sensitivity in all groups. Other antibiotics that showed high sensitivity in each group were as follows. Amikacin (84.5%), cefepime (83.7%), piperacillin/tazobactam (73.9%), ofloxacin (70.3%), ceftazidime (66.0%), cefotetan (62.1%), Augmentin (61.3%), and tobramycin (61.3%) showed high sen-

TABLE 5. Result of antimicrobial sensitivity tests according to voiding method

	CIC (%)	SPC (%)	UF (%)	SV (%)
Penicillin	49.2	67.1	33.3	23.1
Ampicillin	9.5	13.3	6.7	18.3
Augmentin	61.3	33.7	45.7	44.1
Cefazolin	52.6	26.5	36.1	43.2
Cefoxitin	59.2	48.7	43.8	59.7
Cefotetan	62.1	47.6	77.3	65.5
Cefuroxime	34.4	23.4	34.6	47.7
Ceftazidime	66.0	54.3	64.4	74.6
Ceftriaxone	50.6	36.5	42.1	51.3
Cefepime	83.7	73.2	76.6	80.3
Ofloxacin	70.3	59.5	87.5	54.5
Ciprofloxacin	33.9	41.8	50.0	36.1
Levofloxacin	36.3	38.3	57.1	36.7
Gentamicin	58.2	55.9	50.5	49.4
Tobramycin	61.3	59.2	70.5	56.9
Amikacin	84.5	74.0	86.0	72.2
Piperacillin	36.4	50.5	45.1	47.0
Piperacillin/tazobactam	73.9	62.4	74.0	77.7
Imipenem ^a	95.1	94.4	92.2	96.5
Meropenem ^a	93.2	95.0	100	94.8
Vancomycin ^a	100	96.6	100	100
Trimethoprim-sulfamethoxazole	49.5	53.9	54.2	42.4
Tetracycline	30.1	23.5	25.0	31.1

CIC: clean intermittent catheterization, SPC: suprapubic catheterization, UF: urethral Foley catheter, SV: spontaneous voiding, ^a: showed very high (more than 90%) sensitivity in all groups

sitivity in the CIC group. In the SPC group, amikacin (74.0%), cefepime (73.2%), penicillin (67.1%), and piperacillin/tazobactam (62.4%) had high sensitivity. In the UF group, ofloxacin (87.5%), amikacin (86.0%), cefotetan (77.3%), cefepime (76.6%), piperacillin/tazobactam (74.0%), tobramycin (70.5%), and ceftazidime (64.4%) showed high sensitivity. Cefepime (80.3%), piperacillin/tazobactam (77.7%), ceftazidime (74.6%), amikacin (72.2%), and cefotetan (65.5%) showed high sensitivity in the SV group (Table 5).

DISCUSSION

The development of voiding methods for patients with SCI has decreased urologic complications and the mortality rate. Despite these improvements, however, UTI is still a major cause of morbidity in SCI patients.

The definitions for significant bacteriuria in SCI patients are controversial. In a study of patients with SCI, Dedeić-Ljubović and Hukić considered significant bacteriuria to be $\geq 10^4$ CFU/ml [4]. In another study, Menon and Tan reported that all positive urine cultures had $\geq 10^5$ CFU/ml [5]. These thresholds lack sensitivity, however. The National Institute on Disability and Rehabilitation Research (NIDRR) Consensus Statement recommended

the following uropathogen colony count criteria for the diagnosis of significant bacteriuria in persons with SCI: (1) $\geq 10^2$ CFU/ml for catheter specimens from individuals on intermittent catheterization, (2) $\geq 10^4$ CFU/ml for clean-void specimens from catheter-free males using condom collection devices, and (3) any detectable concentration of uropathogens from indwelling catheters or suprapubic aspirates because the vast majority of patients with an indwelling catheter and low-level bacteriuria showed an increase to greater than 10^5 CFU/ml within a short period of time [6]. In our study, more than 10^3 CFU/ml ($\geq 10^3$ CFU/ml) of uropathogens were evaluated; this threshold is identical to that of most Korean hospitals. According to the definition of the NIDRR, all of the positive urine culture results were significant bacteriuria.

Our study reported a positive urine culture rate of 74.8%. In another study of patients with SCI, Dedeić-Ljubović and Hukić reported that 87.3% of samples had a positive urine culture [4]. This modest difference may be because our study population included some patients who were seen for regular periodic follow-up.

In non-SCI patients, more than 10^5 CFU/ml is considered significant bacteriuria. Our results showed that a considerable portion of specimens (41.9%) had colony counts of less than 10^5 CFU/ml. This suggests that a low colony count of a specimen is an important aspect in the diagnosis of UTI in SCI patients.

Most bacteriuria in short-term catheterization is of a single organism, whereas patients catheterized for longer than 1 month will usually demonstrate a polymicrobial flora caused by a wide range of gram-negative and gram-positive bacterial species. Such specimens commonly have two to four bacterial species, each at concentrations of 10^5 CFU/ml or more. Some may have up to six to eight species at that concentration. This phenomenon is due to an incidence of new episodes of bacteriuria approximately every 2 weeks and the ability of these strains to persist for weeks and months in the catheterized urinary tract [7]. The rate of polymicrobial infection was 30.2% in our study, and the CIC group (14.5%) showed a significantly lower rate than did the other groups. In another study of SCI patients, Dedeić-Ljubović and Hukić reported a rate of polymicrobial infection of 44.9% and a lower rate (40.8%) in the CIC group [4]. On the other hand, in studies of UTI in non-SCI patients, the rate of polymicrobial infection ranged from 3.5% to 21.8% and was lower than in the SCI patients [8-12].

In 1966, Guttman and Frankel recommended sterile intermittent catheterization for the initial management of neurogenic bladder in SCI patients [13]. In 1972, Lapidès et al reported that CIC could prevent UTI in patients with incomplete bladder drainage and neurogenic bladder [14]. In many previous studies of SCI patients, CIC showed a low risk of urologic complications [4,15,16]. In the present study, the CIC group showed the lowest rate of positive urine cultures, colony counts, and number of isolates.

The common causative organisms in uncomplicated UTI are *E. coli* (34.4% to 67.0%), followed by *Enterococcus*,

Pseudomonas, *Enterobacter*, *Klebsiella*, and *Staphylococcus* [8-12]. The major organisms causing UTI in patients with SCI differ from those in patients with intact spinal cords in etiology, complexity, and antimicrobial susceptibility and are influenced by the type and duration of catheterization. In most studies of UTI in patients with SCI or indwelling catheter, interestingly, *E. coli* was isolated in less than 20% (4.3% to 19%) of patients and *Pseudomonas aeruginosa*, *Proteus mirabilis* (*P. mirabilis*), or *Enterococcus faecalis* were more common among SCI patients than among patients with intact spinal cords. Other common organisms were *Klebsiella pneumoniae*, *Providencia stuartii*, *Morganella* species, *Acinetobacter* species, *Serratia* species, *Staphylococcus*, and *Candida* species [4,5,17-20]. Especially, urease-splitting organisms including *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, and *Providencia stuartii* were isolated at a relatively high rate of cultures in patients with SCI or indwelling catheters. Mobley and Warren reported that 86% of all specimens were urease-positive bacterial species, and major organisms were *P. mirabilis* and *M. morgani*, and these species made up over half of the specimens [21]. In our results, urea-splitting organisms were isolated in 62% of cultures, and the major organisms were *Pseudomonas* species and *Klebsiella* species.

E. coli, a commensal organism of the bowel and perineum, was most common in the CIC and UF groups, even though *Pseudomonas* species were the most common bacteria in our study. This result suggests that *E. coli* is strongly associated with the periurethra adjacent to the perineum. Munir et al reported that *E. coli* was the most common organism causing bacteriuria in catheterized patients and that there was a significant association between periurethral colonization and subsequent bacteriuria [22]. Also, Schlager et al reported that the origin of *E. coli* isolated from the urine of children with neurogenic bladder receiving CIC was the periurethra [23].

In the treatment of UTIs, selection of antibiotics is a major concern. First-line antibiotics should be chosen in view of effectiveness and prevention of antibiotic resistance. Therefore, urologists have no choice but to use empirical antibiotics considering the antibiotic restriction policy (prefer common antibiotics to restricted antibiotics for preventing resistant bacteria) until the reports of an antimicrobial sensitivity test are available. Unfortunately, few studies have analyzed the results of antimicrobial sensitivity tests according to the voiding method used in SCI patients with UTI. Our study thus provides valuable information about first-line antibiotic treatment in SCI patients with UTI.

Our results showed a difference in antibiotic sensitivity among the groups according to the voiding method used. Vancomycin, meropenem, and imipenem showed very high (more than 90%) sensitivity in all groups. However, these antibiotics are restricted and are considered last resort antibiotics. The initial use of these antibiotics before identification of the causative bacteria can produce resistant

bacteria. We suggest that choosing the first-line antibiotic by considering the result of an antimicrobial sensitivity test according to the voiding method can produce an increased treatment effect and a decreased production of resistant bacteria.

This study has several limitations. First, the voiding methods of patients before 2000 could not be investigated, so the previous voiding method might have influenced the results of the urine culture and antimicrobial sensitivity test. Second, urinary calculi, vesicoureteral reflux, interval of catheter change, and previous antibiotic treatment were not investigated in our study. If these factors were additionally investigated, the relationship between voiding methods and our results could be clarified further.

In conclusion, an appropriate choice of voiding method is extremely important to prevent (recurrent) UTIs in SCI patients. Furthermore, the immediate administration of proper antibiotics according to the voiding method can produce effective treatment in SCI patients with symptomatic UTI and decrease the risk of antibiotic resistance.

CONCLUSIONS

We studied the results of urine cultures and antimicrobial sensitivity tests according to the voiding method used by SCI patients over a recent 10-year period. CIC is generally recognized to reduce UTIs and various urological complications. We determined that the rate of positive urine cultures, the colony counts, and the number of isolates were lower in the CIC group than in the other groups. Furthermore, when immediate use of antibiotics is needed for treatment of UTI, a proper choice of antibiotics can be made according to the voiding method.

Conflicts of Interest

The authors have nothing to disclose.

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