Original Article

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Clinical Data of Urine Culture and Antimicrobial Sensitivity Tests according to the Voiding Method over 15 Years in Patients with Spinal Cord Injury

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Purpose: To analyze the results of urine cultures and antimicrobial sensitivity tests according to the voiding methods in patients with spinal cord injury (SCI) over a 15-year period.

Materials and Methods: A total of 1,579 urine culture samples, obtained from January 2000 to December 2014, for 73 SCI patients were analyzed according to the voiding method. We analyzed the following: positive urine culture rate, colony counts, isolated number of organism, major organisms, and antimicrobial sensitivity tests. The voiding methods were categorized into four methods: clean intermittent catheterization (CIC), suprapubic catheterization (SPC), urethral Foley catheter, and spontaneous voiding (SV).

Results: Among the 1,579 urine samples, 1,250 (79.2%) were positive. The CIC group showed the lowest rate of bacteriuria ($p<0.001$), colony counts ($p<0.001$), and polymicrobial infection ($p<0.001$). Causative organisms were mostly gram-negative bacteria (86.7%). *Pseudomonas aeruginosa* (22.7%) was most common pathogen followed by *Escherichia coli* (22.3%), *Klebsiella* species (9.5%), *Providencia* species (4.4%), and *Serratia marcescens* (4.2%). Major pathogens and antimicrobial sensitivity tests were different according to the voiding method.

Conclusions: CIC is the best voiding method to reduce urinary tract infection (UTI) in SCI patients. To treat UTI in in SCI patients, empirical antibiotics can be chosen according to the voiding method based on the reference of our study prior to the availability of antimicrobial sensitivity results.

Keywords: Bacteriuria; Spinal cord injuries; Urinary tract infections

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INTRODUCTION

Although recent medical advances have greatly enhanced the long-term survival for individuals with spinal cord injury (SCI), SCI patients suffer from many urological complications, like as urinary tract infection (UTI), urinary tract stones, hydronephrosis, and vesicoureteral reflux [1]. Most SCI patients have neurogenic lower urinary tract dysfunction. As a result of impaired storage and voiding function, patients often require catheters for bladder drainage; additionally, UTI occur frequently in this group of patients [2]. Furthermore, UTI is the leading cause for septicemia in patients with SCI, which is associated with a significant increase in morbidity and mortality [3]. Therefore, prevention and proper management of UTI in SCI patients are crucial.

The optimal method of bladder management for SCI patients remains controversial [4]. Many factors must be considered when electing a specific bladder management, including patient convenience, renal function preservation, and prevention of potential urological complications. Bladder management alternatives include clean intermittent catheterization (CIC), suprapubic catheterization (SPC), urethral Foley catheter (UF), and spontaneous voiding (SV).

As for using a catheter, catheter-associated UTI is often recurrent, and the bacterial strains are increasingly resistant to antibiotic treatment [5]. Moreover, the overuse and misuse of antimicrobial agents have contributed to increasing antibiotics resistance, making it even more difficult to choose an appropriate antibiotic.

We already reported the results of urine culture and antimicrobial sensitivity tests for SCI patients according to the voiding method over a period of 10 years [6]. In this study, we investigated the results of urine culture and antimicrobial sensitivity tests according to the method of bladder drainage used in SCI patients over the recent 15-year period.

MATERIALS AND METHODS

From January 2000 to December 2014, a retrospective chart review of 73 SCI patients was performed for analysis. Some patients had a change of voiding method as a result of an inevitable situation. To minimize the impact of voiding method for UTI, urine culture samples obtained when keeping just one voiding method over a period of 6 months were analyzed. The number of included urine culture samples in these patients was 1,646. Among these samples, the results of "multiple species" samples (n=67) were excluded as these were considered contaminated. Finally, a total of 1,579 urine samples were analyzed. These urine culture samples were classified into four groups according to the voiding method used when the samples were obtained: CIC (n=529), SPC (n=555), UF (n=322), and SV (n=173).

Urine samples were collected by aseptic catheterization or by using a clean catch technique for patients who were able to void spontaneously. In patients who kept the catheter, urine samples were collected by aseptically aspirating the clamped and disinfected catheter with a sterile syringe after a catheter change. All culture specimens were examined in the laboratory, and minimum isolation for the diagnosis of bacteriuria was 10^3 colony-forming units (CFU)/ml.

Antimicrobial sensitivity for cultured organisms was analyzed, and the results were stratified according to the voiding method. The antibiotics analyzed in our study were as follows: penicillin, ampicillin, augmentin, cefazolin, cefoxitin, cefotetan, cefuroxime, ceftazidime, ceftriaxone, cefepime, ofloxacin, ciprofloxaxin, levofloxacin, gentamycin, tobramycin, amikacin, piperacillin, piperacillin/tazobactam, imipenem, meropenem, ertapenem, teicoplanin, vancomycin, trimethoprim-sulfamethoxazole, and tetracycline.

Chi-square test (with Fisher's exact test) was used for statistical analysis by PASW Statistics ver. 18.0 (IBM Co., Armonk, NY, USA). A p-value of <0.05 was considered to be statistically significant.

RESULTS

1. Results of Urine Cultures

1) Positive urine culture

Among the 1,579 urine culture samples, 1,250 (79.2%) showed a positive result. In the CIC group, 383 (72.4%) urine samples were positive, which was significantly lower than in the other groups ($p<0.001$; Table 1).

2) Colony counts

Table 2 showed the colony counts of the isolated bacteria. The CIC group had lower colony counts than the other groups ($p<0.001$).

3) Isolated number of organism

Of all (1,250) positive urine cultures, multiple organisms

Table 1. Positive urine cultures according to voiding method

Voiding method	Sterile cultures	Positive cultures	Total	p-value[a)]
Clean intermittent catheterization	146 (27.6)	383 (72.4)	529 (100)	<0.001
Suprapubic catheterization	82 (14.8)	473 (85.2)	555 (100)	
Urethral Foley catheter	64 (19.9)	258 (80.1)	322 (100)	
Spontaneous voiding	37 (21.4)	136 (78.6)	173 (100)	

Values are presented as number (%).
[a)]Analyzed by chi-square test.

Table 2. Colony counts of the positive urine cultures

Voiding method	Colony counts (CFU/ml)					p-value[a)]
	$10^3 \leq <10^4$	$10^4 \leq <10^5$	$10^5 \leq <10^6$	$\geq 10^6$	Total (%)	
Clean intermittent catheterization	2 (0.5)	32 (8.4)	182 (47.5)	167 (43.6)	383 (100)	<0.001
Suprapubic catheterization	0	34 (7.2)	192 (40.6)	247 (52.2)	473 (100)	
Urethral Foley catheter	0	25 (9.7)	118 (45.9)	115 (44.4)	258 (100)	
Spontaneous voiding	0	6 (4.4)	58 (43.0)	72 (52.6)	136 (100)	

Values are presented as number (%).
CFU: colony-forming units.
[a)]Analyzed by chi-square test.

Table 3. Isolates of urine cultures according to voiding method

Voiding method	Isolated number				p-value[a)]
	1	2	3	Total	
Clean intermittent catheterization	326 (85.1)	54 (14.1)	3 (0.8)	383 (100)	<0.001
Suprapubic catheterization	284 (60.0)	186 (39.3)	3 (0.6)	473 (100)	
Urethral Foley catheter	188 (72.9)	68 (26.4)	2 (0.8)	258 (100)	
Spontaneous voiding	106 (77.9)	27 (19.9)	3 (2.2)	136 (100)	

Values are presented as number (%).
[a)]Analyzed by chi-square test.

Table 4. Major causative organisms (top 1-10)

Causative organism	Voiding method				Total
	CIC	SPC	UF	SV	
Pseudomonas aeruginosa	45 (10.2)	210 (31.6)	69 (20.9)	41 (24.3)	365 (22.7)
Escherichia coli	146 (33.0)	90 (13.5)	81 (24.5)	42 (24.9)	359 (22.3)
Klebsiella species	71 (16.0)	45 (6.8)	23 (7.0)	14 (8.3)	153 (9.5)
Streptococcus species	36 (8.1)	60 (9.0)	15 (4.5)	14 (8.3)	125 (7.8)
Providencia species	14 (3.2)	40 (6.0)	7 (2.1)	10 (5.9)	71 (4.4)
Serratia marcescens	21 (4.7)	27 (4.1)	15 (4.5)	4 (2.4)	67 (4.2)
Citrobacter species	25 (5.6)	23 (3.5)	11 (3.3)	5 (3.0)	64 (4.0)
Staphylococcus species	24 (5.4)	16 (2.4)	6 (1.8)	10 (5.9)	56 (3.5)
Acinetobacter species	13 (2.9)	21 (3.2)	13 (3.9)	8 (4.7)	55 (3.4)
Morganella morganii	10 (2.3)	24 (3.7)	19 (5.8)	2 (1.2)	55 (3.4)
Proteus species	7 (1.6)	22 (3.3)	10 (3.0)	6 (3.6)	45 (2.8)

Values are presented as number (%).
CIC: clean intermittent catheterization, SPC: suprapubic catheterization, UF: urethral Foley catheter, SV: spontaneous voiding.

were identified in 346 (27.7%) urine samples. The CIC group show the lowest, polymicrobial infection rates (14.9%) with statistical significance ($p<0.001$; Table 3).

4) The major organisms in the urine samples

Most bacteriuria was caused by gram negative bacteria (86.7%). The two major gram negative bacteria were *Pseudomonas aeruginosa* (22.7%) and *Escherichia coli* (22.3%), followed by *Klebsiella* species (9.5%), *Providencia* species (4.4%), *Serratia marcescens* (4.2%), *Citrobacter* species (4.0%), *Acinetobacter* species (3.4%), *Morganella morganii* (3.4%), and *Proteus* species (2.8%). Gram positive organisms were isolated in 13.3%. *Streptococcus* species (7.8%) and *Staphylococcus* species (3.5%) were the two main organisms. In the CIC, UF, and SV groups, *E. coli* was the most common pathogen, and in the SPC group, *P. aeruginosa* was the most common pathogen (Table 4).

2. Results of Antimicrobial Sensitivity Tests

In the antimicrobial sensitivity tests, the most widely used quinolones, such as ciprofloxacin and levofloxacin, showed low (32.3-43.9%) sensitivity in all groups (Table 5).

Imipenem, meropenem, teicoplanin, and vancomycin showed very high (more than 90%) sensitivity in CIC, SPC, and SV groups; but relatively low (63.6-78.2%) sensitivity in the UF group. Other carbapenem series, like ertapenem,

Table 5. Results of antimicrobial sensitivity tests according to voiding method

Antibiotics	Voiding method			
	CIC	SPC	UF	SV
Penicillin	51.4	66.4	36.6	21.9
Ampicillin	10.4	9.8	7.4	12.4
Augmentin	52.3	43.8	44.0	44.6
Cefazolin	46.5	33.5	35.5	41.3
Cefoxitin	61.8	58.3	55.1	60.5
Cefotetan	59.3	39.0	69.7	72.7
Cefuroxime	32.5	18.4	30.8	47.1
Ceftazidime	64.9	60.6	60.6	76.7
Ceftriaxone	47.8	32.9	43.2	49.0
Cefepime	82.7	71.0	64.8	75.6
Ofloxacin	65.1	53.4	92.9	75.0
Ciprofloxacin	37.2	41.1	35.5	36.7
Levofloxacin	43.9	33.9	32.4	32.3
Gentamicin	59.8	56.4	50.1	46.2
Tobramycin	64.4	54.6	61.1	51.9
Amikacin	89.5	76.3	76.1	74.2
Piperacillin	35.7	47.8	33.2	42.8
Piperacillin/tazobactam	76.9	66.5	61.1	81.3
Imipenem	94.9	92.5	78.2	94.8
Meropenem	95.0	92.3	76.0	95.7
Ertapenem	100	97.9	98.1	100
Teicoplanin	100	93.5	63.6	100
Vancomycin	100	96.8	69.2	100
Trimethoprim-sulfamethoxazole	50.6	44.0	43.9	43.0
Tetracycline	30.2	31.6	42.7	32.7

Values are presented as a percentage.
CIC: clean intermittent catheterization, SPC: suprapubic catheterization, UF: urethral Foley catheter, SV: spontaneous voiding.

showed very high (more than 97%) sensitivity in all groups.

Other antibiotics with high sensitivity in each group, according to the test, were as follows. In the CIC group, Amikacin (89.5%), cefepime (82.7%), piperacillin/tazobactam (76.9%), ofloxacin (65.1%), ceftazidime (64.9%), tobramycin (64.4%), and cefoxitin (61.8%) showed high sensitivity. Amikacin (76.3%), cefepime (71.0%), piperacillin/tazobactam (66.5%), penicillin (66.4%), and ceftazidime (60.6%) had high sensitivity in the SPC group. In the UF group, ofloxacin (92.9%), Amikacin (76.1%), cefotetan (69.7%), piperacillin/tazobactam (61.1%), and ceftazidime (60.6%) showed high sensitivity. Piperacillin/tazobactam (81.3%), ceftazidime (76.7%), cefepime (75.6%), ofloxacin (75.0%), amikacin (74.2%), cefotetan (72.7%), and cefoxitin (60.5%) showed high sensitivity in the SV group.

DISCUSSION

Improvement in the management of neurogenic bladder has dramatically reduced the rate of death from urinary tract complications. Despite improved treatment however, urinary tract complications, especially UTI, are still ranked as the second leading cause of death in SCI patients [7].

Bacteriuria is almost universal in SCI patients, and is often an asymptomatic colonization. However, its recurrence is still prevalent throughout their lives with the potential to cause serious problems, such as pyelonephritis, bacteremia, calculi, and renal failure. With respect to SCI patients, the definition of 'significant bacteriuria' remains controversial; but in general, the definition provided by the National Institute on Disability and Rehabilitation Research (NIDRR) Consensus Statement has been accepted. This definition is as: (1) $\geq 10^2$ CFU/ml in CIC patients, (2) $\geq 10^4$ CFU/ml for clean void specimens from catheter-free males, and (3) any detectable concentration of uropathogens from indwelling catheters [8]. In our study, more than 10^3 CFU/ml of uropathogens were defined as bacteriuria; this limit is generally accepted in most Korean hospitals, and according to the definition provided by NIDRR, all of the positive urine culture results were considered as significant bacteriuria.

In our study, the rate of positive urine culture was 79.2%, and the lowerest positive urine culture rate was observed in the CIC group. These results are similar to other published studies. In a previous study analyzed 5 years ago in our hospital, we reported that the positive urine culture rate was 74.8%, and similarly, the lowest rate of bacteriuria was observed in the CIC group [6]. In another report by Dedeic-Ljubovic and Hukic [9], 87.3% of the samples had positive urine culture.

There are several published guidelines for the management of neurogenic bladder after SCI [10-13]. In most guidelines, CIC was considered to be ideal management or the 'gold standard' of neurogenic bladder only if the patient is willing and both physically and mentally able to perform the task or has caregivers who are able to provide assistance. These guidelines are based on considerable literature review showing that CIC is associated with relatively low risk of urologic complications [9,13,14]. Actually, CIC has been increasing in popularity with time. Cameron et al. [15] reported their experience in bladder management of SCI patients in United States from 1972 to 2005. They reported that the use of CIC has increased from 12.6% in 1972 to a peak of 56.2% in 1991. Compared with CIC, the use of an indwelling catheter (suprapubic or urethral) significantly increases the risk of renal failure, bladder and renal stones, urethral fistulas, strictures, erosions, and bladder cancer [16-18].

In our study, the CIC group showed advantageous with respect to all infection conditions, such as positive culture rates, colony counts, and polymicrobial infection.

For the proper treatment of UTI in SCI patients, identifying common causative organisms are important. There was a difference of pathogens between SCI patients and non-SCI patients. In uncomplicated UTI, *E. coli* (34.4-67.0%) was the most common pathogen, as shown in many studies, followed by *Enterococcus*, *P. aeruginosa*, *Enterobacter*, *Klebsiella* species, and *Staphylococcus* [19-21]. On the contrary, urea splitting bacteria—i.e., *P. aeruginosa*, *P. mirabilis*, *Enterococcus faecalis*, *Klebsiella* species, *Providencia* species, and *Morganella* species—are more common in most studies of UTI in patients with SCI or indwelling catheter [22-24]. In our study, urea splitting organisms were isolated in 57.9% of cultures, and the two major organisms were *P. aeruginosa* and *Klebsiella* species. Generally, UTI caused by urea- splitting bacteria is a more complicated condition and more difficult to treat due to their association with calculi. Moreover, such bacteria form ammonium hydroxide raises the urinary pH, thereby creating an unfavorable condition for most antimicrobials.

In the occurrence of UTI, appropriate antibiotic selection is critical. Antibiotic treatment should be initiated according to the results of microbiologic sensitivity testing. It is important to select an appropriate antibiotic for empirical treatment of UTI before obtaining the bacterial culture results. Our reports about antimicrobial sensitivity tests provide information regarding empirical treatment in SCI patients with UTI.

Prolonged or repeated exposure to antimicrobial agents and the consequent antibiotic pressure increase the risk of colonization and infection with multiresistant bacteria [25]. Moreover, the overuse and misuse of antibiotics have increased the resistance rates. Recently, fluoroquinolone resistance was emerging in gram-negative pathogens worldwide. In our study, ciprofloxacin and levofloxacin showed low (32.3-43.9%) sensitivity in all groups. Conversely, ofloxacin showed relatively high (53.4-92.9%) sensitivity than other quinolone series in our analysis.

In the report published in our institution 5 years ago, imipenem, meropenem, and vancomyin had very high (more than 90%) sensitivity in all voiding method groups [6]. However, this present study showed different results. Imipenem, meropenem, teicoplanin, and vancomycin showed very high (more than 90%) sensitivity in CIC, SPC, and SV groups; but in the UF group, they showed relatively low (63.6-78.2%) sensitivity. Because chronic indwelling of urethral catheter encourages more urologic complications, like as urethritis, epididymitis, and prostatitis, frequent use of antibiotics, like as imipenem, meropenem, teicoplanin, and vancomycin, has increased bacterial resistance in these patients recently. Ertapenem—a kind of carbapenem—had a relatively lower prescription rate than imipenem or meropenem, but showed very high (more than 97%) sensitivity in all groups in the present study.

There was a difference in antibiotics sensitivity among the groups according to the voiding method. Based on these results, the empirical antibiotics with high antimicrobial sensitivity can be selected. With this, we can expect an increase in the efficacy of treatment. Furthermore, an appropriate use of antibiotics can decrease the production of resistant bacteria.

There are several limitations to consider. First, due to the retrospective nature of this study, urine culture samples were not schedule for all patients. There was a tendency to perform urine studies when patients complained of urologic symptoms. However, this suggests that the collected urine samples most likely represented symptomatic UTI, making our results clinically more useful. Second, other factors that may influence UTI, like as vesicoureteral reflux, high intravesical pressure, urinary tract stones, previous antibiotics treatment, and interval of catheter change, were not analyzed in our study. Third, some patients have changed the voiding method due to inevitable situations, resulting in a possibility for partial bias. However, as we only analyzed the specimens from patients who persisted on using one voiding method for more than 6 months, the bias should be minimal.

CONCLUSIONS

Out study shows that CIC is perhaps the best voiding method for reducing bacteriuria in SCI patients. Most common organisms of urine culture in SCI patients with a follow-up of more than 15 years were *P. aeruginosa* in the SPC group, and *E. coli* in other groups. In antimicrobial sensitivity tests, ofloxacin had a higher rate of susceptibility than other fluoroquinolones, such as ciprofloxacin and levofloxacin, in all groups. Especially, ofloxacin was susceptible in 92.9% of the UF group. Ertapenem also had a higher rate of susceptibility than other carbapenems, such as imipenem and meropenem, in all groups. Recently, antimicrobial resistance for imipenem, meropenem, vancomycin, and teicoplanin in the UF group has gradually increased; thus, according to our results, it is reasonable to select ofloxacin or ertapenem as an empirical antibiotic therapy for this group.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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