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Bacteriuria in Spinal Cord Injured Patients with Neurogenic Bladder Dysfunction

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ABSTRACT

The occurrence of bacteriuria in spinal cord injured patients with neurogenic bladder dysfunction who used clean intermittent catheterisation to empty their bladders was studied in order to examine cut-off concentration breakpoints for significant bacteriuria in this group of patients using procedures of the European Urinanalysis Guideline.

344 samples were cultured, yielding 285 isolates. Coagulase-negative staphylococci (27 %), Enterococci (25 %), *Klebsiella* spp (19 %), and Escherichia coli (12 %) were the most common findings. Bacteria grew at concentrations of 10^5–10^8 cfu/L, but only a few at 10^4 cfu/L.

It is concluded that low bacterial concentrations in the urine (10^5 cfu/L) of patients with neurogenic bladder dysfunction who are on intermittent catheterisation might be as significant for bladder contamination with bacteria as a high bacterial concentration and can possibly be responsible for bladder infections.

INTRODUCTION

Patients with neurogenic bladder dysfunction are often unable to empty their bladders sufficiently. If this condition is left untreated, urinary tract infection is unavoidable, with potentially lethal consequences. The use of indwelling urinary catheters makes it possible to empty the bladder, but the risk for complicating urinary tract infections (UTI) is still high (1). Following the introduction of intermittent catheterisation with sterile technique, the prognosis for these patients improved (2). Lapides et al. (3) showed that non-sterile, clean catheterisation is a safe way to maintain sterile urine and decrease the risk for urinary tract infection (UTI). Since then, several studies have indicated that clean intermittent catheterisation is a safe and effective means of managing neurogenic bladder dysfunction and to decrease the risk for renal complications (1, 4–7).

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Usually, UTI is associated with clear symptoms. Persons with spinal cord injuries, however, often have subtle symptoms which may not be recognized as being related to UTI (8). In otherwise healthy persons with symptomatic UTI a significant bacteruria of *Escherichia coli* or *Staphylococcus saprophyticus* is 10^6 cfu/L (10^3 cfu/mL) and a higher bacterial concentration when other species are isolated (9). In order to establish breakpoints for significant bacteruria for persons with neurogenic bladder due to spinal cord injury on intermittent catheterisation, Gribble et al. compared cultures of samples obtained through suprapubic aspiration with those obtained through intermittent catheterisation at the same time (10). They reported a strong correlation between the presence of bacteria in urine obtained via suprapubic aspiration and via intermittent catheterisation (10). In their study they suggested that 10^5 cfu/L should be used as a diagnostic cut-off for significant bacteriuria in samples obtained through intermittent catheterisation for this group of patients. Accordingly, for persons with spinal cord injuries and neurogenic bladder dysfunction a National Institute on Disability and Rehabilitation Research Consensus Statement recommended a criterion for significant bacteriuria of at least 10^5 cfu/L for most clinical, epidemiological and research purposes (11). To our knowledge, however, no study since then has been published in which this criterion has been used to validate the suggested cut-off in a clinical study of neurogenic bladder dysfunction and to relate the usefulness of the reported cut-off to published guidelines used in urinary tract infection diagnostics (11, 12).

This study investigated the prevalence of bacteriuria in spinal cord injured patients with neurogenic bladder dysfunction at the neuro-rehabilitation clinic at Linköping University Hospital who were practising clean intermittent catheterisation. The aim was to examine cut-off concentration breakpoints for significant bacteriuria in this group of patients using the procedures suggested by the European Urinanalysis Guidelines in order provide a platform for further studies of the clinical importance of bacteriuria in this group of patients (9).

MATERIAL AND METHODS

Patients

The study took place at the rehabilitation clinic at the University Hospital in Linköping, Sweden. Twenty patients (16 males and 4 females) with complete or partial spinal cord lesions causing neurogenic urinary bladder dysfunction were investigated regarding signs of bacteriuria. All patients drained their urinary bladder through clean intermittent catheterisation (CIC, n = 14) by themselves, or assisted by nursing personnel (assisted CIC; n = 6). Patients with a recent spinal injury were investigated in this study as soon as intermittent catheterisation was introduced. There were 9 inpatients and 11 outpatients. Since catheterisation was not done solely for the sake of the study, approval from the ethical committee was considered unnecessary. The patients, who had given their informed consent, were questioned regarding the presence of dysuria, a burning sensation, increased spasticity, diffuse

pain, general discomfort, a feverish feeling, sweating, headache, a foul smell, turbid urine, macroscopic haematuria, and incontinence.

Urinary samples were collected three times a week from the inpatients. Samples from the outpatients were collected when they visited the outpatient clinic, usually for scheduled follow-up or for some complication due to their injuries. Blood samples were not taken in this study.

Cultures

Urine was refrigerated after sampling and reached the laboratory within 24 h. The media were prepared from dehydrated powders. Upon receipt, 1 µL of urine was cultured on CLED (Cystein lactose electrolyte deficient) agar, 10 µL on aerobic horse blood agar, and 100 µL each on haematin agar and on anaerobic horse blood agar. All agarplates were incubated at 35°C for 48 h. Anaerobic blood agar plates were incubated anerobically, and the others were incubated in an atmosphere of 10% CO_2. A positive culture was defined as a maximum of three isolates at a urinary concentration of at least 10^4 cfu/L in accordance to the European Urinanalysis Guidelines. Counting of bacteria was done, to be accurate, on plates of aerobic horse blood agar, haematin agar and on anaerobic horse blood agar. Colonies in a positive culture were picked for identification. Other findings were considered irrelevant for the study and were thus not reported.

RESULTS

Three hundred and forty-four samples were cultured. Of these, 242 were considered positive and contained 285 isolates. Five cultures contained three isolates and 33 cultures contained two isolates. Seven cultures contained more than three species and were considered negative in this study.

Ninety-seven percent (96.8%) of all positive cultures grew in a urinary concentration of B10^5 cfu/L (Table 1).

The most frequent finding was coagulase negative staphylococci (27%), which was recovered at all concentrations, but mostly at 10^8 cfu/L. Klebsiella (19%) and Escherichia coli (12%) were recovered most frequently at 10^8 cfu/L. Enterococci (25%) was recovered most frequently at 10^7 cfu/L (Table 1) .

The presence of dysuria, a burning sensation, increased spasticity, diffuse pain, general discomfort, a feverish feeling, sweating, headache, a foul smell, turbid urine, macroscopic haematuria, and incontinence among the patients provided no useful information for grouping the patients (data not shown).

Distribution of bacterial species in different patient groups

The differences in bacterial distribution with respect to gender, care and catheterisation method were generally small (Table 2). However, Klebsiella was more common in inpatients, especially in those with assisted CIC.

Table 1. Bacterial species isolated from all patients in relation to their concentration in urine.

Isolate	Frequency, % (number, n) of all isolates	Frequency, %, at different concentrations [cfu/L]				
	Total (n)	10^8	10^7	10^6	10^5	10^4
Coagulase-negative staphylococci	26.7% (76)	11.6%	4.9%	4.6%	3.2%	2.5%
Enterococci	24.9% (71)	5.3%	7.0%	8.8%	3.2%	0.7%
Klebsiella spp.	18.6% (53)	9.1%	4.6%	4.2%	0.7%	
Escherichia coli	12.3% (35)	8.4%	1.8%	1.1%	1.1%	
Alpha-haemolytic streptococci	3.2% (9)	1.4%	0.4%	0.7%	0.7%	
Enterobacter spp.	2.8% (8)	2.5%	0.4%			
Streptococci group B	2.5% (7)			1.8%	0.7%	
Pseudomonas spp.	2.1% (6)	1.8%		0.4%		
Citrobacter spp.	1.8% (5)	1.4%		0.4%		
Lactobacilli	1.1% (3)	0.7%		0.4%		
Corynebacteria	0.7% (2)		0.7%			
Haemophilus spp.	0.7% (2)			0.4%	0.4%	
Other*	2.8% (8)	0.7%	0.4%	1.1%	0.7%	
Total	100.0% (285)	42.8%	20.0%	23.5%	10.5%	3.2%

* One isolate each of aerobic Gram positive cocci, *clostridium perfringens,* untyped coliform bacteria, non-haemolytic streptococci, non-fermenting gram-negative rods, *Proteus mirabilis, Staphylococcus aureus,* and *S. saprophyticus.*

Table 2. Frequencies of the four most common bacterial species in different group of patients.

		Voiding regime		Gender		Level of care	
	Culture positive patients, n (%)	assCIC (n=6)	CIC (n=14)	Female (n=4)*	Male (n=16)	Inpatients (n=9)	Outpatients (n=11)
Coagulase-negative staphylococci	76 (26.7%)**	21.4%**	30.4%	36.2%	24.2%	28.2%	24.1%
Enterococci	71 (24.9%)	31.6%	20.2%	6.9%	29.5%	25.4%	24.1%
Klebsiella	53 (18.6%)	29.9%	10.7%	8.6%	21.1%	25.4%	7.4%
E. coli	35 (12.3%)	11.1%	13.1%	17.2%	11.0%	11.3%	13.9%

* All CIC, one inpatient. ** The frequency is given as the percentage of the total number of findings in each group (column).

Distribution of bacterial concentrations in different patient groups

A bacterial concentration in urine of 10^6–10^7 cfu/L was more common in samples from males, and 10^8 cfu/L was more common in samples from female patients. There were no differences with respect to voiding regime or level of care.

Table 3. Bacterial concentrations in urine from inpatients on intermittent catheterisation.

Patient	Total number of findings	Number of cultures containing different bacterial concentrations [cfu/L]					
		Negative culture	10^4	10^5	10^6	10^7	10^8
A	2	2					
B	39	7	2	4	4	3	19
C	38	21	1	4	6	3	3
D	35	8		2	7	2	16
E	14	8		1	1		4
F	4	2					2
G	8	2	1	1	2		2
H	70	10	1	5	14	24	16
I	42	15	2	2	6	5	12
Total	252	75	7	19	40	37	74

Table 4. Urine isolates from inpatients on intermittent catheterisation.

Patient	Total isolates	Coagulase-negative staphylococci	Enterococci	*Klebsiella* spp.	*E. coli*	*Pseudomonas* spp.	*Citrobacter* spp.	Alfastreptococci	Anaerobic Gram positive cocci	*C. perfringens*	*Enterobacter* spp.	Gamma haemolytic streptococci	Lactobacilli	*S. aureus*
A	0													
B	32	18	1	1	2	1	4	2	1	1			1	
C	17	3	5	4	4									1
D	27	7	10	9								1		
E	6		1		5									
F	2			2										
G	6	2	2		2									
H	60	2	21	26	6	4					1			
I	27	18	5	3	1									
Total	177	50	45	45	20	5	4	2	1	1	1	1	1	1

Distribution over time for inpatients

Two hundred and twenty-nine samples from nine inpatients were sent to the laboratory. Of these, 75 were negative (Table 3). Seven cultures grew at a bacterial concentration of 10^4 cfu/L, 19 at 10^5 cfu/L, 40 at 10^6 cfu/L, 37 at (10^7 cfu/L), and 74 at 10^8 cfu/L (Table 3).

Coagulase negative staphylococci, enterococci, *Klebsiella, E.coli,* and P. aeruginosa were all found in at least two patients (Table 4). Citrobacter was found four

times in one patient and was otherwise an occasional finding. In patient B, coagulase negative staphylococci were found twelve times in a row. Coagulase-negative staphylococci were repeatedly found in patient D.

DISCUSSION

In this study 73% of the samples from patients using clean intermittent catheterisation contained bacteria at a concentration of 10^4 cfu/L. If 10^8 cfu/L was used as a criterion for bacteriuria, 31% of the samples were positive. Neither bacteriuria at concentrations of 10^4 and 10^8 cfu/mL nor growth of any particular bacterial species, was correlated with particular symptoms or physical and biochemical laboratory findings. This study can therefore provide a starting point for further clinical studies on the relationship between bacteriuria and UTI in the practice of CIC using the well defined European Urinanalysis Guidelines recommendations for laboratory identification of urinary tract infections.

In order to diagnose urinary tract infections in patients with spinal cord injuries and neurogenic bladder dysfunction, of use of urine culture with proper cut-off breakpoints for significant bacteruria is particularly important. In our study urine was cultured quantitatively in order to detect bacteriuria to allow counts from B10^8 cfu/L to 10^4 cfu/L. This was necessary, since bacterial growth was found even at 10^4 cfu/L; (Table 1) The four most found species were found at a concentration down to 10^5 cfu/L or lower (Table 1). Gribble et al. cultured urine using pour-plate technique to allow counts from 10^{11} cfu/L to 10^4 cfu/L (10). They showed that the bacterial content in suprapubic urine aspirate was similar to that in urine immediately following catheterisation(10). A practical criterion for significant bacteriuria when samples were taken through intermittent catheterisation was defined as 10^5 cfu/L This breakpoint had a high sensitivity and specificity in relation to cultures after suprapubic aspiration. They stated that culture of urine obtained with intermittent catheterisation was a reliable method for detection of low bacterial concentrations in the bladder. Significant bacteriuria is defined by Hooton (13) as the quantity of uropathogens in urine that reliably distinguishes bladder bacteriuria, but not necessarily infection, from contamination. This concept is also useful and applicable regarding spinal cord injured patients with neurogenic bladder dysfunction, since the sensitivity and specificity of symptoms and signs for detecting UTI, including pyuria is poor in patients with spinal cored injuries (8). This is in agreement with our findings, where urine dip sticks for nitrate and leukocyte esterase were inconclusive (data not shown).

Using their data, Gribble *et al.* suggested that 10^5 cfu/L was a reliable breakpoint, with high sensitivity and specificity for significant bacteriuria in persons on intermittent catheterization (10). In a Consensus Statement by the National Institute on Disability and Rehabilitation Research (11), it was stated that the criterion for bacteriuria in people with spinal cord injuries who use intermittent catheterisation should be B10^5 cfu/L, and that the traditional criterion (Kass criterion) of B10^8 cfu/L has an unacceptably low sensitivity when used for clinical and research purposes

among in people with spinal cord injuries who use intermittent catheterisation. In some later studies, the bacterial concentrations used to indicate significant bacteriuria are higher than 10^5 cfu/L or else information is lacking making direct comparison of data difficult (6, 14–17) We find our results to be in agreement with those obtained by Gribble *et al.* (10)

The four most common categories of bacteria isolated in this study were coagulase negative staphylococci, enterococci, *Klebsiella*, and *Escherichia coli.* The bacteria found in this study do not differ from those in other studies, although the frequencies of the categories differ. Coagulase-negative staphylococci were, as in the study by Gribble *et al.* (10) quite frequent, and *E. coli* were less frequent than in some reports (6, 8, 14, 18). *Klebsiella* and *Pseudomonas* were the most frequently isolated species in the study by Perkash and Giroux (6). The different patterns of species between the studies probably reflect differences in the hospital flora. The variety of findings in published articles show that the mechanisms of urinary tract infections we are familiar with in patients with undisturbed bladder voiding (20) do not apply in persons with spinal cord injuries who are on intermittent catheterisation. Due to the disturbed urodynamics in the neurogenic bladder, these colonising bacteria may more easily infect the urinary tract. There is, of course, a risk that during catheterisation the genito-urethral flora contaminates the urine used for culture, thus giving a false positive culture. However, the results reported by Gribble *et al.* (10) show that this risk is small since the suprapubic aspiration was made before the intermittent catheterisation and the cultures of the paired samples often yielded the same results.

In the inpatients, as shown in Table 4, coagulase-negative staphylococci were very frequent findings in two patients, suggesting that these strains had heavily colonised the urinary tracts of these patients. Most of the isolates were found at urinary concentrations down to 10^5 cfu/L (Table 3).

The lack of symptoms and physical and biochemical laboratory findings make the diagnosis of urinary tract infection quite difficult in spinal cord injured persons with neurogenic bladder dysfunction. The results reported by Gribble (10) show that a finding of at least 10^5 cfu/L is a significant bacteriuria. There are in this group of persons no simple signs to determine when bacteriuria becomes an infection(19). In our study there were no clear differences in bacterial numbers between those bacteria often found in urinary tract infections and those regarded as genito-urethral flora in persons with normal bladder function. Our results are thus a validation and extension of the findings of Gribbles *et al.* The results show that a low bacterial concentration in the urine of patients with neurogenic bladder dysfunction who are on intermittent catheterisation might, even if the bacteria are of urethral origin, be as significant for bladder contamination with bacteria as a high bacterial concentration and thus can possibly be responsible for bladder infections.

REFERENCES

1. Wyndaele JJ, De Sy WA, Claessens H. Evaluation of different methods of bladder drainage used in the early care of spinal cord injury patients. Paraplegia 1985;23(1):18–26.

2. Guttmann L, Frankel H. The value of intermittent catheterisation in the early management of traumatic paraplegia and tetraplegia. Paraplegia 1966;4(2):63–84.
3. Lapides J, Diokno AC, Silber SJ, Lowe BS. Clean, intermittent self-catheterization in the treatment of urinary tract disease. J Urol 1972;107(3):458–61.
4. McGuire EJ, Savastano JA. Long-term followup of spinal cord injury patients managed by intermittent catheterization. J Urol 1983;129(4):775–6.
5. Pearman JW. Urological follow-up of 99 spinal cord injured patients initially managed by intermittent catheterisation. Br J Urol 1976;48(5):297–310.
6. Perkash I, Giroux J. Clean intermittent catheterization in spinal cord injury patients: a followup study. J Urol 1993;149(5):1068–71.
7. Wyndaele JJ, Maes D. Clean intermittent self-catheterization: a 12-year followup. J Urol 1990; 143(5):906–8.
8. Cardenas DD, Hooton TM. Urinary tract infection in persons with spinal cord injury. Arch Phys Med Rehabil 1995;76(3):272–80.
9. Kouri TT, Gant VA, Fogazzi GB, Hofmann W, Hallander HO, Guder WG. European urinary guidelines. Scand J Clin Lab Invest 2000;60(Suppl. 231):1–96.
10. Gribble MJ, McCallum NM, Schechter MT. Evaluation of diagnostic criteria for bacteriuria in acutely spinal cord injured patients undergoing intermittent catheterization. Diagn Microbiol Infect Dis 1988;9(4):197–206.
11. The prevention and management of urinary tract infections among people with spinal cord injuries. National Institute on Disability and Rehabilitation Research Consensus Statement. January 27-29, 1992. J Am Paraplegia Soc 1992;15(3):194–204.
12. Clarridge JE, Pezzlo MT, Vosti KL. Laboratory Diagnosis of Urinary Tract Infections. In: Weissfeld AS, editor. Cumulative Techniques and Procedures in Clinical Microbiology. Washington DC: American Society for Microbiology; 1987.
13. Hooton TM. The epidemiology of urinary tract infection and the concept of significant bacteriuria. Infection 1990;18(Suppl 2):S40–3.
14. Bakke A, Digranes A. Bacteriuria in patients treated with clean intermittent catheterization. Scand J Infect Dis 1991;23(5):577–82.
15. Bakke A, Digranes A, Hoisaeter PA. Physical predictors of infection in patients treated with clean intermittent catheterization: a prospective 7-year study. Br J Urol 1997;79(1):85–90.
16. Hellström P, Tammela T, Lukkarinen O, Kontturi M. Efficacy and safety of clean intermittent catheterization in adults. Eur Urol 1991;20(2):117–21.
17. Kuhn W, Rist M, Zaech GA. Intermittent urethral self-catheterisation: long term results (bacteriological evolution, continence, acceptance, complications). Paraplegia 1991;29(4):222–32.
18. Stover SL, Miller JMd, Nepomuceno CS. Intermittent catheterization in patients previously on indwelling catheter drainage. Arch Phys Med Rehabil 1973;54(1):25–30.
19. Gribble MJ, Puterman ML, McCallum NM. Pyuria: its relationship to bacteriuria in spinal cord injured patients on intermittent catheterization. Arch Phys Med Rehabil 1989;70(5):376–9.
20. Mulvey MA, Schilling JD, Martinez JJ, Hultgren SJ. Bad bugs and beleaguered bladders: interplay between uropathogenic Escherichia coli and innate host defenses. Proc Natl Acad Sci U S A 2000;97(16):8829–35.

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