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Bacteriology

The clinical significance of isolation of two different organisms from the urine of patients with an indwelling catheter

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ABSTRACT

Background: We evaluated the clinical significance of urine cultures from patients with an indwelling urinary catheter (UC) from which 2 different pathogens were isolated.
Methods: Urine cultures from patients with a UC from which 2 different organisms were isolated were randomly divided into a control group (culture results were reported as usual) and a study group (culture results were reported as "mixed growth"). Endpoints included change in antibiotic treatment, use of broad spectrum agents, time for clinical improvement, and duration of admission.
Results: A total of 81 cultures met the inclusion criteria. Antibiotic treatment was changed after 72–96 h in 19 (48%) study patients and in 25 (61%) controls (NS). There was no difference regarding narrowing or broadening of antibiotic spectrum, and duration of hospitalization was similar. In each group, 15 (36%) patients died.
Conclusion: Our findings imply that laboratory work-up of 2 pathogens from patients with an indwelling catheter may be discarded.

1. Introduction

Urinary tract infections are a common cause for hospital admissions (Gupta and Trautner, 2012). Determination of quantity and identification of bacteria in the urine are time-honored diagnostic tools, and antimicrobial susceptibility testing is important for adjusting empiric treatment. Pre-therapy cultures and susceptibility testing are essential especially in patients with a permanent indwelling urinary catheter (UC), due to the variety of pathogens that may be involved (Raveh et al., 2003, 2006). Bacteriuria develops in almost all patients catheterized for more than 1 month, but is usually without clinical or laboratory signs of infection (Nicolle, 2001; Tambyah and Maki, 2000a). Catheter-associated urinary tract infection (CAUTI (is suspected when symptoms such as fever, lower abdominal or flank pain, decreased consciousness, or delirium appear (Garner et al., 1988; Kunin, 2006; Tambyah and Maki, 2000b; Tenke et al., 2008). Only a minority of patients with CAUTI will develop symptoms of sepsis with associated bacteremia (Tambyah and Maki, 2000a), and CAUTIs are not associated with increased mortality (Warren, 2001).

CAUTI is likely when urine cultures grow $\geq 10^5$ bacteria of a single species per milliliter (Garner et al., 1988; Schreckenberger, 2001). The clinical significance of isolation of more than 1 species is not clear; whether multiple different bacteria in urine culture is associated with asymptomatic bacteriuria or clinical infection is unknown (Garner et al., 1988; Tenke et al., 2008). Covering each of different bacteria in case of polymicrobial growth inevitably leads to use of broader spectrum antimicrobial agents, which may precipitate *Clostridium difficile*–associated colitis, development of multidrug-resistant bacteria (Bahagon et al., 2007; Cope et al., 2009; Friedmann et al., 2003; Milan and Ivan, 2009; Raveh et al., 2003, 2006), and increased expense.

Urine cultures from which 2 different organisms were isolated are currently fully processed in the microbiology laboratory—with identification of each pathogen and determination of susceptibilities for each one separately. When 3 or more organisms are isolated in urine culture, identification and sensitivity are not done, and the culture is reported as mixed growth with no further workup. Identification of each organism and susceptibility testing consume laboratory time and effort, and are expensive. The purpose of the current study was to evaluate the clinical significance of urine cultures

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from patients with an indwelling UC from which 2 different pathogens were isolated.

2. Methods

Shaare Zedek Medical Center is a 750-bed university-affiliated general hospital in Jerusalem, Israel. The clinical microbiology department accepts annually 4000–4500 urine cultures from patients with an indwelling catheter. In a prospective possibility survey carried out during 11 working days, 301 urine cultures from patients with an indwelling catheter were processed in the microbiology laboratory. Of these urine cultures, 70% were found sterile, 18% contained 1 species of organism, 7% contained 2 different pathogens, and 6% had 3 or more pathogens.

We conducted a prospective, randomized, and controlled study over a 6-month period. Included were all consecutive urine cultures from adult patients (≥18 years old) with a UC from which 2 different organisms were isolated. The patients were randomly divided into a control group (their culture results, pathogen identification, and susceptibilities were reported as usual) and a study group (their culture results were reported as mixed growth, without identification and susceptibility report). The physicians were blinded to the study groups. In order to ensure safety of participants, we excluded patients with positive blood cultures (obtained between 48 h prior to and till 24 h after the index urine culture) or with a systemic inflammatory response syndrome (SIRS) (Rangel-Frausto et al., 1995) unless their simultaneous blood cultures were negative.

2.1. Microbiological intervention

Included in the study were urine cultures obtained from patients with an indwelling UC with growth of 2 different pathogens, each one of which was $\geq 10^4$ CFU/mL. All urine cultures were processed routinely, with determination of identification and sensitivity of the 2 pathogens. At the completion of laboratory work, cultures were randomized. The difference between the study group and the control group was the final report of the culture to the physicians: either "mixed growth, consider sending a new culture according to clinical relevance" in the study group or the usual report of pathogens and susceptibility testing in the control group. Sterile urine cultures or cultures with growth of 1, 3, or more pathogens were excluded from this study.

The primary endpoints were the change in prescription of antibiotic treatment 72–96 h after urine culture was obtained (this being the time interval after which culture results could be expected to impact on antibiotic usage) and use of broad-spectrum antibiotic regimens including amikacin, colistin, carbapenems, and piperacillin–tazobactam. Secondary endpoints included clinical measures of time to defervescence, resolution of leukocytosis, and length of hospital stay from the day of index urine culture to discharge. Demographic, clinical, and laboratory data were collected for each patient, including records regarding antibiotic treatment, duration, and outcome of hospitalization. The conduct of the study was approved by the hospital's institutional review board.

2.2. Statistical analysis

Sample size was estimated based on the expected difference in antibiotic use between the study and control groups. We assumed a 60% change in antibiotic therapy in the control group and only a 30% change in antibiotic use prescribed in the study group (in which the attending physicians would receive a note of "mixed growth"). At least 60 cultures (30 in each study group) were required to detect a statistically significant difference with a power of 80%. Proportions were compared using Fisher's exact test, and continuous variables were compared by Student's *t* test or the Mann–Whitney test. A *P* value of <0.05 was considered statistically significant.

3. Results

During the 6-month study, 81 consecutive urine cultures met the inclusion criteria. Baseline demographic, clinical, and laboratory data of the patients are depicted in Table 1. The study population consisted mainly of elderly patients, of whom 38% lived in nursing homes, 90% were disabled, and 58% suffered from dementia. There was a (statistically insignificant) greater use of latex UC as opposed to silicone UC in the study group. Only a minority of patients in both groups had symptoms characteristic of urinary tract infection. Approximately half of the cultures were taken more than 48 h after admission to hospital. No significant differences regarding baseline characteristics were found between the 2 groups.

The total number of isolates was 80 for the study group and 82 for the control group. The most frequently isolated organisms in the study and control group were Enterobacteriaceae (57/80 [71%] versus 53/82 [64%], respectively, NS), *Pseudomonas* sp. (11 [14%] versus 13 [16%], NS), *Enterococcus* sp. (6 [7.5%] versus 7 [9%], NS), and *Candida* sp. (2 [2.5%] versus 6 [7%], NS) (Table 2). In the study and control group, 22 (63%) and 16 (48%) of the Enterobacteriaceae, respectively, were extended spectrum β-lactamase producers (NS). The frequency of combinations of pathogens in urine cultures is shown in Table 3, with no significant differences between the groups.

Antibiotic treatment was prescribed on the day the culture was obtained for 22 (55%) study patients and for 30 (73%) control patients (NS). Seventy-two to 96 h after cultures were obtained, at the time culture results could be expected to influence prescribing, no significant differences were found between the 2 groups in the rate of antibiotic change and spectrum of antibiotic therapy.

Table 1
Demographic data and clinical and laboratory baseline characteristics of patients in the study and control groups.

Variable	Study group, $n = 40$ (%)	Control group, $n = 41$ (%)	*P* value
Female gender	23 (57)	25 (61)	NS
Mean age (years) ± SD	80 ± 11	79 ± 12	NS
Nursing home residence	17 (42.5)	14 (34)	NS
Performance status[a]			
Independent	3 (8)	5 (12)	NS
Disabled	37 (92)	36 (88)	NS
Comorbidities			
Diabetes mellitus	13 (33)	20 (49)	NS
Renal failure	15 (37)	15 (37)	NS
Dementia	25 (62)	22 (54)	NS
Decubitus ulcers	15 (37)	11 (27)	NS
Indwelling time of UC (days, mean ± SD)	111 ± 179	76 ± 120	NS
UC type			NS
Latex	36 (90)	30 (73)	
Silicon	0	8 (20)	
Unknown	4 (10)	3 (7)	
Symptoms of UTI[b]			NS
Present	2 (5)	3 (7)	
Not present	21 (52)	19 (46)	
Unknown	17 (42)	19 (46)	
Minimal systolic BP (mmHg, mean ± SD)[b]	119 ± 20	115 ± 20	NS
Maximal temperature (°C, mean ± SD)[b]	37.3 ± 0.8	37.8 ± 0.9	NS
WBC (10^3/μL, mean ± SD)[b]	12.1 ± 5.2	13.2 ± 6.6	NS
Creatinine (mg/dL, mean ± SD)[b]	1.4 ± 1.2	1.4 ± 1.2	NS
Culture obtained >48 h after admission	23 (58)	20 (49)	NS
Duration of hospital stay (days, mean ± SD)[b]	16 ± 21	21 ± 37	NS

UC = Urinary catheter; UTI = urinary tract infection; BP = blood pressure; WBC = white blood cell count.
[a] Prior to admission.
[b] On the day the index culture was obtained.