MAJOR ARTICLE

Inappropriate Treatment of Catheter-Associated Asymptomatic Bacteriuria in a Tertiary Care Hospital

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(See the editorial commentary by Kunin on pages 1189–90)

Background. Evidence-based guidelines state that asymptomatic bacteriuria is not a clinically significant condition in men and nonpregnant women and that treatment is unlikely to confer clinical benefit. We hypothesized that, among patients with indwelling catheters or condom collection systems, many who receive a diagnosis of and are treated for catheter-associated urinary tract infection (CAUTI) actually have asymptomatic bacteriuria and, therefore, that antibiotic therapy is inappropriate.

Methods. We reviewed all urine culture results at a veterans affairs medical center during a 3-month period. Cultures yielding $\geq 10^4$ colony-forming units/mL were included if the urine had been collected from a hospitalized patient with an indwelling (Foley) catheter or a condom collection system. We applied standardized definitions to determine whether the episode represented catheter-associated asymptomatic bacteriuria (CAABU) or CAUTI. Antibiotic therapy was considered appropriate for patients who met criteria for symptomatic UTI.

Results. Overall, 280 episodes met criteria for inclusion: 164 CAABU and 116 CAUTI. Of the 164 episodes of CAABU, 111 (68%) were managed appropriately (no treatment), whereas 53 (32%) were treated with antibiotics (inappropriate treatment). In multivariate analysis, older patient age, having predominantly gram-negative bacteriuria, and higher urine white blood cell count were significantly associated with inappropriate treatment of CAABU ($P < .05$, by logistic regression).

Conclusions. Better recognition of CAABU and the distinction between this condition and CAUTI, consistent with evidence-based guidelines, may play a key role in reducing unneeded antibiotic usage in hospitalized patients.

Approximately 560,000 catheter-associated urinary tract infections (CAUTIs) are reported to the Centers for Disease Control and Prevention (CDC) each year [1]. In 2002, the annual incremental costs attributed to nosocomial CAUTI were estimated to exceed $451 million [2]. New regulations that went into effect in October 2008 state that Medicare will no longer reimburse hospitals for costs associated with certain nosocomial infections, including CAUTI [1]. As a consequence, hospitals and health care providers have a substantial financial incentive to reduce rates of nosocomially acquired CAUTI.

CAUTI arises through bacterial entry into the urinary tract via the urinary catheter. Formation of a biofilm on the urinary catheter perpetuates the bacterial presence in the urinary tract [3]. Persons with a catheterized urinary tract acquire bacteriuria at the rate of ~3%–10% per day [4, 5]. However, in the majority of cases, no symptoms result, and secondary complications such as bacteremia are rare [6]. Thus, the majority of cases of CAUTI indicate unrecognized or subclinical infection. Confusion exists on this point in the literature, because most studies of prevention of CAUTI use bacteriuria, both symptomatic and asymptomatic, as the outcome measure and as a surrogate marker for UTI [7]. The CDC definitions for nosocomial infections illustrate this point [8]. Although CDC definitions distinguish between symptomatic UTI and asymptomatic

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bacteriuria, they are both coded as "UTI," the former as UTI-SUTI and the latter as UTI-ASB.

Because treatment of asymptomatic bacteriuria in adults is generally unlikely to confer clinical benefit, antibiotics are recommended only for pregnant women and for individuals who are about to undergo urological procedures [9]. Indeed, treatment of asymptomatic bacteriuria in diabetic women was found to incur harm, because the treated group had a higher incidence of adverse antimicrobial reactions yet had the same incidence of symptomatic UTI as did the untreated group [10]. The presence of asymptomatic candiduria is, likewise, not an indication for antifungal therapy [11]. The case for nontreatment of catheter-associated bacteriuria or funguria is particularly strong in persons who require long-term indwelling urinary catheters, because nearly all such individuals are infected with multiple species [12]. Antimicrobial treatment of such patients fails to eradicate the catheter-associated biofilm and facilitates the emergence of antimicrobial-resistant flora [13, 14]. Avoidance of unnecessary antibiotic use in the hospital setting is particularly relevant given the current epidemic of nosocomially acquired *Clostridium difficile* colitis [15].

Our clinical experience suggested that, in many instances of CAUTI, treatment is given inappropriately (because the condition is asymptomatic) for a condition that we have termed "catheter-associated asymptomatic bacteriuria" (CAABU). The present study was designed to demonstrate the extent of the problem that results from the failure of clinicians to distinguish between CAABU and CAUTI.

METHODS

The purpose of our study was to study the current management of catheter-associated bacteriuria in our tertiary care, academic teaching hospital. The unit of analysis for this study was an episode of bacteriuria, regardless of whether the bacteriuria arose from symptomatic CAUTI, CAABU, or possibly contamination of the specimen. For practical reasons, we use the term "bacteriuria" throughout to connote the presence of cultivatable microorganisms in the urine, either bacterial or fungal.

Patients

Case patients were identified by reviewing all urine culture results reported by the microbiology laboratory at Michael E. DeBakey Veterans Affairs Medical Center (Houston, Texas), from 1 July 2007 to 30 September 2007. A positive result of urine culture was defined as the presence of $\geqslant 10^4$ cfu/mL of any bacterium or yeast. The medical records of individuals with positive urine cultures during the study period were carefully reviewed by one of us (M.C.). To be included in the study, the individual had to have been an inpatient or in the process of admission when the urine was collected, so that the culture result, when reported, was for a hospitalized patient. The urine had to have been collected from a patient who had either a transurethral indwelling (Foley) catheter or an external (condom) collection system in place for $\geqslant$24 h during the preceding 7 days. Patients were excluded if they had a suprapubic catheter, were practicing intermittent catheterization without use of an external catheter, or had undergone urinary diversion surgery with creation of a urinary stoma. Patients who died or were discharged from the hospital between the time the culture specimen was obtained and the time the culture results were available were also excluded. Finally, we excluded patients who were being treated with an antibiotic for UTI at the time of hospital admission. Data captured by chart review included age and sex of the patient, temperature, duration of catheter use, catheter type, hospital ward or service, types and quantities of organisms found in the urine, reason for treatment of bacteriuria (if stated in the medical record), antibiotics given, duration of treatment, and outcomes of therapy. Quantitative data on WBC counts in urine were obtained from automated readings that are reported as cells per high-power field (hpf) but are not, in fact, read microscopically.

Definitions

Infection. To define nosocomial CAUTI, we used modified CDC criteria [8] that distinguish between symptomatic infection and asymptomatic bacteriuria on the basis of the presence or absence of symptoms. Specifically, we defined a UTI as the presence of $\geqslant$1 of the following signs and symptoms with no other recognized cause: fever (temperature, $\geqslant$37.8°C), urgency, frequency, dysuria, suprapubic tenderness, altered mental status, or hypotension in a patient who had a positive urine culture ($\geqslant 10^4$ cfu/mL). We omitted the provision that no more than 2 species of microorganisms could be present, because we were not trying to distinguish between true bacteriuria and contamination of the urine sample; our interest was in whether the perceived bacteriuria was treated. We defined CAABU as occurring when the patient had a positive urine culture ($\geqslant 10^4$ cfu/mL) but did not have any of the symptoms or signs that would lead to classification of having a CAUTI (unless these signs or symptoms had another obvious cause), again omitting the requirement that no more than 2 species of microorganisms could be present. Our other noteworthy modification was that we used a cutoff of $\geqslant 10^4$ instead of $\geqslant 10^5$ cfu/mL for positive urine cultures. Our rationale for this decision was that once organisms appear in the catheterized urinary tract, the organisms rapidly multiply to $\geqslant 10^5$ cfu/mL [16]. A lower cutoff is frequently used for both therapeutic decisions and for epidemiological research [3], and we wanted to capture as many cases of bacteriuria as possible. All episodes of bacteriuria in

this study were catheter associated and thus were either CAUTI or CAABU.

Appropriate therapy. Our definition of appropriate therapy for bacteriuria incorporated CDC guidelines [8] as well as those from the Society for Healthcare Epidemiology of America [17]. In accordance with Society for Healthcare Epidemiology of America guidelines, the minimum criteria for initiation of antibiotic therapy in patients with a chronic, indwelling catheter include the presence of at least 1 of the following: fever (temperature, >37.9°C), new costovertebral tenderness, rigors, or new onset of delirium. Accordingly, to make our criteria for appropriate treatment of bacteriuria as inclusive as possible, we judged administration of antibiotic therapy to be appropriate if the patient met our criteria for symptomatic UTI or if the patient was being prepared for urological surgery or for placement of a prosthetic device. In all other cases, the administration of antibiotics for treatment of bacteriuria was regarded as inappropriate. We strove to analyze each urine culture by using only the information the health care team would have had at the time that they received the culture result. In other words, even when the patient's fever was subsequently attributed to another etiology, such as pneumonia, if the patient initially had fever of unclear origin and bacteriuria, we scored the episode as CAUTI rather than CAABU. If a single patient had multiple urine culture specimens collected during the same inpatient stay, results of urine cultures were defined as separate episodes if they were collected ⩾24 h apart and if distinct organisms were isolated from them.

Our protocol was approved by the Institutional Review Board of Baylor College of Medicine, and the investigation was conducted in accordance with ethical and human principles of research.

Statistical Analysis

SAS, version 9.1 (SAS Institute) was used for analysis. The outcome of interest (i.e., the dependent variable) was whether the treatment of CAABU was appropriate or inappropriate. The following variables were analyzed using Fisher's exact test or the χ^2 test to determine whether they were associated with CAABU versus CAUTI or with appropriate versus. inappropriate management of CAABU: type of catheter, number of organisms in the urine, quantity of predominant organism in the urine, types of organisms in the urine, and hospital ward or service. The following continuous variables were analyzed by Fisher's exact test or the Wilcoxon rank-sum test to determine whether they were associated with CAABU versus CAUTI or with appropriate versus inappropriate management of CAABU: patient age, duration of catheterization, peripheral blood WBC count, and urine WBC count. In converting continuous variables to dichotomous variables, we tried to use cutoffs that were clinically relevant—for example, we chose an age cutoff close to the average age of our inpatients. Variables significantly associated with inappropriate treatment of CAABU were subjected to multivariate analysis using logistic regression.

RESULTS

Overall, 280 episodes of culture-proven catheter-associated bacteriuria occurred during 3 months of study, 164 CAABU episodes and 116 CAUTI episodes. These episodes occurred among 197 unique patients, and all but 15 episodes represented urine cultures of specimens collected ⩾7 days apart. Patient demographic characteristics associated with the 2 conditions are shown in table 1. Of the 280 episodes, 143 (51%) had urine culture specimens collected from patients whose catheter had been in place for ⩾30 days. Not surprisingly, a smaller proportion of patients with CAABU were febrile, because fever was part of our definition of UTI. Urinalysis results were available for 250 episodes, of which 197 had documented pyuria (WBC count, ⩾5 cells/hpf). Of these cases of pyuria, 103 (52%) involved patients with CAABU, and 94 (48%) involved patients with CAUTI, with median WBC counts of 177 cells/hpf in patients with CAABU and 484 cells/hpf in patients with CAUTI. Similarly, in 195 episodes, the quantity of the predominant organism was $>10^5$ cfu/mL. Of these episodes, 105 (54%) occurred in patients with CAABU, and 90 (46%) occurred in patients with CAUTI. A greater proportion of patients with CAABU had urine culture specimens obtained on the extended care unit rather than the medical, surgical, or rehabilitation services.

Of the 164 episodes of CAABU, 111 (68%) were managed appropriately (no treatment), whereas 53 (32%) were treated with antibiotics (inappropriate treatment). Of the episodes of CAUTI, all but 1 were appropriately treated with antibiotics.

We further analyzed the episodes of CAABU for variables associated with inappropriate use of antibiotic therapy (table 2). Patients hospitalized on the extended care service were significantly more likely to be treated for CAABU, in pairwise comparison with other services ($P = .02$, by Fisher's exact test). If the predominant organism was gram negative rather than gram positive or fungal, and if the quantity of the predominant organism was $>10^5$ cfu/mL rather than 10^4–10^5 cfu/mL, antibiotics were more likely to be given inappropriately ($P < .05$, by Fisher's exact test). A higher urine WBC count and older age of the patient were also significantly associated with inappropriate treatment ($P < .05$, by Fisher's exact test). In multivariate analysis, patient age, type of predominant organism, and urine WBC count remained significantly associated with inappropriate treatment of CAABU ($P < .05$, by logistic regression). The number of species present in the urine, the patient's sex, body temperature, type of urinary catheter, duration

Table 1. Demographic characteristics of groups with catheter-associated asymptomatic bacteriuria (CAABU) and catheter-associated urinary tract infection (CAUTI).

Characteristic	CAABU group (n = 164)	CAUTI group (n = 116)	P
Age, median years (range)	67 (21–88)	69 (21–89)	.72[a]
Male sex	157 (96)	114 (98)	.31[b]
Hospital service			.001[c]
Medicine	78 (48)	80 (69)	
Surgery	29 (18)	15 (13)	
Extended care	29 (18)	6 (5)	
Rehabilitation	28 (17)	15 (13)	
Catheter type			.37[c]
Foley	126 (77)	97 (84)	
Condom	38 (23)	19 (16)	
Predominant organism			.66[c]
Gram negative	51 (31)	31 (27)	
Gram positive	81 (49)	63 (54)	
Fungal	32 (20)	21 (18)	
Quantity of predominant organism, cfu/mL			.018[b]
10^4–10^5	59 (36)	26 (22)	
$>10^5$	105 (64)	90 (78)	
Temperature, median °C (range)	37.1 (34.7–40.8)	37.7 (31.7–40.2)	<.001[a]
WBC count, median cells/mL (range)			
Peripheral blood	11.3 (3.1–28.4)	13.7 (1.9–111)	.05[a]
Urine	177 (0–3654)	484 (0–4340)	<.001[a]
Duration of catheterization, days			.81[b]
<30	77 (47)	57 (49)	
⩾30	87 (53)	59 (51)	

NOTE. Data are no. (%) of patients, unless otherwise indicated.

[a] By Wilcoxon rank-sum test.
[b] By Fisher's exact test.
[c] By χ^2 test.

of catheterization, and peripheral blood WBC count were not significantly associated with inappropriate treatment of CAABU.

In cases where treatment was given for either CAUTI or CAABU, we sought the reason for this decision in the electronic medical record. We accepted clinical signs and symptoms, as well as specific documentation of the physician's thought process, as justification for treatment of the episode. Of 116 cases of CAUTI, the reasons for treatment were fever in 72 (62%), altered mental status in 37 (32%), hypotension in 19 (16%), urinary symptoms in 17 (15%), hematuria in 6 (5%), and other in 7 (6%). Patients with CAUTI frequently had documentation of ⩾1 reason for treatment (e.g., fever and hypotension), and some justification was given in 115 (99%) of 116 cases. In contrast, in 53 patients treated for CAABU, a reason for treatment was stated in 19 (36%), including peripheral leukocytosis in 6 (11%), hematuria in 4 (8%), pyuria in 3 (6%), and other in 6 (11%).

Three patients developed *C. difficile*–associated diarrhea shortly after receiving inappropriate antibiotics for CAABU. Two of these patients had not received any other antibiotics during their hospital stay, and neither had diarrhea at admission. The third patient was receiving multiple antibiotics for other conditions. No cases of *C. difficile* colitis were noted among the patients with CAUTI.

DISCUSSION

In a 3-month period in our large, academic, tertiary care hospital, 280 patients had bacteriuria associated with a urinary catheter or collection system. In 164 cases, the infection was asymptomatic. Nevertheless, nearly one-third of these patients were treated with antibiotics—by official guidelines, inappropriately so. In other words, of 169 episodes of bacteriuria that were treated as CAUTI, 53 (31%) were actually CAABU, even by our lenient interpretation of CDC and Society for Healthcare Epidemiology of America guidelines. Therefore, the first strategy for decreasing the number of reported cases of CAUTI in

Table 2. Comparison of patients with catheter-associated asymptomatic bacteriuria (CAABU) treated appropriately and those with CAABU treated inappropriately.

Characteristic	Patients with CAABU	Patients with CAABU treated appropriately (n = 111)	Patients with CAABU treated inappropriately (n = 53)	P[a]
Sex				.21
Male	157	108 (69)	49 (31)	
Female	7	3 (43)	4 (57)	
Age, years				.04
<63	56	44 (79)	12 (21)	
⩾63	108	67 (62)	41 (38)	
Hospital ward or service				.02
Extended care unit	29	14 (48)	15 (52)	
Other[b]	135	97 (72)	38 (28)	
Catheter type				.35
Foley	126	85 (67)	41 (33)	
Condom	38	26 (68)	12 (32)	
Predominant organism				.004
Gram negative	81	46 (57)	35 (43)	
Gram positive or fungal	83	65 (78)	18 (22)	
Quantity of predominant organism, cfu/mL				.02
10^4–10^5	59	47 (80)	12 (20)	
>10^5	105	64 (61)	41 (39)	
Peripheral blood WBC count, cells/mL				.61
<11	89	62 (70)	27 (30)	
⩾11	75	49 (65)	26 (35)	
Urine WBC count, cells/mL				<.001
<90	125	96 (77)	29 (23)	
⩾90	39	15 (38)	24 (62)	
Duration of catheterization, days				.86
<30	77	53 (69)	24 (31)	
⩾30	87	58 (67)	29 (33)	

NOTE. Data are no. (%) of patients, unless otherwise indicated.

[a] By Fisher's exact test.

[b] Includes medicine, surgery, and rehabilitation wards.

medical centers may be simply to encourage physicians not to screen for CAABU, because this is a condition that does not require treatment, an approach that is supported by evidence-based guidelines.

Older patients, patients with gram-negative organisms in their urine, and patients with higher urinary WBC counts were more likely to receive inappropriate treatment for CAABU. These findings suggest that the treatment decision to give antibiotics for treatment of CAABU may be influenced by the care provider's perception of how sick the patient is or by how dangerous the provider perceives the bacteriuria to be. Because our data collection was retrospective, we could not fully explore the thought process that went into the treatment decisions. However, neither in previous reports [9] nor in our present study are such inappropriately treated patients likely to receive clinical benefit from eradication of the organisms in their urine. Indeed, 3 patients developed *C. difficile* colitis subsequent to receiving inappropriate antibiotics, and in 2 of these cases, the only antibiotics given to the patient were those given to treat CAABU. We also know from our results that many of the patients who are likely to receive inappropriate antibiotics for CAABU are located on extended care units. Because we are currently designing a strategy to increase adherence to CAABU nontreatment guidelines, these findings will be useful to focus our efforts.

Our results are likely to be an underestimate of the proportion of cases of CAABU that were treated inappropriately. We used lenient criteria for appropriate treatment, including temperature ⩾38°C and any change in mental status. Many episodes that we classified as UTI on the basis of fever were subsequently determined to have another source of infection, such as pneumonia, and thus, in retrospect, were in fact CAABU.

Given that our method for capturing cases of CAABU required a positive urine culture, patients who were treated empirically (without culturing) because their urine was visibly cloudy or because the urinalysis showed pyuria would have been missed. Also, patients who had negative urine cultures because they received their first dose of antibiotics before the urine culture specimen was collected would not be included in our analysis. Finally, we excluded outpatients with indwelling catheters and all patients with suprapubic catheters.

On the other hand, it is possible that we misclassified some episodes of bacteriuria on the extended care units as CAABU when they were, in fact, febrile CAUTI. Vital signs are charted 2 times daily on the extended care units, in comparison with 3 times daily on the acute care wards. However, any change in the patient's clinical status prompts more frequent measurement of vital signs on the extended care units.

Recently, *Clinical Infectious Diseases* published a call for national performance measures to encourage nontreatment of asymptomatic bacteriuria [18]. This goal has been reaffirmed by the US Preventive Services Task Force in a recent publication stating that men and nonpregnant women should not be screened for asymptomatic bacteriuria [19]. Our study documents poor adherence to these guidelines. The well-described barriers to physician adherence to guidelines include gaps in knowledge, attitudes, and behavior [20]. We suspect that the discrepancy we observed between guidelines and clinical practice reflects barriers in all 3 domains. Current guidelines concerning asymptomatic bacteriuria do not adequately distinguish between CAUTI and CAABU, thus creating a knowledge barrier. Furthermore, we suspect even many infectious disease specialists are not entirely certain of the terms of the CDC definitions; thus, general practioners' awareness of the guidelines for asymptomatic bacteriuria and their understanding of how to implement them are also likely to be limited. Our observation that older patients with higher levels of pyuria and gram-negative organisms in their urine were more likely to receive unnecessary antibiotic treatment suggests that practitioners do not feel comfortable ignoring bacteriuria once they are aware of its presence. Although our study was performed in single center in the United States, a recent evaluation at The Ottawa Hospital in Canada concluded that antimicrobial agents were prescribed in 68% of patients with asymptomatic CAUTI (i.e., CAABU) [21]. Thus, health care providers' misunderstanding about the clinical significance of bacteriuria is an international problem.

One of the first steps to implementing evidence-based practice guidelines, such as those concerning nontreatment of asymptomatic bacteriuria, is to survey the knowledge and attitudes that create barriers to implementation [20, 22]. The baseline data from this study will help us to design a qualitative survey and an interventional strategy that are appropriately targeted to local conditions. Our ultimate goal is to create and disseminate a strategy that improves adherence to guidelines for asymptomatic bacteriuria, in turn leading to improvement in the quality of patient care.

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