

Antimicrobial Prophylaxis for Catheter-Associated Bacteriuria

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We evaluated short-term systemic antimicrobial prophylaxis for catheter-associated bacteriuria in women undergoing elective gynecological operations in a prospective, controlled, double-masked study. Nine of 100 placebo-treated patients acquired bacteriuria during catheterization compared with 3 of 96 of the drug-treated group. However, at the time of hospital discharge, clean-voided urine specimens were positive as frequently in the drug-treated group (8 of 82 patients cultured) as in the placebo group (8 of 75 patients cultured). No difference in febrile morbidity due to bacteriuria was noted between the prophylaxis and placebo groups. The incidence of catheter-associated bacteriuria may be reduced by antimicrobial prophylaxis. However, because the protective effect is transient and is associated with the selection of resistant organisms, prophylaxis is not indicated for patients at low risk for acquired bacteriuria and in whom the sequelae of catheter-associated infections are infrequent.

In a prospective survey of patients with indwelling urethral catheters, we observed a lower rate of acquired bacteriuria in patients who were receiving systemic antimicrobials than in untreated patients (3). The apparent protective effect of antimicrobial treatment was noted during each of the first 4 days of catheterization, and was evident for both female and male, old and young, and critically ill and non-critically ill patients. Overall, the average daily incidences of acquiring bacteriuria were 4.1% for patients who received antimicrobials and 12.2% for patients who did not. However, microbial species associated with increased antibiotic resistance were cultured more often from treated patients than from the untreated comparison group. We undertook the present study to evaluate, in a prospective, double-masked trial, the effects of short-term use of an antimicrobial on the rate of acquired bacteriuria.

MATERIALS AND METHODS

From April 1974 to February 1975, data were collected from patients admitted to a 23-bed gynecological division of the LDS Hospital. Patients were included in the study if they gave informed consent, underwent a gynecological operation, received an indwelling urethral or suprapubic urinary catheter, and did not have a rapidly or ultimately fatal disease, an active clinical infection, or allergy to penicillins or cephalosporins. Patients with positive urine cultures at the time of insertion of the catheter

were analyzed separately. The study patients received either antimicrobial or placebo provided through the hospital pharmacy by a randomization schedule. Neither the attending physicians, study personnel, nor nursing personnel were aware of the treatment regimen assigned by the pharmacy. If a complication occurred which required release of this information, a note was made in the study record. The first dose of the antimicrobial (cefazolin sodium [Kefzol], 500 mg) was given at the time of operation, and each subsequent dose was given at 8-h intervals, intravenously or intramuscularly, for a total of nine doses.

A clean-voided urine specimen for culture was collected preoperatively upon entry to the study. Additional specimens were collected at the time of catheter insertion and daily during indwelling catheterization by aseptic needle puncture of the catheter tubing. A clean-voided specimen was also collected on the day of discharge from the hospital. All urine specimens were refrigerated within 1 h of collection and 0.1- and 0.01-ml samples were streaked on blood and MacConkey agar plates, respectively. We considered gram-negative bacilli and/or enterococci with colony counts of 10^5 or more per ml from clean-voided specimens and 10^2 or more per ml from catheter specimens indicative of colonization of bladder urine. Colony counts of this magnitude were reproducible by our culture method and were not considered to reflect bacterial contamination during specimen collection or processing. Bacterial identification was performed by standard methods.

The indwelling urinary catheters were inserted by physicians at the time of operation. Povidone-iodine solution was used for meatal cleansing before

catheter insertion. The same commercially available closed-drainage bag system was used throughout the study. Nursing personnel were instructed in, and closely monitored, regarding the techniques of closed sterile drainage. A member of the study team visited each patient daily to monitor the quality of catheter care and to collect clinical data and urine specimens. Blood cultures were obtained according to study protocol from patients who had fever greater than 38.3°C orally. Febrile morbidity was defined as an oral temperature of 38.0°C or greater for at least 2 consecutive days, excluding the first 24 h after operation.

RESULTS

Patient population. A total of 215 patients were entered into the study; 14 patients were subsequently excluded because the first clean-voided or catheterized specimen was positive, and five patients were excluded because they were catheterized for less than 1 day. The final study population included 100 in the placebo group and 96 in the active-drug group. The two treatment groups were similar in age (40.6 years in the prophylaxis group versus 38.3 years in the placebo), type of surgery (Table 1), quality of catheter care, and type of catheterization (6 suprapubic catheters in the prophylaxis group versus 12 in the placebo group).

Acquired bacteriuria. Overall, 24 patients acquired bacteriuria; 12 patients became colonized during their period of catheterization and 12 additional patients had more than 10^5 colonies per ml in clean-voided specimens at time of hospital discharge (Table 1). Four patients who acquired bacteriuria during catheterization also had more than 10^5 colonies per ml in clean-voided specimens at the time of hospital dis-

charge. Of those patients who acquired bacteriuria during indwelling catheterization, three had received antimicrobial prophylaxis and nine had received placebo. Only one of the patients in the active-drug group acquired bacteriuria during the period of drug administration. The other two patients acquired bacteriuria while still catheterized but were colonized 2 and 5 days after the prophylaxis has been discontinued. All nine patients in the placebo group who acquired bacteriuria were colonized during the first 3 days of catheterization. The average daily rate of acquired bacteriuria was 1.7% for the prophylaxis group compared with 3.8% for the placebo group. *Enterococcus* (two) and indole-negative *Proteus* (one) were cultured from the three antimicrobial-treated patients who were colonized during their period of catheterization. The nine placebo-treated patients who acquired bacteriuria were colonized with *Escherichia coli* (eight) and *Enterobacter* (one). No significant differences in rates of bacteriuria were observed between patients who had undergone vaginal versus abdominal hysterectomies. None of the patients who had received suprapubic catheters became bacteriuric.

At the time of hospital discharge, the rates of positive cultures of clean-voided specimens were similar for the prophylaxis and placebo groups (Table 1). The bacterial isolates from patients who received prophylaxis included *E. coli* (three), *Enterobacter* (three), *Pseudomonas* (one), and both *E. coli* and enterococcus (one). Patients who had received placebo were colonized with *E. coli* (six) and enterococci (two).

TABLE 1. Effect of antimicrobial prophylaxis on acquired bacteriuria

Acquired bacteriuria	Prophylaxis group (N = 96)		Placebo group (N = 100)	
	Abdominal hysterectomy (N = 82)	Vaginal hysterectomy (N = 14)	Abdominal hysterectomy (N = 82)	Vaginal hysterectomy (N = 18)
During catheterization				
Day 1-3 of catheterization ^a				
10 ² -10 ⁴ colonies/ml	1	0	6	0
≥10 ⁵ colonies/ml	0	0	2	1
Day ≥4 of catheterization				
10 ² -10 ⁴ colonies/ml	0	0	0	0
≥10 ⁵ colonies/ml	2	0	0	0
Positive clean-voided specimen at discharge	0	0	4 ^b	0
After catheterization^c	6 ^d	2 ^d	4 ^b	0

^a $P < 0.01$ by Fisher exact test for difference between prophylaxis and placebo groups.

^b Eight positive cultures of 63 clean-voided specimens collected at time of discharge from patients who had not received nonprotocol antimicrobial therapy.

^c First positive culture was obtained at time of discharge.

^d Eight positive cultures of 72 clean-voided specimens collected at time of discharge from patients who had not received nonprotocol antimicrobial therapy.

Morbidity. No reduction in febrile morbidity occurred among the abdominal hysterectomy patients who received antimicrobial prophylaxis (Table 2). However, among patients with vaginal hysterectomies, postoperative fever occurred less often in those who received prophylaxis. In addition, significantly fewer of the patients who had received prophylaxis required subsequent therapy with nonprotocol antimicrobial drugs. The average duration of indwelling catheterization was less in vaginal hysterectomy patients who received prophylaxis than in those who received placebo. The prolonged period of catheterization in the placebo group, however, was not associated with an increased risk of acquired bacteriuria. The single instance of acquired bacteriuria in the vaginal hysterectomy group receiving placebo occurred during day 1 of catheterization.

Only 1 of the 29 febrile patients had concurrent bacteriuria, suggesting that urinary tract colonization or infection was not a major cause of fever in these patients. Attending physicians, often without obtaining additional bacterial cultures, diagnosed pelvic, respiratory, urine, or wound infections, or infection at an unknown site, as causes of the febrile episodes. No instance of fever was attributed to drug sensitivity or drug-associated phlebitis. All protocol blood cultures were negative.

We also evaluated the effect of the randomly assigned antimicrobial prophylaxis on the hospital course of the 14 patients found to have positive cultures from their first clean-voided or catheterized specimens. Bacterial isolates included *E. coli* (seven), *Klebsiella* (three), enterococcus (three), and *Enterobacter* (one). Seven patients received cefazolin and seven received placebo. Mean ages, severity of underlying diseases, and types of operations were similar for the two groups. All seven of the patients treated with the antimicrobial were cleared of

their bacteriuria within 24 h after drug administration. Only one of the seven had a subsequent febrile episode, and this occurred after the catheter had been removed. Additional antimicrobials were not required, and none of six specimens obtained at time of discharge was positive.

On the other hand, four of the seven patients who received placebo, including two who had fever above 38.9°C orally for 2 or more consecutive days, required subsequent nonprotocol antimicrobial treatment. The other three had persistent bacteriuria at time of discharge. The mean duration of hospitalization was 5.6 days for the seven patients who received cefazolin versus 6.7 days for the seven who received placebo.

DISCUSSION

The results suggest that a brief course of prophylactic antimicrobial may reduce the incidence of catheter-associated bacteriuria. We observed that the group which received antimicrobial prophylaxis had a lower overall rate, as well as a lower average daily incidence, of acquired bacteriuria. This apparent efficacy of antimicrobials for the prevention of catheter-associated bacteriuria has been noted in several studies (1, 3, 4, 6, 7, 10, 12). Allen et al. (1), in a controlled prospective study, demonstrated beneficial effects of prophylaxis against urinary tract infections in gynecological surgery patients who were not studied with daily urine cultures. Their rates of clinical urinary tract infection in placebo and prophylaxis groups (11 and 0%, respectively) are similar to our observed rates of acquired bacteriuria (12 and 3%, respectively).

Quantitative criteria for bacteriuria during constant bladder drainage with an indwelling catheter have not been determined. In a previous study (3), we found that, among patients

TABLE 2. Effect of antimicrobial prophylaxis on morbidity

Determination	Prophylaxis group		Placebo group	
	Abdominal hysterectomy (N = 82)	Vaginal hysterectomy (N = 14)	Abdominal hysterectomy (N = 82)	Vaginal hysterectomy (N = 18)
No. with febrile morbidity	11	1	12	5
No. treated with nonprotocol antimicrobial	10	2	10	12 ^a
Avg duration of catheterization (days)	1.8	2.4	1.7	5.0
Avg daily incidence of acquired bacteriuria (%)	2.1	0	5.5	1.1
Avg duration of hospitalization (days)	6.0	6.1	5.6	7.6

^a $P < 0.01$ by Fisher exact test.

who showed colony counts between 10^2 and 10^5 organisms per ml, the first positive culture was noted on the last day of catheterization (so that subsequent cultures were not obtained) or systemic antimicrobials were being used in those with low colony counts on 2 or more days. In the present study, a higher proportion of patients had low colony counts because of the brief duration of catheterization in this population and the frequent occurrence of positive cultures on the last day of catheterization.

The indwelling urinary catheter has been cited as a prime causal factor for nosocomial urinary tract infection and resultant bacteremia. Obviously, certain efforts should be extended to minimize the frequency of these complications. However, our enthusiasm for using antimicrobial prophylaxis for catheter-associated bacteriuria in gynecological surgery patients is dampened by other results of our study. These include: (i) the low incidence of acquired bacteriuria in this population, (ii) the lack of relation between febrile morbidity and acquired bacteriuria, (iii) the failure of prophylaxis to reduce the prevalence of positive urine cultures at the time of discharge, and (iv) the lack of effect of prophylaxis in reducing febrile morbidity or duration of hospitalization of the abdominal hysterectomy patients. However, we noted a trend toward less febrile morbidity and shorter hospital stays for the vaginal hysterectomy patients who received prophylaxis, a finding consistent with a number of previous reports (2, 5, 8, 9, 11).

In our previous report, we noted that the major morbidity and mortality of indwelling urinary catheterization are related to the patients' age, sex, and severity of underlying disease. The patient selection criteria for this study excluded higher-risk patients, thus explaining the low incidence of acquired bacteriuria.

We have no explanation for the high prevalence of bacteriuria at time of discharge in patients who had negative cultures during indwelling catheterization. It seems likely that these patients acquired bacteriuria after subsequent ("straight") catheterizations for urinary retention after their period of constant bladder drainage. However, this aspect of care was not monitored.

The efficacy of antimicrobials was more apparent in patients who had a positive urine culture at time of insertion of the catheter. In these patients, antimicrobial therapy probably reduced subsequent catheter-associated morbidity. On the basis of these observations, we

recommend that a urine specimen for culture be submitted from all patients either before or at the time of urethral catheterization. Bacteriuric patients should be treated with a specific antimicrobial as soon as possible. Antimicrobial prophylaxis is not indicated for patients with noncritical underlying diseases undergoing short-term urinary catheterization. Additional study is needed to determine the possible efficacy and potential benefits of prophylaxis in higher-risk patient populations.

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