Published in final edited form as:
Infect Control Hosp Epidemiol. 2011 January ; 32(1): 84–86. doi:10.1086/657664.

Adverse Outcomes of Increasing Episodes of Observed Bacteriuria in Nursing Home Residents

Rituparna Das, MD, **Virginia Towle, MPhil**, **Peter H. Van Ness, PhD, MPH**, and **Manisha Juthani-Mehta, MD**
Yale School of Medicine

Abstract

We examined the association of increasing episodes of observed bacteriuria on adverse clinical outcomes in non-catheterized nursing home residents. While bacteriuria was not associated with hospitalization for UTI or change in mental status, it was associated with antibiotic utilization for UTI and isolation of MDRGNR uropathogens, suggesting a causal relationship.

Keywords

bacteriuria; urinary tract infection; nursing home residents

Introduction

Infections with antibiotic-resistant bacteria are a major public health concern, leading to increased healthcare costs and greater mortality. Antimicrobial prescriptions are frequent in nursing homes and inappropriate use fosters the development of antibiotic resistance. Suspected urinary tract infection (UTI) prompts the greatest usage of antimicrobials by nursing home clinicians.[1] Nursing home residence is a risk factor for bacteremia with antibiotic-resistant pathogens.[2] Colonization with antibiotic-resistant bacteria is highly prevalent, affecting as many as 51% of residents,[3] and is associated with longer duration of residence and antibiotic exposure.[4] Among hospitalized patients with UTI, age >65 years, recurrent episodes of infection, and prior antibiotic use have been associated with isolation of antibiotic-resistant bacteria from urine culture.[5] Stool colonization with amoxicillin-resistant *Escherichia coli* has been demonstrated after amoxicillin therapy for UTI.[6]

Bacteriuria is common in nursing home residents (15–50% prevalence). Without classic genitourinary symptoms, bacteriuria has not been associated with adverse outcomes.[7] We examined the impact of increasing episodes of observed bacteriuria on adverse clinical outcomes in this population, particularly its relationship with antibiotic usage and isolation of antibiotic-resistant bacteria.

Methods

Setting and Participants

This cohort was comprised of residents from five Connecticut nursing homes followed from 2005–2007. Exclusion criteria were: 1)short-term residents; 2)<65 years old; 3)indwelling

Corresponding Author: Rituparna Das, MD, Yale School of Medicine, Department of Internal Medicine, Section of Infectious Diseases, P.O. Box 208022, New Haven, CT 06520.

Conflicts of interest: No conflicts for all authors

catheter; 4)dialysis; 5)chronic suppressive anti-infective therapy for recurrent UTI; or 6)residence for < 4 weeks. All eligible residents (or surrogates) were approached for verbal consent. Of 942 residents screened, 644 were eligible, and 551 enrolled (86% participation rate). Participants were followed for one year, until death, or meeting an exclusion criterion. The study was approved by the Yale Human Investigation Committee, the participating hospitals' IRBs, and each nursing home Medical Board.[8]

Data Collection

Demographics were obtained via chart review. Interviews with nurses and aides determined baseline level of incontinence, functional dependence, and mental status. When the participant's physician or nurse clinically suspected UTI,[8] nursing home staff obtained a urine culture with susceptibility testing to identify multi-drug resistant gram negative rods (MDRGNR), defined as resistance to three or more of the following antibiotics: ampicillin/sulbactam, cefazolin, ceftriaxone, ceftazidime, fluoroquinolones, piperacillin/taxobactam, meropenem, imipenem, and trimethoprim-sulfamethoxazole.[2] Antibiotic utilization (none, one, or 2 or more courses during the one year surveillance period), hospitalization, and mental status (worsening of level of consciousness, periods of altered perception, disorganized speech, or lethargy) were also assessed at the time of clinically suspected UTI episode.[8–9] The main predictor was a three-level ordinal variable for none, one, or 2 or more episodes of observed bacteriuria (>100,000 colony forming units per milliliter). An episode of observed bacteriuria was defined as the presence of bacteriuria during a clinically suspected UTI episode.

Analysis

In addition to descriptive statistics, four unadjusted logistic regression models were fit, each with the ordinal episodes of bacteriuria main predictor and one of the four adverse outcomes (antibiotic utilization, MDRGNR urinary isolates, change in mental status, and hospitalization for UTI, present in any clinically suspected UTI episode). Since change in mental status is often attributed to UTI, this adverse outcome was explored. Then, four multivariable logistic regressions were fit, using the same main predictor and outcomes as in the unadjusted analyses, adding covariates for age, gender, baseline level of incontinence, and number of baseline ADL dependencies. Although some values were missing, complete case results are reported because results from multiply imputed models did not substantively differ. Model fit was assessed with residual analysis and goodness-of-fit statistics. Two-sided tests with p-values < 0.05 were interpreted as being statistically significant. All analyses were performed using SAS® version 9.2.

Results

Of 551 participants, 311 had no clinically suspected UTI episodes, while 240 participants had one or more clinically suspected UTI episodes; 92 participants had no episodes of observed bacteriuria, 100 participants had one episode, and 48 participants had at least 2 episodes (33 with two episodes and 15 with three episodes). Participants were predominantly female (202/240;84.2%) and white (213/240;88.7%), with a mean age of 86.7 years (SD 6.8 years). They had an average of 2.2 comorbidities (SD 1.1) and 4.3 ADL dependencies (SD 3.4) at baseline,[8–9] with 15 (6.2%) having either bladder or bowel incontinence, and 91 (37.9%) having both bladder and bowel incontinence. Of those participants with at least one clinically suspected UTI, 27.1% (65/240) received no antibiotics, 47.9% (115/240) had one antibiotic course, and 25% (60/240) had at least 2 courses of antibiotic therapy. Of these 240 participants with suspected UTI, 102 (42.5%) had a change in mental status from baseline, 31 (12.9%) were hospitalized for UTI, 35 (14.6%)

died prior to the end of surveillance, and 185 (77.1%) had a change in functional status from baseline.[9] Forty participants (40/218,18.3%) had MDRGNR urinary isolates.

Bivariate and multivariable associations of the number of episodes of bacteriuria with adverse clinical outcomes (antibiotic utilization for UTI, MDRGNR urinary isolates, change in mental status, and hospitalization for UTI) were explored. These data are shown in Table 1. In the unadjusted model, antibiotic utilization, isolation of MDRGNRs from urine culture, and change in mental status were associated with increasing episodes of observed bacteriuria during the study period ($p<0.001$, $p=0.004$, and $p=0.041$ respectively). In the adjusted model, only the associations with antibiotic utilization and isolation of MDRGNRs were maintained ($p<0.001$, and $p=0.014$). Further, when antibiotic utilization was added to the model, the association between bacteriuria and isolation of MDRGNR was no longer significant ($p=0.965$).

Discussion

During the study period, almost two-thirds of participants demonstrated bacteriuria with one or more uropathogenic organisms. Since urine cultures were obtained from residents with clinically suspected UTI, our rates of observed bacteriuria were higher than those reported previously in nursing homes surveillance studies.[7] Increasing episodes of observed bacteriuria was associated with increased antibiotic utilization and with MDRGNR urinary isolates. Although UTI is a commonly reported reason for transfer of nursing home residents to hospitals, in this population, there was no association between increasing episodes of observed bacteriuria and hospitalization for UTI. These data suggest that although bacteriuria is common in this population, it is not associated with clinical illness warranting hospitalization for UTI. Finally, although change in mental status is a common reason for investigating UTI and was associated with bacteriuria plus pyuria in our previous study,[8] increasing episodes of observed bacteriuria alone was not associated with altered mental status. This study further suggests that change in mental status is likely multi-factorial in nursing home residents, and alone, should not prompt empiric UTI antibiotic therapy.

While the criteria for diagnosis of UTI in this population continue to evolve,[8] the majority of participants with bacteriuria received antibiotics, with one-quarter receiving more than one course during the study period. Because antibiotics are commonly prescribed in nursing homes, exploring the relationship between antibiotic utilization and isolation of MDRGNRs is important. This study is the first, to our knowledge, to demonstrate a relationship between increasing episodes of observed bacteriuria and isolation of MDRGNR uropathogens in nursing home residents. When the multivariable model is adjusted for antibiotic utilization, the association between bacteriuria and isolation of MDRGNR uropathogens becomes negligible (OR 1.02, $p=0.965$). Antibiotic utilization is associated with MDRGNR urinary isolates (OR 2.42, 95% CI 1.09, 5.38, $p=0.031$) suggesting that antibiotic utilization is a mediator for the emergence of MDRGNR urinary isolates. Our findings corroborate data demonstrating an association of MDRGNR infections with antibiotic exposure.[10]

Confirming a causal relationship between antibiotic use and isolation of MDRGNR uropathogens was beyond the scope of this work. Whether some antibiotics have more propensities to enable resistance than others should be further studied. As this work focused on urine cultures rather than groin or rectal swabs, we identified a smaller number (40,18.3%) of MDRGNR colonized residents than previously reported (51%).[3] The impact of more MDRGNR uropathogens in nursing home residents is important for future study, since these residents may become vehicles for transfer of resistant pathogens to other residents or acute care hospitals.

These data suggest that increasing episodes of observed bacteriuria among nursing home residents in this cohort are not associated with hospitalization for UTI or change in mental status, but are associated with antibiotic utilization and occurrence of MDRGNRs. With more resistant uropathogens, treatment options with oral antibiotics will become increasingly difficult in nursing homes. Restricting antibiotic prescriptions for bacteriuria should continue to be the guiding principle in nursing home practice. Continued inappropriate utilization may increase hospital transfers and provide a vehicle for the transmission of resistant organisms to the inpatient setting.

Acknowledgments

Funding: NIA T32-AG019134; NIH/NIA Claude D. Pepper Older Americans Independence Center (P30-AG21342); NIA R03-AG028057; NIA K23-AG028691; Atlantic Philanthropies; IDSA/NFID; John A. Hartford Foundation; Association of Specialty Professors; CTSA Grant Number UL1 RR024139 from the National Center for Research Resources (NCRR)

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Table 1

Unadjusted and Multivariable Logistic Regression Models – Association of Increasing Episodes of Observed Bacteriuria (0, 1, 2 or more episodes) with Adverse Clinical Outcomes*

Adverse Clinical Outcomes	Unadjusted Odds Ratio (95% Confidence Interval)	P-value
Antibiotic Utilization	29.01 (15.63, 53.83)	<0.001
MDRGNR Urinary Isolates†	1.99 (1.25, 3.19)	0.004
Change in Mental Status	1.44 (1.02, 2.04)	0.041
Hospitalization for UTI	1.12 (0.67, 1.85)	0.662
Adverse Clinical Outcomes	**Adjusted Odds Ratio (95% Confidence Interval)‡**	**P-value**
Antibiotic Utilization§	30.57 (15.98, 58.49)	<0.001
MDRGNR Urinary Isolates†	1.91 (1.14, 3.18)¶	0.014
Change in Mental Status	1.18 (0.80, 1.76)	0.405
Hospitalization for UTI	1.16 (0.67, 2.02)	0.595

*92 participants had no episodes of observed bacteriuria, 100 participants had one episode, and 48 participants had at least 2 episodes (33 with two episodes and 15 with three episodes)

†The N for all adverse clinical outcome categories is 240 except for MDRGNR Urinary Isolates for which it is 218 since 22 participants did not have susceptibility data available.

‡All adverse outcomes in the multivariable logistic regression models were adjusted for age, gender, baseline level of incontinence, and number of baseline ADL dependencies.

§Since the outcome is ordinal with 3 levels (0, 1, 2 or more episodes of antibiotic use for UTI), this logistic regression model is a proportional odds model in which the odds ratios represent the odds of study participants having a higher level of antibiotic utilization (regardless as to how the ordinal outcome is dichotomized into higher and lower groups) for each additional episode of bacteriuria. The proportional odds assumption was examined and satisfied.

¶When antibiotic utilization is added to this multivariable model, the effect for the number of episodes of bacteriuria becomes negligible (OR 1.02, 95% CI 0.49, 2.12, p=0.965). Additionally, in this multivariable model, antibiotic utilization was associated with MDRGNR Urinary Isolates (OR 2.42, 95% CI 1.09, 5.38, p=0.031).