



Major Article

Male veterans with complicated urinary tract infections: Influence of a patient-centered antimicrobial stewardship program



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Background: The influence of antimicrobial stewardship programs (ASPs) on outcomes in male veterans treated for complicated urinary tract infection has not been determined.

Methods: This was a retrospective cohort study encompassing the study period January 1, 2005–October 31, 2014, which was conducted at a 150-bed Veterans Affairs Healthcare System facility in Buffalo, NY. Male veterans admitted for treatment of complicated urinary tract infection were identified using ICD-9-CM codes. Outcomes before and after implementation of a patient-centered ASP, including duration of antibiotic therapy, length of hospitalization, readmission within 30 days, and *Clostridium difficile* infection were compared. Interventions resulting from the ASP were categorized.

Results: Of the 1,268 patients screened, 241 met criteria for inclusion in the study (n = 118 and n = 123 in the pre-ASP and ASP group, respectively). Duration of antibiotic therapy was significantly shorter in the ASP group (10.32 days vs 11.96 days; $P < .0001$), as was length of hospitalization (5.76 days vs 6.76 days; $P = .015$). There was no difference in 30-day readmission. A total of 170 interventions were identified that resulted from the ASP (1.39 interventions per patient).

Conclusions: ASPs may be useful to improve clinical outcomes in men with complicated urinary tract infection. Implementation of an ASP was associated with significant decreases in duration of antibiotic therapy and length of hospitalization, without adversely affecting 30-day readmission rates.

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Urinary tract infections (UTIs) are among the most commonly diagnosed bacterial infections in the United States, leading to more than 8 million physician office visits and 365,000 hospitalizations in the year 2000.^{1–3} In general, the elderly population may be at greater risk for developing a UTI due to a higher prevalence of urinary incontinence, urologic abnormalities (such as those leading to outlet obstruction), cognitive impairment, and catheterization.^{4–6} When UTIs do occur in men, they are by definition classified as complicated.^{7–9}

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The inappropriate use of antimicrobial agents is relatively common in current practice and may be associated with a number of undesirable consequences.^{10–13} In the short-term, suboptimal design of an antimicrobial drug regimen may lead to avoidable adverse drug reactions, bacterial superinfections, and lengthier hospital stays.^{14–16} Persistent misuse of antimicrobial agents may contribute to an increasing prevalence of drug-resistant organisms and may complicate treatment of future patients, because infections with resistant pathogens have previously been associated with increased morbidity, mortality, and health care costs.^{17–20} Because of these implications, methods to improve antimicrobial prescribing practices are necessary.²¹

The Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America have encouraged the establishment of antimicrobial stewardship programs (ASPs) to promote the appropriate use of antimicrobial agents.²¹ Interventions such as prescription review and feedback, restricted formularies, guideline development, and education can be administered via an ASP

and are useful in modifying prescribing practices.^{12,22,23} The ASP at our institution is unique in that it is patient-centered. Automated protocols are not used, and the infectious diseases pharmacist reviews each patient's chart daily. Complex cases are reviewed with the infectious diseases physician. The Infectious Diseases Society of America and Society for Healthcare Epidemiology of America guidelines also recognize the importance of a multidisciplinary approach to antimicrobial stewardship.

Despite the impetus to establish ASP programs, few studies to date have demonstrated their utility in terms of clinical outcomes. The objective of this study is to evaluate the influence of an ASP on outcomes such as duration of antibiotic therapy, length of hospitalization, and readmission within 30 days in male veterans treated for complicated UTI.

METHODS

A retrospective chart review using the Veterans Affairs Computerized Patient Record System was conducted for male veterans admitted to the Veterans Affairs Western New York Healthcare System (VAWNYHS) with a primary admission diagnosis of complicated UTI between January 1, 2005, and October 31, 2014. This facility has 150 acute-care beds and an internal 20-bed community living center. The study period was selected to correspond with implementation of an ASP in 2009. It was further divided into pre-ASP (January 1, 2005-December 31, 2007) and ASP (January 1, 2012-October 31, 2014) periods. The time period including 2008-2011 was excluded because this was the ramp-up period for the stewardship team and there was inconsistent staffing of the program during this timeframe. The local institutional review board approved this study.

The patient-centric stewardship team consists of a board-certified pharmacist and infectious diseases physician support. Interventions consist of prospective audit and feedback regarding antibiotic selection, microbiology, and duration of therapy. Care of each patient is individualized based on prior history and response to treatment. In addition, brief monthly educational conferences on antimicrobial stewardship and local antimicrobial resistance patterns are provided to the medical staff to underline the importance of microbial cultures and to promote appropriate use of antimicrobial agents. In an effort to further decrease inappropriate use, VAWNYHS uses a partially restricted formulary that requires infectious diseases service approval of certain antimicrobial agents. These restrictions remained consistent throughout the entire study period (ie, pre-ASP and ASP).

Male patients were included for analysis if they had a primary admission diagnosis of UTI (as determined using ICD-9-CM codes 599, 599.8, and 599.9). UTIs in men are by definition classified as complicated UTIs and these patients had to have symptoms consistent with a UTI.⁷⁻⁹ Symptoms included urgency, dysuria, burning on urination, suprapubic pain, or flank pain. Symptoms were coupled with fever and/or leukocytosis to meet inclusion. Patients with negative urine cultures were included if they had received antibiotics before the urine culture. Patients who were receiving hemodialysis could also be included if they routinely produced small amounts of urine. Female patients were excluded, as were patients with an inpatient stay < 24 hours, a duration of inpatient intravenous (IV) antibiotics < 24 hours, prostatitis, abscess, urinary stents or nephrostomy tube, genitourinary fistula, a concurrent and active infection other than UTI during admission, or severe immunosuppression (defined by active and systemic cancer receiving chemotherapy within 28 days before admission, a diagnosis of HIV with AIDS, solid organ and/or bone marrow transplant, or absolute neutrophil count < 1,500 cells/ μ L within 28 days before admission). Eligible patients were assigned to either the pre-ASP or ASP cohort based on the date of their admission.

Primary outcomes included duration of antibiotic therapy, length of hospitalization, and readmission within 30 days. Because VAWNYHS is a vertical health care system (ie, provides integrated acute and nonacute care), total duration of antibiotic therapy was defined as the patient's entire course of therapy, including both inpatient and outpatient antibiotic days. Additional outcomes such as the appropriateness of initial antibiotic therapy, frequency of antibiotic drug regimen modification, frequency of antibiotic drug regimen narrowing, and incidence of bacterial superinfection (eg, *Clostridium difficile* infection) were also assessed. *C difficile* infection was collected until 30 days after discharge. ASP interventions were identified and categorized, although only interventions related to modification of the antimicrobial drug regimen were included in the analysis. Routine dosing and pharmacokinetic monitoring recommendations related to the management of vancomycin or aminoglycoside therapy were not included in this total. Other data related to baseline characteristics (eg, age, race, weight, height, and serum creatinine level), the presence of underlying comorbidities (eg, Charlson comorbidity index and presence of diabetes), presence of sepsis or bacteremia on admission, and health care-associated risk factors before admission (eg, recent hospitalization, long-term-care residence, urologic surgery, systemic antibiotic exposure, catheter use, or chronic hemodialysis) were recorded.²⁴ Sepsis was defined using criteria from the Surviving Sepsis Campaign.²⁵ Microbiology data, including frequency of culture, timing of culture (in relation to first dose of antibiotics), and causative pathogen (including incidence of drug-resistant organisms such as carbapenem-resistant Enterobacteriaceae and those producing extended spectrum β -lactamases) were also collected.

Baseline characteristics, comorbidities, severity of illness, and health care-associated risk factors were compared for the pre-ASP and ASP periods in a bivariate model. Categorical data were analyzed using the χ^2 test and continuous data were analyzed using the Student *t* test. Duration of antibiotic therapy and length of hospitalization were analyzed using ordinary least-squares regression. Factors that differed significantly ($P < .05$) between the pre-ASP and ASP periods were built into a least-squares regression model, which was used to adjust for the influence of these variables on primary outcomes, including length of hospitalization, total duration of antibiotics, and total duration of IV antibiotics.

A bivariate analysis of baseline characteristics, comorbidities, severity of illness, and health care-associated risk factors were compared for 30-day readmission and incidence of *C difficile* infection. Significant factors in the bivariate analysis were built into a multivariate logistic regression analysis to calculate odds ratios. Statistical analyses were performed using JMP version 11 (SAS Institute Inc, Cary, NC).

RESULTS

Of the 1,268 patient encounters screened, 241 met criteria for inclusion in the final analysis ($n = 118$ and $n = 123$ in the pre-ASP and ASP groups, respectively). Exclusions occurred as follows: inpatient stay less than 24 hours ($n = 304$), concurrent infection ($n = 203$), no symptoms of UTI ($n = 138$), being female ($n = 125$), duplicate patient ($n = 55$), stents or nephrostomy tube ($n = 48$), death or transition to comfort care ($n = 46$), IV antibiotics < 24 hours ($n = 37$), immunosuppression ($n = 25$), abscess ($n = 12$), prostatitis ($n = 10$), fistula ($n = 10$), duration of antibiotics not documented ($n = 10$), or transferred to VAWNYHS ($n = 4$). Baseline characteristics of the pre-ASP and ASP groups were generally well matched (Table 1). The average age of the study population was approximately 76 years and did not differ between groups. There was a statistically significant difference in average serum creatinine level between groups (1.97 mg/dL in the pre-ASP group vs 1.50 mg/dL in the ASP group; $P = .023$),

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