Data Mining Derived Treatment Algorithms From the Electronic Medical Record Improve Theoretical Empirical Therapy for Outpatient Urinary Tract Infections

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Purpose: We determined whether data mining derived algorithms from electronic databases can improve empirical antimicrobial therapy in outpatients with a urinary tract infection.

Materials and Methods: The electronic medical records from 3,308 visits associated with a positive urine culture at Northwestern's outpatient Urology and Internal Medicine clinics and Emergency Department from 2005 to 2009 were interrogated. Bacterial species and susceptibility rates for trimethoprim-sulfamethoxazole, ciprofloxacin and nitrofurantoin were compared. Using data mining techniques we created algorithms for empirical therapy of urinary tract infections and compared the theoretical outcomes from data mining derived therapy to those from conventional therapy.

Results: Patients were significantly older in the Department of Urology vs Internal Medicine vs Emergency Department, and more patients in the Department of Urology were male. During the 5-year period the susceptibility rates for ciprofloxacin in the Department of Urology and trimethoprim-sulfamethoxazole in Internal Medicine decreased significantly. In the Department of Urology the susceptibility rate for nitrofurantoin was greater than for ciprofloxacin, which was greater than for trimethoprim-sulfamethoxazole. In all departments, bacteria were more resistant to trimethoprim-sulfamethoxazole than to ciprofloxacin or nitrofurantoin. All drugs were more effective in the Emergency Department and Internal Medicine than the Department of Urology. Prior resistance patterns were the strongest predictor of current susceptibility profiles. In the Department of Urology the algorithms for patients with or without prior cultures theoretically outperformed conventional therapy in men (13.2%) and women (10.1%).

Conclusions: Antimicrobial resistance patterns in outpatient urinary tract infections are time dependent, and drug and site specific. Data mining directed therapy significantly improved theoretical outcomes compared to conventional therapy for Department of Urology outpatients and for female patients in the Emergency Department.

Key Words: urinary tract infections, bacteria, data mining, anti-bacterial agents, drug resistance

Abbreviations and Acronyms

CIP = ciprofloxacin

ED = Emergency Department

EDW = Enterprise Data Warehouse

IDSA = Infectious Disease Society of America

IM = Internal Medicine

NFN = nitrofurantoin

NU = Northwestern University

TMP-SMX = trimethoprim-sulfamethoxazole

URO = Department of Urology

UTI = urinary tract infection

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URINARY tract infections afflict millions of individuals in the United States causing significant morbidity and costs up to $3.5 billion annually. UTIs account for more than 9 million outpatient visits to physician offices annually. The lifetime risk of UTIs in women and men is approximately

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60% and 12%, respectively.[1–3] In ambulatory women the national cost of uncomplicated UTIs approaches $2.5 billion per year, while costs of recurrent UTIs in this population are close to $1.6 billion.[4–7] In men the total annual health care expenditures for UTIs have also been estimated to be greater than $1 billion.[8] At a time when control of spiraling health care costs is a national priority, improving the management of UTIs is imperative.

A presumptive diagnosis of a UTI is made by a history of irritative voiding symptoms and a urinalysis that suggests an infection but does not identify the bacterial species or antimicrobial susceptibility.[6] UTIs are difficult to treat because the pathogens and their related antimicrobial susceptibility vary widely depending on the clinical scenario. Because the bacterial pathogens responsible for uncomplicated UTIs in women are reasonably predictable, the IDSA recommends that urine cultures, which take up to 72 hours, not be performed.[9]

In practice, even if a culture is done, UTI symptoms warrant empirical treatment driven by historical data of probable pathogens, antimicrobial susceptibility patterns and treatment guidelines. The 1999 IDSA guidelines for uncomplicated UTIs in women recommend 1 tablet of TMP-SMX double strength taken orally twice a day for 3 days.[2] When TMP-SMX resistance exceeds 10% to 20% in the community, empirical treatment of UTI should be switched to another agent, of which the fluoroquinolones (eg CIP) have the greatest efficacy.[2] To our knowledge no guidelines exist for empirical outpatient UTI therapy in men. However, as UTIs in men are considered complicated, a fluoroquinolone is often used as first line therapy. However, bacterial resistance in UTIs is increasing, and is site and patient sensitive.[10] Thus, reevaluation of these recommendations and practices appears warranted. We hypothesize that the uncertainty about the proper course of treatment for UTIs can be reduced and outcomes improved if comprehensive, up-to-date data are available to generate and maintain patient and site specific UTI management guidelines.

MATERIALS AND METHODS

Northwestern Memorial Hospital is an 873-bed teaching hospital for Northwestern University's Feinberg School of Medicine. Physicians at Northwestern's Urology, Internal Medicine and Emergency Departments are affiliated with the Northwestern Medical Faculty Foundation. The Northwestern University EDW is a data warehouse containing electronic medical records, laboratory results and billing data from Northwestern Memorial Hospital and Northwestern Medical Faculty Foundation for patients treated in the last dozen years. We queried the NU EDW to obtain the results of urine cultures for patients who were seen as outpatients between January 1, 2005 and December 31, 2009 with a diagnosis of UTI, symptoms of UTI (ie dysuria) and a positive urine culture. In addition to ICD-9 coding (associated with the office visit or the urine culture order), ED, IM and URO visits were queried for the phrases UTI, urinary tract infection or dysuria. A positive urine culture was defined as a uropathogen present in clinically significant colony counts (greater than 10,000 cfu/ml) for which susceptibility data were available. Results of the urine culture were linked to patient medical records, from which we obtained age, race, gender, zip code of billing address and other demographic characteristics for use in our analysis.

Urine cultures contained the name of the organism detected and susceptibility to a laboratory determined panel of antimicrobials. We limited our analysis to NFN, CIP and TMP-SMX, the 3 commonly used antimicrobials at NU that can be administered orally for the treatment of UTIs. Susceptibility to each antimicrobial was considered a binary outcome (susceptible or resistant), with partial or intermediate susceptibility being categorized as resistant. If multiple organisms were detected, a drug was presumed to be effective if all of the bacterial species identified in the culture were susceptible. The NU EDW was also used to query records for prior urine cultures. Patients whose most recent culture was susceptible were categorized as not previously resistant. Patients whose most recent cultures were resistant were categorized as previously resistant.

To evaluate the potential efficacy of data mining to improve empirical therapy for UTIs, we used an association rule algorithm to interrogate the data and derive algorithms for empirical therapy. Algorithms were derived for patients with (NU Algorithm+) and without (NU Algorithm–) previous cultures. We compared theoretical outcomes with data mining directed therapy to those with conventional therapy. For conventional empirical therapy in women we used the 1999 IDSA guidelines for uncomplicated UTI (ie TMP-SMX if resistance to TMP-SMX during the prior year in question was less than 20%, or CIP if resistance to TMP-SMX during the prior year was greater than 20%).[9] The 1999 guidelines were used because the 2010 IDSA guidelines were not available during the period queried. For women seen in the ED in the years 2005, 2006 and 2009, IDSA guidelines would have resulted in the use of TMP-SMX. For all other years and sites CIP would have been indicated because the resistance to TMP-SMX was greater than 20%. For conventional empirical therapy in men we assigned CIP in all cases.

To determine theoretical outcomes for UTI therapies we made several assumptions. We assumed that each patient received the assigned antimicrobial. In addition, we assumed that if the bacterial pathogens were susceptible to the assigned antimicrobial, the treatment would have been effective (ie resulting in cure and resolution of symptoms). As a corollary, if the pathogens were resistant, the assigned treatment would have been ineffective.

Statistical analysis was performed using SAS® 9.2 and SPSS® 19. A significance level of $\alpha = 0.05$ was used