Evaluation of Outpatient Antibiotics for the Treatment of Urinary Tract Infections in the Emergency Department

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Abstract

Introduction

Urinary tract infections (UTIs) are a frequent diagnosis made in the emergency department (ED). Solely, in the United States more than 2 million ED visits are attributable to UTIs annually. However, antibiotics for UTIs are often inappropriately prescribed in the ED. Sub-therapeutic and/or supra-therapeutic treatment can lead to resistant urinary isolates, recurrent infections, or treatment failure. Beta-lactam antibiotics are commonly used for UTI treatment despite lack of guideline support. This lack of support can be attributed to outdated guidelines and possible increase in resistance to first line agents with a need for alternative agents. The main purpose of this research is to aid in quality improvement of outpatient antibiotic prescribing for UTIs in the emergency departments across three Dignity Health St. Rose Dominican campuses.

Methodology

This is a retrospective chart review, quality improvement evaluation on the rate of UTI treatment success with beta-lactam antibiotics compared to an alternative acceptable agent. Patients to be included were those that presented to a Dignity Health Siena, San Martin, or Rose De Lima emergency department from August 2020 – July 2023 and were discharged with an antibiotic for an uncomplicated or complicated UTI. The primary outcome was to evaluate UTI treatment success with the use of beta-lactam antibiotics compared to an alternative acceptable agent. Secondary outcome included evaluating appropriateness of initial empiric regimens prescribed for UTI treatment in the emergency department. Exclusion criteria included catheter associated urinary tract infections (CAUTIs) and patients that were admitted to the hospital for treatment.

Results

This study included 171 patients in the final analysis. There was a statistical difference found regarding the primary outcome of treatment success between the alternative agent group and the beta-lactam antibiotic group. Treatment success in the alternative agent group was 74% compared to 53% in the beta-lactam antibiotic group ($p = 0.0131$). There was not a statistical difference concerning individual components of the primary outcome. For secondary outcomes, empiric regimens in the alternative agent group were inappropriate 61% of the time compared to 49% in the beta-lactam antibiotic group. It was more common for duration of therapy to be inappropriate in the alternative agent group (61% vs 30%, $p < 0.0001$.) Conversely, it was more common for inappropriate dosing in the beta-lactam antibiotic group (12% vs 2%, $p = 0.0171$.)

Conclusion

There was a statistical difference in UTI treatment success favoring alternative agent antibiotics vs beta-lactam antibiotics. It is also evident that there is much improvement to be made in prescribing patterns for UTI treatment across the three Dignity Health system emergency departments. The results of this study support the need for further empiric regimen standardization for efficacious and safe UTI outpatient treatment.

Keywords:

Antimicrobial Agents, Infectious Disease

Introduction

Urinary tract infections (UTIs) are a frequent diagnosis made in the emergency department (ED). Solely, in the United States more than 2 million ED visits are attributable to UTIs annually.[1-3] UTIs can have several classifications. Uncomplicated UTI is classified as lower urinary symptoms in a healthy non-pregnant woman in the absence of fever, flank pain or suspicion for systemic infection.[4,5] Otherwise, the UTI can be classified as complicated. The highest incidence of uncomplicated UTI appears in young sexually active women aged 18-24 years.[5] Considering this high number of encounters, it is crucial to have effective treatment for the appropriate duration.

Antibiotics for UTIs are often inappropriately prescribed in the ED which poses the issue of increasing resistant urinary isolates.[6,7] Sub-therapeutic and/or supra-therapeutic treatment can also lead to recurrent infections. Recurrent urinary tract infections are classified as two infections within 6 months or > 3 infections in one year.[8] Relapse of a UTI is defined as a recurrence within 2 weeks of previous treatment, with the same organism.[9] Recurrent UTIs are difficult to treat and decrease the quality of life for patients.[8] When patients are diagnosed in the emergency department with a UTI, they are typically discharged on antibiotics without definitive cultures to aid in selection of antibiotics. This highlights the importance of utilizing first line agents for treatment success. Beta-lactam antibiotics are commonly used for UTI treatment despite proven inferior efficacy compared to other agents (nitrofurantoin, fluoroquinolones and sulfamethoxazole-trimethoprim) and lack of guideline support.[5] The lack of guideline support for beta-lactam antibiotics in the treatment of UTI can be attributed to outdated guidelines and increase in resistance to first line agents with a need for alternative agents.[10] A lack of response to initial treatment within 72 hours would warrant further workup or change in treatment.[5] Overall, there is an opportunity for improvement in empiric antibiotic regimen selection for UTIs.

Methods

This study was a retrospective chart review, quality improvement evaluation on the rate of UTI treatment success with beta-lactam antibiotics compared to an alternative acceptable agent. This study was conducted from November 1, 2023 through May 1, 2024. Patient charts were reviewed for data that aid in reporting UTI antibiotic prescribing from emergency departments across three different campuses in the Dignity Health system. Patients included in the study are those that presented to a Dignity Health Siena, San Martin, or Rose De Lima emergency department from August 2020 – July 2023 and discharged with an antibiotic for a UTI. This study included patients aged 18 and older that were diagnosed with an uncomplicated or complicated UTI in the emergency department and discharged with an antibiotic for treatment. Exclusion criteria included catheter associated urinary tract infections (CAUTIs) and patients that were admitted to the hospital for treatment. The primary outcome is to evaluate UTI treatment success with the use of beta-lactam antibiotics compared to an alternative acceptable agent, defined as absence of recurrent UTI, relapse UTI, and treatment failure.

Statistical Analysis

Statistical analyses performed include a two-sample independent t-test for patient characteristics and chi-squared test for categorical outcomes. To achieve an 80% power level and a significance threshold of $p < 0.05$, it was estimated that a sample size of 134 patients in totality would be needed to detect a difference in the primary outcome. A logistic regression model was utilized controlling for age, sex, flank pain, duration of therapy (DOT), and temperature.

Table 1: Baseline Characteristics

	Alternative Agent (n = 46)	Beta-Lactam (n = 115)	p-value
Female	42 (89%)	99 (86%)	0.57
Age (years)	49 (± 21)	53 (± 20)	0.33
Pregnant	1 (2%)	8 (8%)	0.21
Temperature (°C)	36.7 (± 0.27)	36.8 (± 0.38)	0.10
Flank Pain	5 (10%)	46 (40%)	0.0003
UA LCE +	43 (91%)	108 (93%)	0.58
UA Nitrites +	18 (38%)	47 (41%)	0.76
DOT (days)	6.8 (± 1.93)	8.2 (± 2.16)	0.0002
UTI Diagnosis	**Alternative Agent (n = 46)**	**Beta-Lactam (n = 115)**	**p-value**
Asymptomatic Bacteriuria	1 (2.13%)	3 (2.61%)	—
Uncomplicated	37 (78%)	38 (33%)	—
Complicated	9 (19%)	74 (64%)	< 0.0001

Results

Of the total 289 charts reviewed, 171 patients were included in the final analysis of this study. Charts were reviewed from August 2020 – July 2023 for inclusion/exclusion. A total of 46 patients were included in the alternative agent group and 115 patients were included in the beta-lactam antibiotic group. Baseline characteristics, as presented in Table 1, were fairly even between both groups. As seen, a majority of patients in both groups were female with an average age around 50 years of age. More patients in the beta-lactam antibiotic group presented with flank pain (40% vs 10%, p = 0.0003). The duration of antibiotic therapy in the beta-lactam group (8.2 ± 2.16 days) was longer compared to the alternative agent group (6.8 ± 1.93 days) with a p-value 0.0002. More patients in the beta-lactam antibiotic group had a complicated UTI diagnosis compared to the alternative agent group (64% vs 19%, p < 0.0001.) As seen in Table 2, the most utilized agent in the alternative agent group was nitrofurantoin (80%) and the most utilized beta-lactam antibiotic was cephalexin (61%.) The primary outcome, indicated in Table 3, showed more treatment success in the alternative agent group (74%) versus the beta-lactam antibiotic group (53%) with a p-value of 0.0131. The individual components of the composite primary outcome did not show any differences between the two groups. The most utilized agents in each group, nitrofurantoin and cephalexin, had individual treatment success rates of 75% and 47% respectively. Cefdinir, the next most utilized beta-lactam antibiotic, had a treatment success of 66%.

Table 2: Antibiotic Empiric Selection

Alternative Agent (n = 46)	Utilization
Nitrofurantoin	37 (80%)
Bactrim	7 (15%)
Levofloxacin	2 (5%)
Beta-Lactam (n = 115)	**Utilization**
Cephalexin	70 (61%)
Cefdinir	36 (31%)
Cefuroxime	3 (2.6%)
Cefpodoxime	3 (2.6%)
Cefadroxil	1 (1%)
Augmentin	1 (1%)

The secondary outcome, represented in Table 4, shows that empiric regimens prescribed for outpatient UTI treatment were often inappropriate with 61% inappropriate in the alternative agent group and 49% inappropriate in the beta-lactam antibiotic group. There were more instances of inappropriate dosing in the beta-lactam antibiotic agent group (2% vs 12%; p = 0.0171) and more instances of inappropriate DOT in the alternative agent group (61% vs 30%; p < 0.0001.)

Table 3: Primary Outcome

	Alternative Agent (n = 46)	Beta-Lactam (n = 115)	p-value
Treatment Success	35 (74%)	62 (53%)	0.0131

Table 4: Secondary Outcome

	Alternative Agent (n = 46)	Beta-Lactam (n = 115)	p-value
Empiric Dose Inappropriate	1 (2%)	14 (12%)	0.0171
DOT Inappropriate	29 (61%)	34 (30%)	<0.0001
Empiric Regimen Inappropriate	29 (61%)	56 (49%)	0.2605

Discussion

While beta-lactam antibiotics have been more frequently utilized for outpatient UTI treatment, the results of this study show that beta-lactam antibiotics had treatment success only 53% of the time. First line IDSA guideline recommended agents such as nitrofurantoin showed a higher rate of treatment success, however, were utilized less often in this trial. Despite the utilization amount in each group, both groups showed that improvement in empiric prescribing is essential.

Alternative trials have assessed beta-lactam use for UTI treatment. In this trial the beta-lactam antibiotic that was used most often and had the highest percent of treatment success was cefdinir. There is controversy over use of cefdinir for UTIs due to a low percentage of concentration in the urine. However, The Cefdinir vs. Cephalexin in Urinary Tract Infections trial showed that there was not a difference in overall treatment failure at 7 days when compared to cephalexin. An upcoming trial Cephalosporins for Outpatient PYelonephritis in the Emergency Department: COPY-ED Study will be assessing rate of treatment failure of cephalosporins compared to fluoroquinolones and Bactrim in pyelonephritis.

Given the single center retrospective trial design, there were several limitations to this study. A main limitation of this study was the inappropriateness of empiric regimens in both groups. Being that treatment success is highly reliant on the correct drug, dose, duration and adherence, inappropriate regimens makes it difficult to adequately compare treatment success between the two groups. Reliance on an outpatient Rx history tool was also a limitation of this study as this tool was not able to incorporate patients that paid out of pocket for antibiotics or patients that filled prescriptions at the VA. Utilizing this tool may have also included more patients in the primary outcome as assumptions were made if an outpatient antibiotic regimen was similar to that of a regimen used for UTI treatment. Determination of regimen appropriateness was highly dependent on documented physician notes as there were instances in which laboratory values were not collected on every patient to support diagnosis.

Conclusion

While in this trial there was a statistical difference in UTI treatment success favoring alternative agent antibiotics vs beta-lactam antibiotics, empiric regimens were often inappropriately prescribed. The most often utilized effective agents in each group were nitrofurantoin and cefdinir. It is evident that there is much improvement to be made in prescribing patterns for UTI treatment across the three Dignity Health system emergency departments. The results of this study support the need for further empiric regimen standardization for efficacious and safe UTI outpatient treatment.

Conflicts of Interest

This author does not have any conflicts of interest to declare.

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