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Less workup, longer treatment, but no clinical benefit observed in women with diabetes and acute cystitis

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ABSTRACT

Aims: There is a lack of evidence on the optimal approach for treating acute cystitis in women with diabetes. We performed an outpatient database study to compare management of women with and without diabetes and to assess the effect of treatment duration on early and late recurrence.

Methods: We used the EPIC Clarity database (electronic medical record system) to identify all female patients aged ≥ 18 years with acute cystitis in two family medicine clinics and a urology department. An index case was defined as the first cystitis episode during the study period (2011–2014) with follow-up data of at least 12 months. Recurrence was defined as a Urinary Tract Infection (UTI) episode, plus a new prescription for an antibiotic, between 6 and 29 days (early), or between 30 days and 12 months (late).

Results: We included 2327 visits for cystitis representing 1845 unique patients. Women with diabetes and acute cystitis were less likely to receive urinary tests to work up cystitis, and received significantly longer treatment courses of antibiotics. There was a higher risk of early recurrence in women with treatment duration >5 days (odds ratio 2.17, 95% confidence interval 1.07–4.41) in multivariate analyses. Longer treatment was not associated with late UTI recurrence. Presence of diabetes, and Charlson comorbidity score were independent determinants of late recurrence.

Conclusions: Longer treatment of cystitis was not associated with lower recurrence rates. This calls into question whether many episodes of diabetic cystitis may be managed with a short course of antibiotics, as for uncomplicated disease.

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1. Introduction

Diabetes mellitus is associated with increased risk of urinary tract infections (UTI) [1–3].

According to a recent study using the United Kingdom General Practice Database, the incidence of UTI among patients with diabetes, both male and female, was 46.9 per 1000 person-years versus 29.9 for patients without diabetes [4]. Various immunologic impairments, incomplete bladder emptying and glycosuria are some of the factors that may contribute to an increased risk of UTI in persons with diabetes [1].

One of the controversial issues in UTI management is whether women with and without diabetes and acute cystitis should receive the same type and duration of antibiotics, and whether women with diabetes perform better have “complicated” cystitis simply by having diabetes. International guidelines suggest that women who have well-controlled diabetes without urological sequelae may be considered to have uncomplicated cystitis [5,6]. A more recent comprehensive systematic review identified only a single study addressing treatment of UTI in women with diabetes since 2000 [7]. That observational study using pharmacy dispensing data in The Netherlands found that pre-menopausal and post-menopausal women with diabetes had a higher recurrence rate within 30 days after the treatment despite receiving a longer course of antibiotics in comparison with women without diabetes [8]. The crux of the clinical question about optimum duration of therapy in women with diabetes is that insufficient duration may lead to therapeutic failure, whereas unnecessarily lengthy duration can increase costs and side effects, and promote the development of antibiotic resistance in urinary and gastrointestinal pathogens [9]. The steadily rising prevalence of diabetes, the increased risk of UTI in patients with diabetes, and the rapid rise of resistance in urinary pathogens underscore the importance of defining the optimal antibiotic management for women with diabetes and acute cystitis. We therefore performed a large outpatient database study to compare management of acute cystitis in women with and without diabetes and to assess the effect of treatment duration on early and late recurrence of UTI.

2. Methods

2.1. Setting and study population

This retrospective cohort study included 2 private family medicine faculty clinics and 1 private urology department in a large urban area. Patients in these clinics are predominantly white with private insurance. We used de-identified records from the EPIC Clarity database (electronic health record system) to identify all female patients aged ≥ 18 with any of 3 *International Classification of Diseases, Ninth Revision* (ICD-9) codes for UTI listed as a diagnosis: 595.0 (acute cystitis) and 595.9 (unspecified cystitis) and 599.0 (UTI) during the period of 2011–2014. For each eligible visit we extracted the following variables: patient age, race, presence of diabetes, date of office visits, type of antibiotic prescribed, duration of treatment, chronic disease score, and diagnostic workup (dipstick urinalysis and urine culture). This study was not considered human

subject research by the Baylor College of Medicine Institutional Review Board (IRB), and IRB approval was not required.

2.2. Inclusion and exclusion criteria

Fig. 1 shows our selection process for identifying uncomplicated cystitis visits. We included outpatient clinical encounters that had both an ICD-9 code for UTI and an associated prescription for an antibiotic course prescribed during the same visit. We excluded visits with factors suggesting complicated UTI by excluding visits with additional ICD-9 codes for pregnancy, genitourinary malignancies, genitourinary abnormalities, chronic indwelling catheters, HIV or AIDS, sexually transmitted diseases, active malignancies, daily prednisone of >10 mg. Genitourinary abnormalities included hydronephrosis and calculus of the kidney, for example. We excluded visits with antibiotics prescribed for >14 days or those with refills provided on the initial prescription, as both of these prescribing details suggest that antibiotics were prescribed as prophylaxis for recurrent UTI. We also excluded visits with prophylactic antibiotics to be taken after intercourse. Visits were excluded if we could not determine the duration of the antibiotic course prescribed or if more than one UTI-relevant antibiotic was prescribed on the same visit, as this might indicate a complicated infection. UTI-relevant antibiotics included nitrofurantoin, trimethoprim alone or in combination with sulfamethoxazole, fosfomycin-trometamol, fluoroquinolones, β lactams, tetracyclines, aminoglycosides, and macrolides. We excluded patients for whom we did not have follow up data for at least 12 months after the visit for UTI.

2.3. Outcome variables

All UTI visits were classified as an index case, an early recurrence, or a late recurrence. An index case was defined as the first cystitis episode (clinical encounter with an associated ICD-9 code for UTI, plus a prescription for an antibiotic course) during the study period with follow-up data of at least 12 months. For index cases, we excluded visits with recorded fever (>100.4 °F) as this may indicate pyelonephritis. Early recurrence was an episode of upper or lower UTI between 6 and 29 days after the index case, plus a new prescription for an antibiotic course. We did not include visits with a second prescription within 5 days after the initial cystitis treatment because this likely represented continued treatment for the index event, with a new prescription resulting from an adverse effect or loss of initial prescription or inactivity of the original agent. Late recurrence was defined by a UTI episode between 30 days and 12 months after the index case plus a new prescription for antibiotic course.

2.4. Covariates

Duration of treatment was dichotomized to shorter (≤ 5 days) or longer (>5 days) duration based on the 2010 IDSA guidelines that recommend 3–5 day duration of treatment for uncomplicated cystitis, depending on the agent prescribed [5]. Patients were classified as having diabetes if the diagnosis was in their problem list or if their glycosylated hemoglobin

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