Urogynecology: Original Research

Antibiotic Prophylaxis During Catheter-Managed Postoperative Urinary Retention After Pelvic Reconstructive Surgery

A Randomized Controlled Trial

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OBJECTIVE: To estimate whether nitrofurantoin prophylaxis decreases the incidence of culture-documented urinary tract infection for women with catheter-managed urinary retention after pelvic reconstructive surgery.

METHODS: This double-blind, placebo-controlled, randomized trial was conducted at five academic institutions. Women with urinary retention after surgery for prolapse or incontinence were randomized to oral nitrofurantoin 100 mg daily during indwelling or clean intermittent self-catheterization. The primary outcome was the incidence of symptomatic urinary tract infection within 6 weeks of surgery, confirmed by culture demonstrating more than 1,000 colony forming units per milliliter of uropathogenic bacteria. Secondary outcomes were adverse symptoms possibly attributable to nitrofurantoin and bacterial resistance to nitrofurantoin. A sample size of 154 would detect a decrease in urinary tract infection incidence from 33% to 13%, with 80% power, two-sided alpha of 0.05, and allow 10% dropout.

RESULTS: Of 154 participants randomized from September 2016 to May 2018, 151 were eligible for analysis: 75 received nitrofurantoin, and 76 received placebo. Demographics were similar between groups. The indication for surgery was prolapse (46%), incontinence (20%), or a combination (34%). Participants were discharged with an indwelling catheter (58%) or performing self-catheterization (42%). Median duration of catheter use was 4 days (interquartile range 3–7). Thirteen women in the nitrofurantoin group and 13 women in the placebo group experienced urinary tract infection (17.3% vs 17.1%, P=0.97, relative risk [RR] [95% CI] 1.01 [0.50–2.04]). Adverse symptoms possibly attributable to nitrofurantoin were common in both groups (68% vs 61%, P=0.54, RR [95% CI] 1.12 [0.88–1.43]). Resistance to nitrofurantoin was identified in seven urine cultures, four among nitrofurantoin and three among placebo recipients. In total, 52 urine cultures were obtained to evaluate symptoms of urinary tract infection, and only 27 of 52 grew at least 1,000 cfu/mL of uropathogenic bacteria.

CONCLUSION: Daily nitrofurantoin did not reduce the incidence of culture-proven urinary tract infection.
The incidence of urinary tract infection after surgery for urinary incontinence or pelvic organ prolapse ranges from 7%–40%. Given that women in the United States have a 20% lifetime risk of undergoing surgery for pelvic organ prolapse or urinary incontinence, the absolute number of women at risk for urinary infectious morbidity associated with surgical correction of incontinence or pelvic organ prolapse is substantial.

The frequency of postoperative urinary tract infection is attributed to intraoperative manipulation and instrumentation of the genitourinary tract and is compounded by the rate of postoperative urinary retention requiring short-term catheterization, which is up to 50%. The substantial baseline risk of urinary tract infection after pelvic organ prolapse or incontinence surgery, combined with the well-established increase in risk associated with catheterization, leads many practitioners to prescribe prophylactic oral antibiotics to women undergoing short-term catheterization in the postoperative period. Although there is strong evidence that prophylactic antibiotics reduce the rate of catheter-associated bacteriuria among patients who undergo postoperative bladder drainage, the Infectious Disease Society of America recommends against routine antibiotic prophylaxis owing to concerns regarding antimicrobial resistance, cost, and potential for adverse events based on minimal and conflicting data. This recommendation includes women undergoing urogynecologic surgery but is based on expert opinion owing to a paucity of data. Furthermore, the trial-level data that do exist are limited by reliance on bacteriuria or symptom-based diagnosis of urinary tract infection instead of urine culture.

The objective of this trial was to determine whether nitrofurantoin is more effective than placebo in decreasing the incidence of symptomatic and culture-confirmed urinary tract infection among women with acute postoperative urinary retention after surgery for prolapse or incontinence. Secondary outcomes included incidence of nitrofurantoin-resistant bacterial isolates from urine cultures and adverse symptoms possibly caused by nitrofurantoin use.

METHODS

This double-blind, placebo-controlled, randomized trial was conducted at five sites between September 2016 and May 2018 through the Fellows Pelvic Research Network of the American Urogynecologic Society and the Society of Gynecologic Surgeons. Patients were recruited from the University of Pittsburgh, MedStar Washington Hospital Center, Washington University, University of Texas Southwestern, and the University of Iowa. Eligible women were those with postoperative urinary retention that required outpatient catheter management after reconstructive surgery for pelvic organ prolapse or urinary incontinence. Reconstructive surgery was considered any procedure performed for correction of urinary incontinence or pelvic organ prolapse of any compartment, and intraoperative cystoscopy was performed at surgeon discretion. Sacral neuromodulation procedures and intradetrusor onabotulinumtoxinA (Botox) injections were excluded. Postoperative urinary retention was diagnosed by retrograde or spontaneous fill voiding trial and defined as a postvoid residual volume of more than 100 mL. Women were discharged with either an indwelling catheter or clean intermittent self-catheterization at surgeon discretion. Patients were excluded if they had an allergy to nitrofurantoin, renal impairment defined as glomerular filtration rate of less than 60 mL per minute, three or more urinary tract infections in the preceding 12 months, a history of nephropathy, a renal transplant, or an immunocompromised condition. Patients were prescreened for eligibility and introduced to the study before surgery. Consent was provided either preoperatively when the study was introduced or postoperatively at the time of urinary retention diagnosis. Women who consented preoperatively but passed a postoperative voiding trial were not randomized.

Participants were allocated 1:1 to extended release nitrofurantoin 100 mg or an identical-appearing placebo capsule, taken once daily during catheter use. Nitrofurantoin was chosen owing to its common use for urinary tract infection prophylaxis, tolerability with few adverse effects, and low rate of resistance. Stratified randomization was performed using computer-generated fixed blocks of four, stratified by site. All participants, clinicians and study team members were masked to study allocation except the University of Pittsburgh Presbyterian...
voided urine specimen. Urinary tract infection was considered positive if there were more than 1,000 colony forming units per milliliter of uropathogenic bacteria in a catheterized or midstream clean catch urine culture within 6 weeks of surgery. Culture positive urinary tract infection confirmed with a positive urine culture during the study period women recorded pill compliance, possible side effects of nitrofurantoin exposure, use of other antibiotics, and catheter-related symptoms in a standardized, questionnaire-format daily diary. Catheter use was discontinued when adequate bladder emptying was documented by assessment of post void residual volume, either by straight catheterization, bladder scan, or repeat of void trial.

Patients were seen by research staff and returned unused study drug and completed diaries at a 6-week postoperative visit. The patient chart was reviewed for any urinary tract infections, adverse events, or additional antibiotic use not previously reported, and patients were queried to confirm all outcomes.

Approval was obtained from the data coordinating center and each institution’s internal review board. The protocol was registered with clinicaltrials.gov (NCT02727322). All participants provided written informed consent. The University of Pittsburgh served as the data coordinating center. A data and safety monitoring board reviewed the progress and safety of the study.

The primary outcome was incidence of symptomatic urinary tract infection confirmed with a positive urine culture within 6 weeks of surgery. Culture was considered positive if there were more than 1,000 colony forming units per milliliter of uropathogenic bacteria in a catheterized or midstream clean catch unvoided urine specimen. Urinary tract infection was treated with antibiotics at the discretion of the treating physician. Any woman diagnosed with urinary tract infection one or more times during the study period, by culture or empiric treatment, is included in the primary outcome. After a patient was diagnosed with urinary tract infection, they were considered to have met the primary outcome. Any additional symptom and culture data were collected, however women experiencing more than one episode of urinary tract infection were counted only once in the primary outcome.

Secondary outcomes included the frequency of urine cultures with nitrofurantoin-resistant or intermediate sensitivity isolates. In addition, we measured the frequency of adverse symptoms possibly related to daily nitrofurantoin exposure as reported by daily diary within 6 weeks of surgery which included nausea, vomiting, headache, flatulence, diarrhea, dyspepsia, abdominal pain, constipation, emesis, dizziness, drowsiness, amblyopia, pruritis, urticaria, hair loss, fever, chills, malaise, and acute pulmonary, dermatologic, or hepatic reaction.

Adverse events and serious adverse events were recorded and graded according to Clavien-Dindo classification and U.S. Food and Drug Administration guidelines. Adverse events of Dindo grade II (those requiring pharmacologic treatment with drugs, blood transfusions and total parenteral nutrition) or higher were recorded. In addition, any other event occurring during the study period that warranted reporting in the opinion of the site primary investigator were recorded. An event was considered “serious” if, in the view of either the investigator or sponsor, it resulted in death, life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or congenital anomaly or birth defect.

Based on best available data, we assumed a 60% relative decrease in urinary tract infection attributable to nitrofurantoin from 33% to 13%. Assuming a two-sided alpha of 0.05, and allowing for a 10% dropout rate, a total of 154 patients would provide 80% power to detect a 60% decrease in urinary tract infection. No interim analysis was performed.

Intention-to-treat analysis included all women randomized and not withdrawn from the study. A per protocol analysis was performed including only patients whose urinary tract infection diagnosis was documented by culture, who did not receive additional antibiotics during the study period for other indications, and who were adherent to study medication. Adherence to study medication was defined as use of the study drug on at least 80% of catheter days and confirmed by pill counts. To avoid overidentifying nonadherence, women who used a catheter for less than 5 days were considered adherent if they took study drug ±1 day of total days of catheter use. Additional analysis of the primary outcome stratified by catheter type was performed.
Continuous variables were compared using t-tests or Wilcoxon rank sum tests, where appropriate, and are presented as mean±SD or median (interquartile range). Categorical data were compared using χ2 or Fisher exact tests, where appropriate, and are presented as frequency (%). P<.05 was considered to be significant. SAS 9.4 was used to perform the analysis.

RESULTS

A total of 510 women were screened for eligibility from September 2016 and May 2018 at five participating institutions, and 225 patients were consented. Of those, 71 women provided preoperative consent for participation but ultimately passed void trials and, therefore, were no longer eligible and not randomized. There were 77 participants randomized to each arm, including two participants who were withdrawn per patient request, and one who was deemed ineligible after she was discovered to have a post void residual volume of less than 100 mL before hospital discharge. Thus, 151 participants were included in the intention-to-treat analysis, 75 in the nitrofurantoin group and 76 in the placebo group.

There were no significant differences in baseline demographic characteristics between the study groups (Table 1). Of the total study population, 46% of patients underwent surgery for prolapse, 20% for incontinence, and 34% had combined prolapse and incontinence procedures. The majority of patients underwent cystoscopy as a part of their procedures, with no difference between groups (72/75, 96.0% nitrofurantoin vs 75/76, 98.7% placebo, P=.37). Fifty-eight percent of patients were discharged with an indwelling catheter, and 42% performed clean intermittent self-catheterization, with no difference between study groups (Table 1). Median duration of catheter use was 4 days (interquartile range 3–7) and not statistically different between self-catheterization and indwelling catheter patients.

Of the 151 participants in the primary analysis, 42 women reported urinary tract infection symptoms a total of 55 times (Fig. 1). Cultures were obtained for 52 episodes of symptoms, and three episodes were treated empirically. Overall, 26 women met the primary outcome of urinary tract infection within 6 weeks of surgery, 13 in both the nitrofurantoin group and placebo group (17.3% vs 17.1%, P=.97, relative risk [RR] [95% CI] 1.01 [0.50–2.04], Table 2). The number needed to treat, or number of women who would be exposed to nitrofurantoin prophylaxis to prevent one woman from experiencing postoperative urinary tract infection, is 500 based on these findings. In the subanalysis stratified by catheter type, there was similarly no difference in urinary tract infection incidence between groups (Table 2).

Assessment of compliance to study medication was performed for the 119 women (79.0%) who returned the study drug for pill counts. Based on a priori criteria, 93 (78.2%) patients were compliant with study drug. After excluding women who received antibiotics during the study period for indications other than urinary tract infection and those whose urinary tract infection was treated empirically, there were 87 women eligible for per-protocol analysis, 41 in the nitrofurantoin arm and 46 in the placebo arm. In this subpopulation, incidence of one or more urinary tract infection was 14.6% in the nitrofurantoin group and 8.7% in the placebo group with no significant difference between the two study arms (P=.51, RR [95% CI] 1.68 [0.51–5.55], Table 2).

The rate of endorsing one or more adverse symptoms possibly attributable to nitrofurantoin use was high, but similar between groups (nitrofurantoin 68.0% vs placebo 60.5%, P=.34, RR [95% CI] 1.12 [0.88–1.43], Table 3). Among individual symptoms, constipation was reported more frequently in the nitrofurantoin group; all other symptoms were reported with comparable frequency by all patients. There were no severe respiratory or hepatic complications. A total of 51 participants experienced 68 adverse events during the study, of which 29 were urinary tract infection. The remaining adverse events are listed in Table 4. There was no difference in number of women experiencing one or more adverse event between the groups (24.0% vs 21.1%, P=.67, RR [95% CI] 1.14 [0.63–2.06]). Serious adverse events were uncommon and no different between groups (nitrofurantoin 4.0% vs placebo 2.6%, P=.64, RR [95% CI] 1.52 [0.26–8.84]).

There were two women with multiple urinary tract infections during the study period, both in the placebo group. One patient had two cultures positive for pansensitive *E. coli* 12 days apart, followed by a culture growing *Enterobacter* species 4 weeks later. The other patient was treated for *Enterobacter* cystitis with nitrofurantoin based on sensitivities and grew nitrofurantoin-resistant *Enterobacter* species in a subsequent culture 3 weeks later.

One woman experienced asymptomatic bacteriuria not requiring treatment, which resulted in a total of 27 positive urine cultures during the study period. *Escherichia coli* was the most common predominant isolate found on urine culture (Table 5). Other isolates included *Klebsiella, Enterobacter, Enterococcus, Proteus, Citrobacter, Pseudomonas,* and *Streptococcus* species.
Seven isolates from the 27 cultures demonstrated resistance to nitrofurantoin, 4 of 13 (30.8%) in the nitrofurantoin group compared with 3 of 14 (21.4%) in the placebo group ($P = .58$). No cultures reported more than one resistant organism. Resistant isolates included *Klebsiella*, *Proteus*, and *Enterobacter* species. There was no *E coli* resistance to nitrofurantoin.

**DISCUSSION**

This multicenter, double-blind, placebo-controlled randomized trial found no difference in urinary tract infection incidence among women with urinary retention after pelvic reconstructive surgery treated with nitrofurantoin or placebo during a median 4 days of catheter use. This finding was consistent in both intention-to-treat and per-protocol analyses, as well as analysis stratified by catheter type (self-catheterization vs indwelling catheter). The majority of patients in both groups reported adverse symptoms possibly attributable to nitrofurantoin at comparable rates, suggesting that these symptoms are common in the postoperative period but not attributable to daily nitrofurantoin exposure. Resistance to nitrofurantoin was identified in seven of 27 urine cultures overall, with no significant differences between arms. It is important to note, however, that this study was not powered to detect differences in this resistance rates or analysis stratified by catheter type.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Nitrofurantoin (n=75)</th>
<th>Placebo (n=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>61.7±11.9</td>
<td>60.5±12.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.8±4.4</td>
<td>27.5±5.3</td>
</tr>
<tr>
<td>Gravidity</td>
<td>3±2</td>
<td>3±2</td>
</tr>
<tr>
<td>Parity</td>
<td>3±1</td>
<td>3±1</td>
</tr>
<tr>
<td>Race–ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>64 (85.3)</td>
<td>60 (78.9)</td>
</tr>
<tr>
<td>African American</td>
<td>5 (6.7)</td>
<td>11 (14.5)</td>
</tr>
<tr>
<td>Native American</td>
<td>1 (1.3)</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>5 (6.7)</td>
<td>4 (5.3)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>4 (5.3)</td>
<td>3 (3.9)</td>
</tr>
<tr>
<td>Menopausal status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>15 (20.0)</td>
<td>17 (22.4)</td>
</tr>
<tr>
<td>Postmenopausal, no HT</td>
<td>56 (74.7)</td>
<td>57 (75.0)</td>
</tr>
<tr>
<td>Postmenopausal, oral HT</td>
<td>4 (5.3)</td>
<td>2 (2.6)</td>
</tr>
<tr>
<td>Vaginal estrogen use</td>
<td>20 (26.7)</td>
<td>22 (28.9)</td>
</tr>
<tr>
<td>Diabetes, on medication</td>
<td>4 (5.3)</td>
<td>9 (11.8)</td>
</tr>
<tr>
<td>History of UTI in past year</td>
<td>2 (2.7)</td>
<td>6 (7.9)</td>
</tr>
<tr>
<td>Preoperative POP-Q stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>2 (2.7)</td>
<td>3 (3.9)</td>
</tr>
<tr>
<td>I</td>
<td>4 (5.3)</td>
<td>6 (7.9)</td>
</tr>
<tr>
<td>II</td>
<td>27 (36.0)</td>
<td>16 (21.1)</td>
</tr>
<tr>
<td>III</td>
<td>38 (50.7)</td>
<td>37 (48.7)</td>
</tr>
<tr>
<td>IV</td>
<td>1 (1.3)</td>
<td>5 (6.6)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (4.0)</td>
<td>9 (11.8)</td>
</tr>
<tr>
<td>Preoperative PVR volume (mL)</td>
<td>87.4±147.5</td>
<td>66.4±129.4</td>
</tr>
<tr>
<td>Indication for surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prolapse</td>
<td>38 (50.7)</td>
<td>31 (40.8)</td>
</tr>
<tr>
<td>Incontinence</td>
<td>12 (16.0)</td>
<td>19 (25.0)</td>
</tr>
<tr>
<td>Prolapse and incontinence</td>
<td>25 (33.3)</td>
<td>26 (34.2)</td>
</tr>
<tr>
<td>Catheter type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foley</td>
<td>44 (58.7)</td>
<td>43 (56.6)</td>
</tr>
<tr>
<td>CISC</td>
<td>31 (41.3)</td>
<td>33 (43.4)</td>
</tr>
<tr>
<td>Days of catheter use</td>
<td>4 (3–7)</td>
<td>3 (3–6)</td>
</tr>
</tbody>
</table>

BMI, body mass index; HT, hormone therapy; UTI, urinary tract infection; POP-Q, pelvic organ prolapse quantification; PVR, postvoid residual; CISC, clean intermittent self-catheterization.

Data are mean±SD, n (%), or median (interquartile range).

There were no statistically significant differences between groups (all $P > .05$).
consistent with findings from the few previous reports of culture-documented urinary tract infection among women using transurethral catheters for postoperative urinary retention after urogynecologic surgery.\textsuperscript{4,23} Notably, among women who reported symptoms of urinary tract infection in the postoperative period, only half of urine cultures were positive. Therefore, awaiting culture before treatment of urinary tract infection, as opposed to empiric treatment, could decrease antibiotic administration for urinary symptoms after pelvic reconstructive surgery by up to 50%. These estimates can be used for clinical counseling and care.

Previous studies of antibiotic prophylaxis of urinary tract infection after pelvic reconstructive surgery have included various forms and duration of catheterizations, used varied outcome definitions, and found mixed results. Nitrofurantoin has previously been shown to reduce the incidence of positive urine cultures and symptomatic urinary tract infection in women with suprapubic catheters for a median 11 days after pelvic organ prolapse or urinary incontinence surgery.\textsuperscript{12} In contrast, another study of women undergoing urogynecologic surgery found no protective benefit from prophylactic nitrofurantoin during routine postoperative transurethral catheterization. In that study, median catheter use was 1 day, and 32% of urinary tract infections were treated without culture. Although many practitioners suspect that route of catheterization affects incidence of postoperative urinary tract infection, systematic review data suggest that incidence is not different between types of catheters with catheterization of 15 days or less.\textsuperscript{10} In contrast, the increased rate of catheter-associated bacteriuria and urinary tract infection with increased duration of any catheter use is well established.\textsuperscript{9,24,25} Differences in findings between studies may be more related to differences in duration of catheter use and choice of culture compared with symptom for outcome definitions than route of catheterization.

Our findings are robust and reflect realistic use of antibiotic prophylaxis. The generalizability is strengthened by recruitment from geographically diverse centers, and inclusion of both indwelling and intermittent catheterization. Importantly, this study

Table 2. Primary Outcome: Comparison of Urinary Tract Infection Incidence Between Groups

<table>
<thead>
<tr>
<th></th>
<th>Nitrofurantoin</th>
<th>Placebo</th>
<th>P</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intention-to-treat</td>
<td>13/75 (17.3)</td>
<td>13/76 (17.1)</td>
<td>.97</td>
<td>1.01 (0.50–2.04)</td>
</tr>
<tr>
<td>Stratified by catheter type*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indwelling catheter</td>
<td>8/44 (18.2)</td>
<td>7/43 (16.3)</td>
<td>.81</td>
<td>1.11 (0.44–2.81)</td>
</tr>
<tr>
<td>CISC</td>
<td>5/31 (16.1)</td>
<td>6/33 (18.2)</td>
<td>.83</td>
<td>0.89 (0.30–2.61)</td>
</tr>
<tr>
<td>Per-protocol</td>
<td>6/41 (14.6)</td>
<td>4/46 (8.7)</td>
<td>.51</td>
<td>1.68 (0.51–5.55)</td>
</tr>
</tbody>
</table>

RR, relative risk; CISC, clean intermittent self-catheterization.
Data are n/group total (%) unless otherwise specified.
\* Not powered to detect difference in stratified analysis.
was designed to evaluate the most clinically meaningful definition of urinary tract infection, and this was accomplished by obtaining urine culture for 95% of all episodes of patient-reported urinary tract infection symptoms.

At least 15% of women either did not take medication as directed or were exposed to postoperative antibiotics for alternative indications. Given the low percentage of women available for inclusion in the strictly defined per-protocol criteria, this analysis

Table 3. Adverse Symptoms Reported in Daily Diaries

<table>
<thead>
<tr>
<th></th>
<th>Nitrofurantoin (n=75)</th>
<th>Placebo (n=76)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women endorsing at least 1 symptom</td>
<td>51 (68.0)</td>
<td>46 (60.5)</td>
<td>.34</td>
</tr>
<tr>
<td>Adverse symptom</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>23 (30.7)</td>
<td>12 (15.8)</td>
<td>.03</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>17 (22.7)</td>
<td>12 (15.8)</td>
<td>.79</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>12 (16.0)</td>
<td>17 (22.4)</td>
<td>.32</td>
</tr>
<tr>
<td>Headache</td>
<td>12 (16.0)</td>
<td>11 (14.5)</td>
<td>.79</td>
</tr>
<tr>
<td>Flatulence</td>
<td>11 (14.7)</td>
<td>18 (23.7)</td>
<td>.16</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>11 (14.7)</td>
<td>14 (18.4)</td>
<td>.53</td>
</tr>
<tr>
<td>Dizziness</td>
<td>11 (14.7)</td>
<td>9 (11.8)</td>
<td>.61</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10 (13.3)</td>
<td>7 (9.2)</td>
<td>.42</td>
</tr>
<tr>
<td>Rash or itching</td>
<td>8 (10.7)</td>
<td>6 (7.9)</td>
<td>.56</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>7 (9.3)</td>
<td>7 (9.2)</td>
<td>.98</td>
</tr>
<tr>
<td>Fever or chills</td>
<td>1 (1.3)</td>
<td>6 (7.9)</td>
<td>.06</td>
</tr>
<tr>
<td>Other</td>
<td>1 (1.3)</td>
<td>0</td>
<td>.31</td>
</tr>
<tr>
<td>Amblyopia</td>
<td>0</td>
<td>1 (1.3)</td>
<td>.32</td>
</tr>
</tbody>
</table>

Data are n (%) unless otherwise specified.
Total number of symptoms exceeds number of individuals because many women reported more than one symptom.

Table 4. Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>Nitrofurantoin (n=75)</th>
<th>Placebo (n=76)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious adverse events</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>0</td>
<td>1 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Transfusion</td>
<td>1 (1.3)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Voiding dysfunction requiring surgery</td>
<td>2 (2.7)</td>
<td>1 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Total serious adverse events</td>
<td>3 (4.0)</td>
<td>2 (2.6)</td>
<td>.64</td>
</tr>
<tr>
<td>Adverse events</td>
<td></td>
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</tr>
<tr>
<td>Neurologic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>1 (1.3)</td>
<td>1 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Lower extremity symptoms</td>
<td>1 (1.3)</td>
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</tr>
<tr>
<td>Hematologic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>0</td>
<td>1 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>1 (1.3)</td>
<td>1 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Dermatologic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>3 (4.0)</td>
<td>2 (2.6)</td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysuria</td>
<td>1 (1.3)</td>
<td>2 (2.6)</td>
<td></td>
</tr>
<tr>
<td>Hematuria</td>
<td>3 (4.0)</td>
<td>1 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Prolonged urinary retention</td>
<td>1 (1.3)</td>
<td>2 (2.6)</td>
<td></td>
</tr>
<tr>
<td>Catheter discomfort or obstruction</td>
<td>3 (4.0)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>0</td>
<td>1 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Infectious</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incision</td>
<td>2 (2.7)</td>
<td>3 (3.9)</td>
<td></td>
</tr>
<tr>
<td>Vulvovaginal yeast</td>
<td>1 (1.3)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Infected hematoma</td>
<td>1 (1.3)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Not specified</td>
<td>0</td>
<td>2 (2.6)</td>
<td></td>
</tr>
<tr>
<td>Total adverse events</td>
<td>18 (24.0)</td>
<td>16 (21.1)</td>
<td>.67</td>
</tr>
</tbody>
</table>

Data are n (%) unless otherwise specified.
is underpowered to detect small differences in urinary tract infection incidence when medications are taken as directed. However, it is worth noting that in both this and a prior study, the urinary tract infection incidence was found to be higher among the patients taking antibiotics compared with those taking placebo.11 This may reflect type I error or be related to small sample sizes. Alternatively, it is possible that efforts at antibiotic suppression alter the urinary microbiome or other factors, thereby increasing susceptibility to infection as opposed to suppressing it. We encourage future research evaluating the perioperative urinary microbiome, and potential effect of surgery and prophylactic antibiotics.

Multidrug-resistant uropathogens are a growing threat and a concern which informs the Infectious Disease Society of America recommendation against antibiotic urinary tract infection prophylaxis even among high risk groups such as catheterized patients after pelvic reconstructive surgery.26 The findings of this trial support this recommendation owing to lack of efficacy of nitrofurantoin, an antibiotic often chosen specifically for its relatively low prevalence of resistant isolates and frequency of adverse symptoms.13–16 Although other antibiotics may have better efficacy in urinary tract infection prophylaxis, the safety and resistance profiles are generally less desirable. We therefore recommend against routine antibiotic prophylaxis for women using catheters for postoperative urinary retention after pelvic reconstructive surgery. Further, our findings suggest that treatment for postoperative urinary tract infection should be based on a culture diagnosis, as only half of postoperative urinary symptoms concerning for urinary tract infection were confirmed to be due to infection based on urine culture.

### Table 5. Bacterial Isolates and Nitrofurantoin Resistance Among Positive Urine Cultures

<table>
<thead>
<tr>
<th>Bacterial genus</th>
<th>All Isolates</th>
<th>Nitrofurantoin-Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>n=27</td>
<td>n=7*</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>4 (14.8)</td>
<td>3 (42.9)</td>
</tr>
<tr>
<td>Enterobacter</td>
<td>4 (14.8)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td>Proteus</td>
<td>2 (7.4)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>2 (7.4)</td>
<td>0</td>
</tr>
<tr>
<td>Citrobacter</td>
<td>2 (7.4)</td>
<td>0</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>1 (3.7)</td>
<td>0</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>1 (3.7)</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are n (%) unless otherwise specified.

* Four in the nitrofurantoin group vs three in the placebo group (P=NS).

### REFERENCES


16. Giske CG. Contemporary resistance trends and mechanisms for the old antibiotics colistin, tetracycline, fosfomycin, meccilli-


Authors’ Data Sharing Statement

Will individual participant data be available (including data dictionaries)? Yes.

What data in particular will be shared? Individual participant data that underlie the results reported in the article after deidentification.

What other documents will be available? Study protocol.

When will data be available (start and end dates)? Beginning 6 months after publication. No end date.

By what access criteria will data be shared (including with whom, for what types of analyses, and by what mechanism)? Researchers who provide a methodologically sound proposal may contact the primary author with data requests to achieve aims in the approved proposal. Proposals may be directed to erin.lavelle@ahn.org.

PEER REVIEW HISTORY

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