Assessing ureteral patency using 10% dextrose cystoscopy fluid: evaluation of urinary tract infection rates

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BACKGROUND: Intravenous indigo carmine has routinely been used to confirm ureteral patency after urogynecologic surgery. Recent discontinuation of the dye has altered clinical practice. In the absence of indigo carmine, we have used 10% dextrose in sterile water (D10) as cystoscopic fluid to evaluate ureteral patency. Glucosuria has been associated with urinary tract infection (UTI) in vivo and significantly enhanced bacterial growth in vitro. The concern is that the use of D10 would mimic a state of glucosuria albeit transient and increase the risk of postoperative UTI.

OBJECTIVES: The objectives of this study were to compare the rates of postoperative UTI and lower urinary tract (LUT) injuries between patients who underwent instillation of D10 vs normal saline at the time of intraoperative cystoscopy after urogynecological surgery.

STUDY DESIGN: This was a retrospective cohort study of all women who underwent cystoscopie evaluation of ureteral patency at the time of urogynecological surgery from May through December 2014 at a tertiary care referral center. We compared patients who received D10 cystoscopy fluid vs those who used normal saline. Outcomes included UTI and diagnosis of ureteral or LUT injuries. UTI was diagnosed according to Centers for Disease Control and Prevention guidelines by symptoms alone, urine dipstick, urinalysis, or urine culture. Descriptive statistics compared the rates of UTI between the 2 groups, and a multivariable model was fit to the data to control for potential confounders and significant baseline differences between the groups.

RESULTS: A total of 303 women were included. D10 was used in 113 cases and normal saline (NS) was used in 190. The rate of UTI was higher in the D10 group than the NS group: 47.8% (95% confidence interval [CI], 38.3–57.4) vs 25.9% (95% CI, 19.8–32.8, P < .001). After adjusting for age, pelvic organ prolapse stage, use of perioperative estrogen, days of postoperative catheterization, menopausal status, diabetes mellitus, and history of recurrent UTI, the UTI rate remained significantly higher with the use of D10 (adjusted odds ratio, 3.4 [95% CI, 1.6–7.5], P = .002) compared with NS. Overall, 3 cases of transient ureteral kinking (1.0%) and one cystotomy (0.3%) were identified intraoperatively. However, ureteral and LUT injuries were not different between groups. No unidentified injuries presented postoperatively.

CONCLUSION: Although the use of D10 cystoscopy fluid has been successful in identifying ureteral patency in the absence of indigo carmine, it is associated with an increased rate of postoperative UTI compared with NS.

Key words: cystoscopy, dextrose, ureteral patency, urinary tract infection
glucose concentrations between 100 and 1000 mg/dL significantly enhanced bacterial growth compared with normal urine. In vivo studies in diabetic women have not confirmed this risk, however, one concern is that cystoscopic instillation of D10 may mimic a transient state of glucosuria in the bladder, placing patients at increased risk for postoperative UTI.

The primary objective of this study was to determine whether using D10 cystoscopy fluid to evaluate ureteral patency after pelvic reconstructive surgery affected the postoperative rate of UTI compared with normal saline. We hypothesized that the rate of UTI would be higher in patients who underwent intraoperative cystoscopy with instillation of D10 compared with those patients who underwent cystoscopic evaluation with normal saline. The secondary objective was to compare ureteral and LUT injuries identified during cystoscopy or presenting postoperatively between the D10 and normal saline groups.

**Materials and Methods**

This was a retrospective cohort study of all women who underwent cystoscopic evaluation for ureteral patency at the time of antiincontinence and pelvic reconstructive procedures performed by surgeons in the Department of Urogynecology from May to December 2014 at the main tertiary care referral center and 2 regional hospitals within the Cleveland Clinic Health System. Institutional review board approval for the study was obtained.

All women who underwent intraoperative cystoscopy with either D10 or normal saline distension media were compared. If sterile water was used, these women were included in the normal saline group. If participants received methylene blue, they were included in the normal saline group because their cystoscopy fluid medium was normal saline. Patients were excluded if they did not complete 6 weeks of follow-up or if there was unclear documentation of method used to identify ureteral patency.

After each antiincontinence or pelvic reconstruction operation, transurethral cystoscopy was performed with a 70° rigid cystoscope, and the bladder was systematically inspected for injury, foreign body, and ureteral patency. At our institution, prior to July 2014, intravenous indigo carmine with normal saline fluid medium was routinely used to identify ureteral patency at the time of urogynecological surgery. After indigo carmine was no longer available, the choice of cystoscopic fluid medium was based on surgeon preference and included D10, normal saline, and sterile water. Choice of medium was documented in both the brief and detailed operative notes.

We reviewed all operative notes and clinical encounters for the 6 weeks following surgery. We collected baseline patient characteristics including age, body mass index, parity, menopausal status, smoking status, a history of diabetes, and immunosuppression (defined as chronic steroid use, current immunomodulation, or active chemotherapy). Preoperative clinical measures included pelvic organ prolapse quantification (POPQ) stage, preoperative treatment for UTI, preoperative use of vaginal or oral estrogen, and a history of recurrent UTI.

Operative variables included transient ureteral kinking (resolved by suture release), ureteral injury, lower urinary tract injury, and method used to evaluate ureteral patency. Postoperative outcome measures included postoperative urinary retention, ureteral or lower urinary tract injury, and UTI. Strict definitions for these outcomes were determined a priori to the data collection phase of the study. Postoperative urinary retention was defined as postvoid residual greater than one third the bladder volume used for retrograde fill voiding trial. In patients with urinary retention, we collected the number of days that each patient required catheterization and catheter type (an indwelling Foley or intermittent self-catheterization).

UTI was diagnosed according to Centers for Disease Control and Prevention guidelines (ie, by symptoms alone, urine dipstick alone, urinalysis, or culture). A symptomatic diagnosis required 2 of the following signs or symptoms with no other recognized cause: fever (> 38°C), urgency, frequency, dysuria, or suprapubic tenderness. A urine dipstick diagnosis was made if the dipstick was positive for leukocyte esterase and/or nitrites. A diagnosis by urinalysis was made if it was significant for pyuria (≥ 10 white blood count per milliliter or ≥ 3 white blood count per high-power field of unspun urine). A positive urine culture was defined by ≥ 105 microorganisms/mL (in a voided specimen) ≥ 102 microorganisms/mL (in a no-voided specimen) with no more than 2 species present.

Data were managed and analyzed using JMP Pro version 10.0 (SAS Inc, Cary, NC). Descriptive statistics were used to characterize the overall population. Differences between the groups were tested with χ² tests for categorical variables and t tests or analysis of variance for continuous variables. We performed univariate analyses to compare UTI rates and adverse events between the D10 vs normal saline (NS) groups. We then fit a multivariable logistic regression model using postoperative UTI (yes/no) as the dependent variable.

Significant baseline differences (P ≤ .05) identified in the univariate analyses (age, POPQ stage, estrogen use, days of postoperative catheterization, or use of indigo carmine) were included as covariates in the model. Known risk factors for UTI including menopausal status, diabetes, and recurrent UTI were also included as covariates in the model, even though they were not significantly different between the groups.

Published rates of UTI from our institution were used to determine the sample size for this study. In a retrospective chart review of 983 women who underwent uterosacral colpopexy for pelvic organ prolapse between January 2006 and December 2011, the overall rate of UTI was 20.3% (95% confidence interval [CI], 17.9–23.6). Presuming a 20% baseline UTI rate in our control group and a fixed sample size of 110 patients in the D10 arm and 180 patients in the NS arm, this study had 80% power to detect an absolute increase of 15% in the UTI rate. We used PASS 11 software.
Results
During the study period, 318 anti-incontinence and pelvic reconstructive procedures including an intraoperative assessment of ureteral patency were performed by 6 board-certified female pelvic medicine and reconstructive surgery specialists. Thirteen cases were excluded because of unclear documentation of method used to identify ureteral patency, and 2 patients were excluded because they did not follow up postoperatively.

In the final analysis, 303 patients were included: 113 (37%) participants had cystoscopy performed with D10 and 190 (63%) had NS. Three patients underwent cystoscopy with sterile water instead of normal saline and were included in the NS group. Ninety-eight of the NS participants (52%) received intravenous indigo carmine (from May through July 2014), 4 (2%) received intravenous methylene blue, and 88 (46%) used NS alone.

Univariate analyses comparing those who received NS alone vs methylene blue showed no baseline differences in characteristics between participants. However, in the NS group, those who received indigo carmine vs those who did not were more likely to be older (60.9 ± 11.7 vs 55.8 ± 12.5 years, P = .004) and were more likely to use estrogen supplementation (17.4% [17 of 98] vs 6.5% [6 of 92], P = .02). Because the patients who received indigo carmine did in fact use normal saline as cystoscopy fluid, these participants were combined in the NS group, but age, estrogen use, and use of indigo carmine were included as covariates in our logistic regression model.

Baseline characteristics of participants with D10 and NS groups are found in Table 1. Differences between the D10 vs NS groups included age (62.6 ± 12.1 vs 58.4 ± 12.3 years, P = .04), POPQ stage (median 3 [range 0–4] vs 2.5 [range 0–4], P = .05), use of vaginal or oral estrogen (25.6% [95% CI, 17.9–34.7] vs 12.1% [95% CI, 7.8–17.6], P = .003), and days of postoperative catheterization (4.3 ± 6.1 vs 2.7 ± 4.2 days, P = .01).

There were a total of 102 UTIs in the cohort, 48 UTIs in the NS group and 54 UTIs in the D10 group. The rate of UTI in the 6 weeks after surgery was significantly higher in the D10 group than the NS group: 47.8% (95% CI, 38.3–57.4) vs 25.9% (95% CI, 19.8–32.8, P < .001). On multivariate analysis, the UTI rate remained significantly higher with the use of D10 than NS (adjusted odds ratio, 3.4 [95% CI, 1.6–7.5], P = .002).

Anger et al.31 reported an absolute UTI rate of 34% in the 3 months following a sling procedure, Jackson et al.32 reported a UTI rate of 32% in women undergoing outpatient sling procedures (with or without outpatient pelvic reconstructive procedures) who were not treated with postoperative prophylactic antibiotics. Because these rates of UTI in patients who underwent sling procedures were higher than the 7–25% rate of UTI after reconstructive pelvic surgery, we examined our population specifically for those surgeries that included a midurethral sling vs those that did not. In a univariate analysis, the rate of UTI was not different between those who received a sling (33% [52 of 156] vs those who did not 34% [50 of 146], P = .87). The usage of D10 did not differ between those who received a sling and those who did not. D10 was used in 33% of those patients who received a sling (51 of 156) vs 42% of those patients who did not (62 of 146) (P = .07).

All patients had a urine dipstick obtained at their postoperative visit. Patients who were discharged home with a Foley catheter had a urine dipstick obtained at their voiding trial visit. The
patient was then managed expectantly, treated, or follow-up urine culture was sent at the discretion of the surgeon based on the results of the urine dipstick and/or symptoms. Table 2 details which criteria were followed for the diagnosis of all the UTIs.

There was no difference between groups regarding the way UTIs were diagnosed (Table 2). Six UTIs were treated by the participant’s primary care or emergency room physician and the method of diagnosis was not available (1 in D10 and 5 in NS group). Of those treated by urine dipstick (39 total), 28 were treated with no culture sent, 11 were sent based on a positive dipstick but had a subsequent negative culture. The patients with negative cultures were evenly distributed between the D10 and NS groups. There were 14 dipsticks with positive leaks but cultures were sent and were negative so these were not treated. There were 15 patients who were treated for UTIs initially based on symptoms, urine dipstick, or urinalysis who had follow-up urine cultures that were negative. This occurred equally in both groups: 7 in the NS group vs 8 in the D10 group.

Ureteral and LUT injuries were rare and were not different between groups. Overall, 3 cases of transient ureteral kinking (1%) were recognized by the absence of ureteral jets during intraoperative cystoscopy. This kinking was relieved intraoperatively by removing vaginal vault suspension sutures without any additional clinical consequences. One cystotomy (0.3%) was identified and repaired intraoperatively. There were no unidentified injuries that presented during the 6 week postoperative period.

Comment
The objectives of this study were to compare the rates of postoperative UTI and LUT injuries between patients who underwent instillation of D10 vs normal saline at the time of intraoperative cystoscopy for urogynecological surgery. We found that postoperative rates of UTI were higher in the D10 group than the NS group (47.8% [95% CI, 38.3–57.4] vs. 25.9% [95% CI, 19.8–32.8], P < .001).

The 25.9% rate of UTI in our NS group is consistent with other published data that report a 7–25% rate of UTI in the first 6 weeks after surgery for women undergoing urogynecological procedures. In our population, the use of D10 was associated with a 22% increase in UTI with a number needed to harm of 4.5 (absolute rate in D10 group of 47.8%). Patients whose cystoscopy was performed with D10 had a 3.4 times greater odds of being treated for a UTI in the 6 weeks following surgery, even after adjusting for a history of prolonged postoperative catheterization and preoperative recurrent UTI, which are among the most modifiable risk factors of postoperative UTI in patients undergoing urogynecological procedures. This is a substantial increase and clinically relevant.

D10 may potentiate the risk for UTI by creating an environment, albeit transient, that promotes bacterial growth. Whereas the role of glucosuria in the pathogenesis of UTI has yet to be completely explained, bacterial adherence is a possible explanation. Adherence of *Escherichia coli* to uroepithelial cells is the first step in the pathogenesis of UTIs. If D10 adheres to the urothelium of the bladder, it may mimic the urothelium of a patient with hyperglycemia or glucosuria. It has been shown that the *E coli* with type 1 fimbiae adhere to the uroepithelial cells of diabetic women are twice as well as to the urothelium of nondiabetic controls. Although in this study we did not flush the bladder after concluding a cystoscopy with D10, one could consider attempting to flush the D10 to decrease this adherence. Further study would be necessary to support this practice.

The rate of ureteral obstruction or LUT injury in our study was 1.3% (4 of 303). This is comparable with the published rates of ureteral obstruction or LUT injury during gynecological surgeries that range from 1.3% to 11%. Gustilo-Ashby et al performed a retrospective review of 700 patients who underwent routine intraoperative cystoscopy with indigo carmine at the time of surgery for pelvic organ prolapse at our institution, and the incidence of transient intraoperative ureteral obstruction was 5.1% and the true ureteral injury rate was 0.9%. Intraoperative cystoscopy performed with intravenous indigo carmine was found to be accurate in 99.3% of cases. Three patients showed no ureteral efflux on cystoscopy but had a preexisting genitourinary pathology and were not truly injured or obstructed (false-positive rate of 0.4%), whereas 2 showed bilateral ureteral efflux on cystoscopy but were later diagnosed with a postoperative ureteral obstruction (false-negative rate 0.3%).

In this study, the sensitivity and specificity of intraoperative cystoscopy with intravenous indigo carmine was 94.4% and 99.5%, respectively. Because we did not identify any LUT or ureteral injuries that were undiagnosed at the time of cystoscopy, we are unable to comment on the sensitivity and specificity of D10 in the identification of ureteral patency.

### Table 2

<table>
<thead>
<tr>
<th>Diagnosis of UTI</th>
<th>10% Dextrose (n = 53)</th>
<th>Normal saline (n = 43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms alone, n, %</td>
<td>6 (11.3)</td>
<td>4 (9.3)</td>
</tr>
<tr>
<td>Urine dipstick, n, %</td>
<td>21 (39.6)</td>
<td>18 (41.9)</td>
</tr>
<tr>
<td>Urinalysis, n, %</td>
<td>1 (1.9)</td>
<td>2 (4.6)</td>
</tr>
<tr>
<td>Urine culture, n, %</td>
<td>25 (47.2)</td>
<td>19 (44.2)</td>
</tr>
</tbody>
</table>

*P = .85.
UTI, urinary tract infection.
To date, this is the first study to assess the safety and efficacy of D10 in the evaluation of ureteral patency (Ovid/PubMed search from 1946 to June 2015 using search terms dextrose, D10, cystoscopy, ureter injury, urinary tract injury, and ureteral patency). Another strength of our study is that we evaluated a large cohort of women who underwent cystoscopies performed by 6 experts.

One of the study’s limitations is that we did not identify any undiagnosed ureteral or LUT injuries in our sample size of 303, and as a result, we cannot calculate a sensitivity or specificity for the diagnostic method. Four patients received methylene blue, whereas only 1 of them excreted blue urine (clear jets were identified prior to the excretion of the blue dye in the other 3), and this could influence ureteral patency detection.

We used a broad definition for the diagnosis of UTI. We did, however, adhere to the Centers for Disease Control and Prevention guidelines, and this is representative of our standard practice. There was no difference between the D10 vs NS groups or between surgeons as to how UTIs were diagnosed. Urine cultures were sent in only 32% of patients (98 of 303), which is a limitation of the study. However, in those patients who had cultures sent, the results were similar with UTI rates of 28% [19 of 68] in the NS group vs 55% [25 of 45] in the D10 group (P = .005).

In a retrospective study design, there are potential sources of bias. For example, the choice of fluid media for cystoscopy was chosen based on surgeon preference, which could pose a potential bias. Reporting bias is inherent to the design because we are limited to the data included in the medical record. For example, it is possible that detail of the cystoscopy was omitted from the operative reports or that patients were treated at outside facilities for UTIs. We followed several steps to limit this bias. First, the operative reports were dictated by the same 4 physicians whose standard practice is to report details of ureteral patency including transient ureteral kinking in both the findings and operative details sections of the brief and full operative notes. The 3 transient obstructions (1%) that were recorded were reported in this manner. This documentation would be a limitation in both the D10 and NS groups and should not be biased toward one method. Any patient who had unclear documentation of cystoscopy fluid media was excluded.

Similarly, patients may have been treated for UTIs outside our health care system. We were fortunate to have had excellent follow-up and an electronic medical record that covers both inpatient and outpatient settings at several regional centers. At the 6 week postoperative visit, all patients were asked about complications in the postoperative period. These notes as well as the documentation of all telephone encounters between surgery and the 6 week follow-up visit were extensively reviewed and allowed us to capture 6 UTIs that were treated by emergency room or primary care physicians. We were not, however, able to capture the method of diagnosis for these UTIs. Those patients who did not have 6 week follow-up were excluded.

Although the use of D10 cystoscopy fluid has been successful in identifying ureteral patency in the absence of indigo carmine, it is associated with an increased rate of postoperative UTI compared with normal saline. This novel information can be used in surgical decision making when weighing the risks and benefits of alternative methods to evaluate ureteral patency in the absence of indigo carmine.

References

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