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Evaluating the utility of routine urine culture and antibiotic treatment in children with neurogenic bladder undergoing intradetrusor OnabotulinumtoxinA injection

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Summary

Introduction
OnabotulinumtoxinA is used as treatment for refractory idiopathic and neurogenic detrusor overactivity in children. Many patients perform intermittent self-catheterization and therefore have higher rates of asymptomatic bacteriuria, which may increase their risk of symptomatic urinary tract infection (UTI) following treatment. Multiple injections are often needed due to the short-term efficacy of onabotulinumtoxinA treatment, which may also increase the risk of UTI.

Objective
We aim to evaluate whether a sterile urinary tract is necessary to decrease the risk of postoperative UTI in pediatric patients treated with onabotulinumtoxinA.

Study design
A retrospective review of patients undergoing intradetrusor onabotulinumtoxinA injection from 2014 to 2021 was performed. Demographic data, clinical characteristics, antibiotic treatment and culture results were collected. A positive urine culture was defined as $\geq 10^3$ CFU/ml of uropathogenic bacteria. Our primary outcome was symptomatic UTI within 14 days of the procedure.

Results
103 patients underwent 158 treatments with onabotulinumtoxinA. The incidence of postoperative UTI was 3.2%. The incidence of symptomatic postoperative UTI in patients with asymptomatic bacteriuria compared to those with sterile urine was not significantly different (3.8% vs 0%, $p = 0.57$). Obtaining a preoperative urinalysis or urine culture did not affect the incidence of postoperative UTI ($p = 0.54$). The number needed to treat with antibiotics to prevent one postoperative UTI was 27. The incidence of postoperative UTI was highest in patients with low-risk bladders ($p = 0.043$). Prior history of multi-drug resistant UTI was a risk factor for postoperative UTI ($p = 0.048$).

Discussion
For children undergoing onabotulinumtoxinA injection, there are no evidence-based recommendations regarding antibiotic prophylaxis and the need to screen for and treat asymptomatic bacteruria prior to treatment. Our study addresses this important clinical question, and shows no difference in the rate of postoperative UTI between patients with asymptomatic bacteriuria and those with sterile urine. Patients with a history of multi-drug resistant UTI are at increased risk of symptomatic postoperative UTI and may benefit from preoperative urine testing and treatment. Limitations of our retrospective study include its small sample size in the face of such a low incidence of our primary outcome.

Conclusions
The risk of UTI following onabotulinumtoxinA injection in children is low. The presence of sterile urine at the time of surgery does not significantly decrease the risk of postoperative UTI. Routine treatment of asymptomatic bacteriuria prior to surgery results in a large number of patients receiving unnecessary antibiotics. As a result, we recommend against preoperative urine testing for most asymptomatic patients.

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Summary Table Patient characteristics and relationship to symptomatic postoperative UTI.

	No UTI (N = 153)	Symptomatic UTI (N = 5)	P-value
Age at surgery, median (IQR)	13 (8.5–16.6) yrs	13.3 (11.6–14.9) yrs	0.87
Gender, Female	50% (77/153)	60% (3/5)	0.67
Spina Bifida	60% (92/153)	80% (4/5)	0.37
Urinary incontinence	72% (110/153)	80% (4/5)	0.69
Recurrent UTI	17% (27/153)	40% (2/5)	0.20
Clean intermittent catheterization (CIC)	89% (136/153)	80% (4/5)	0.54
Continuous antibiotic prophylaxis (CAP)	16% (25/153)	0% (0/5)	0.32
History of multi-drug resistant UTI	Yes 21% (15/71)	Yes 60% (3/5)	0.048
	No 79% (56/71)	No 40% (2/5)	
	Unknown 54% (82/153)		
Vesicoureteral reflux	Yes 17% (22/127)	Yes 20% (1/5)	0.88
	No 83% (105/127)	No 80% (4/5)	
	Unknown 17% (26/153)		
History of prior onabotulinumtoxinA injection	43% (66/153)	80% (4/5)	0.10
Bladder risk categorization	Low 9% (13/144)	Low 40% (2/5)	0.043
	Intermediate 34% (49/144)		
	Hostile 57% (82/144)	Hostile 60% (3/5)	
	Unknown 6% (9/153)		
Preoperative urinalysis or urine culture performed	11% (17/153)	20% (1/5)	0.54
Positive preoperative urine culture	43% (6/14)	100% (1/1)	0.27
Positive intraoperative urine culture	Yes 76% (100/131)	Yes 100% (4/4)	0.57
	No 24% (31/131)	No 0% (0/4)	
	Unknown 14% (22/153)	Unknown 20% (1/5)	
IV antibiotic prophylaxis at time of surgery	95% (145/153)	80% (4/5)	0.16
Empiric treatment with oral antibiotics*	15% (23/153)	0% (0/5)	0.35

* Refers to asymptomatic patients who were treated empirically with a treatment course of antibiotics within 7 days before or after their Botox procedure.

Introduction

Pediatric patients with neurogenic bladder often exhibit neurogenic detrusor overactivity (NDO) during bladder filling, which can lead to elevated bladder pressures, urinary tract infection (UTI) and renal damage [1]. First-line interventions to mitigate these risks and improve urinary continence include clean intermittent catheterization (CIC) and anticholinergic medications [2]. OnabotulinumtoxinA is increasingly used for treatment of refractory idiopathic and neurogenic detrusor overactivity in children, as it has been shown to be safe and effective in pediatric patients with NDO who do not respond to anticholinergic therapy [3]. Treatment with intradetrusor onabotulinumtoxinA injection has been shown to significantly improve bladder storage pressures, increase bladder capacity and improve compliance, ultimately helping many children with hostile neurogenic bladders to avoid or delay bladder augmentation [3–6].

Currently there is limited evidence regarding the need for urine culture or antibiotic treatment prior to intradetrusor onabotulinumtoxinA injection. As a result, there are wide variations in clinical practice. The goal of this study is to evaluate whether a sterile urinary tract is necessary to decrease the risk of symptomatic postoperative UTI in pediatric patients undergoing intradetrusor onabotulinumtoxinA injection. We hypothesized that symptomatic UTI is uncommon following intradetrusor onabotulinumtoxinA injection and routine use of preoperative urine culture to guide antibiotic treatment of asymptomatic bacteriuria prior to treatment does not decrease the risk of UTI.

Materials and methods

With institutional review board approval, a retrospective review of neurogenic bladder patients undergoing cystoscopic intradetrusor onabotulinumtoxinA injection (CPT 52287) at our institution from January 2014 to October 2021 was performed. We excluded cases where onabotulinumtoxinA injection was performed in conjunction with other surgical procedures [n = 49]. Patient demographics, clinical characteristics, and postoperative outcomes were abstracted from the electronic medical record. Clinical characteristics of interest included associated diagnoses, indication for onabotulinumtoxinA treatment, urinary continence, current bladder management and medications. A diagnosis of recurrent UTI was defined as three or more UTIs within the last year. Urine culture results within 3 years prior to onabotulinumtoxinA treatment were reviewed to evaluate for history of multi-drug resistant (MDR) UTI. Multi-drug resistance was defined as non-susceptibility to at least one agent in three or more antibiotic classes [7]. Preoperative videourodynamics were reviewed for vesicoureteral reflux (VUR), presence of NDO, detrusor leak point pressure/end fill pressure and bladder risk categorization (low, intermediate, hostile) as defined by the UMPIRE protocol [8].

Preoperative urine testing was defined as any urinalysis or urine culture collected within 2 weeks prior to the procedure. A positive urine culture was defined as $\geq 10^3$ CFU/ml of any uropathogenic bacteria [9]. The decision to obtain preoperative urine testing and treatment of positive preoperative urine cultures was based on surgeon discretion. Surgical IV antibiotic prophylaxis was administered at the discretion of the surgeon. Intraoperative urine culture was obtained at the time of onabotulinumtoxinA injection in the majority of patients. Asymptomatic bacteriuria was defined as a positive urine culture without signs or symptoms of UTI. Asymptomatic patients who received oral antibiotic treatment within 7 days before or after onabotulinumtoxinA injection were classified as having periprocedural antibiotic treatment. The decision to treat empirically with oral antibiotics was based on surgeon discretion. The primary outcome was development of a symptomatic UTI within 14 days of the procedure, defined as a positive urine culture in the presence of at least two of the following symptoms: fever, gross hematuria, abdominal/flank pain, dysuria or pain with catheterization, new or worsening frequency/urgency/incontinence, and malodorous or cloudy urine.

Study data was collected and managed using the REDCap database hosted at our academic tertiary care children's hospital [10,11]. Descriptive statistics were performed. Patients who developed postoperative UTI were compared to those who did not develop postoperative UTI using univariate analysis. Subgroup analysis of patients with intraoperative urine cultures who were not empirically treated with antibiotics was performed. Comparison of categorical and continuous variables were made using Chi-square test and Kruskal Wallis test, respectively. Data analysis was generated using SAS software (Version 9.4). A p-value <0.05 was considered statistically significant.

Table 1 Patient characteristics.

Gender, %	
Female	52 (54/103)
Associated diagnoses, %	
Spina bifida	70 (72/103)
Vesicoureteral reflux	20 (21/103)
Recurrent UTI	18 (19/103)
Tethered cord	7 (7/103)
Spinal cord injury	5 (5/103)
Caudal regression syndrome	4 (4/103)
Transverse myelitis	3 (3/103)
Bladder exstrophy	3 (3/103)
Multiple sclerosis	1 (1/103)
Non-neurogenic neurogenic bladder	1 (1/103)
Posterior urethral valves	1 (1/103)
Other	8 (8/103)
Bladder management, %	
Clean intermittent catheterization (CIC)	88 (140/158)
Overnight catheterization	39 (61/158)
Spontaneous void	11 (17/158)
Vesicostomy	1 (1/158)
Medications, %	
Anticholinergics	87 (137/158)
Mirabegron	7 (11/158)
Dual-therapy	10 (16/158)
None	11 (18/158)
Continuous antibiotic prophylaxis	16 (25/158)
Indication(s) for Botox, %	
Urinary incontinence	72 (114/158)
Hostile bladder	54 (85/158)
NDO with urinary incontinence	37 (59/158)
NDO without urinary incontinence	15 (23/158)

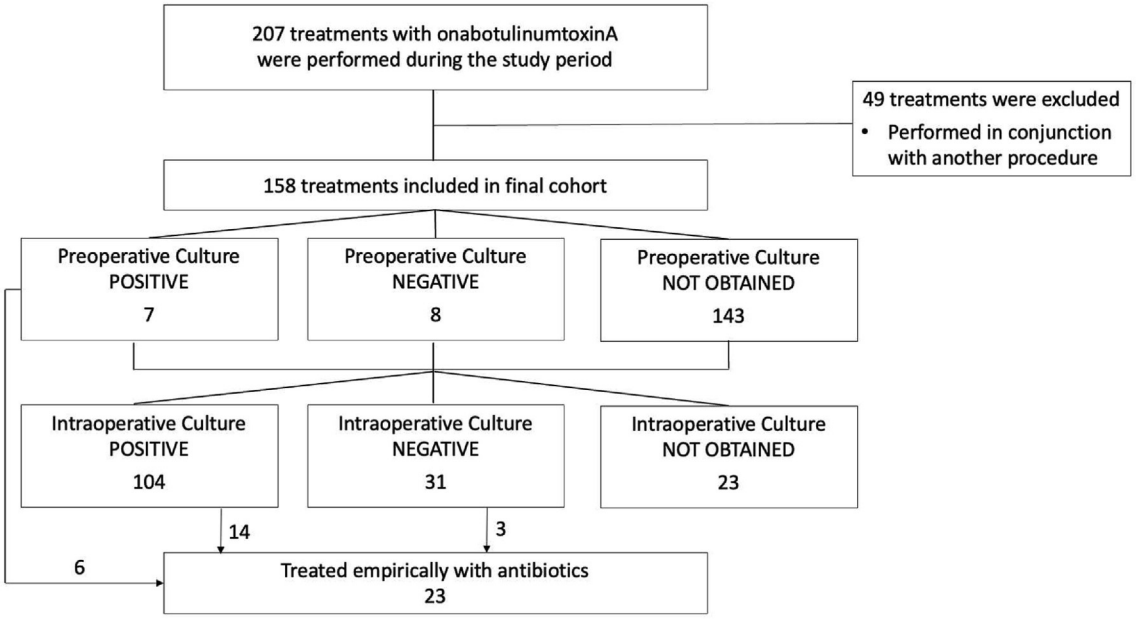

Fig. 1 Description of study cohort.

Table 2 Patient characteristics and culture results of patients who developed symptomatic postoperative urinary tract infection (UTI) following onabotulinumtoxinA injection.

Patient Characteristics	Preoperative Culture	Intraoperative Culture	Surgical Prophylaxis	Time to UTI (days)	Postoperative Course	Postoperative Culture
11.6 yo M with hostile NGB with VUR and recurrent MDR UTI, on oxybutynin status post vesicostomy	10-50k CFU/ml *E. coli*, MDR Treated with IV meropenem	Not performed	Not Given	1	Febrile UTI. Hospitalized for sepsis requiring ICU admission.	10-50k CFU/ml *E. coli*, MDR
18 yo F with neurogenic urinary incontinence, on CIC and solifenacin	Not performed	50-100k CFU *E. coli*	IV Cefazolin	5	Febrile UTI with bacteremia. Hospitalized for sepsis requiring ICU admission.	50-100k CFU/ml *E. coli*, MDR
8.3 yo M with hostile NGB and history of MDR UTI, on CIC and oxybutynin	Not performed	>100k CFU *E. coli*	IV Cefazolin	7	Febrile UTI	50-100k CFU/ml *E. coli*
14.9 yo F with hostile NGB, recurrent UTI, on CIC and solifenacin	Not performed	<10k CFU/ml *E. coli, Pseudomonas*	IV Cefazolin	7	Afebrile UTI	Not available (Treated by PCP)
13.3 yo F with neurogenic urinary incontinence and history of MDR UTI, on CIC	Not performed	<10k CFU/ml *Staphylococcus epidermidis*	IV Cefazolin	12	Possible febrile UTI. Hospitalized with fever and upper respiratory infection requiring ICU admission.	*Enterococcus*, *Staphylococcus aureus*

NGB = neurogenic bladder; CFU/ml = colony-forming unit per milliliter.

Results

During the study period, a total of 103 patients underwent 158 treatments with onabotulinumtoxinA (Fig. 1). For the 158 treatments included in this study, 56% (88/158) were initial treatment in patients with no history of onabotulinumtoxinA injection and 44% (70/158) were subsequent injections in patients previously treated with onabotulinumtoxinA. Mean age at surgery was 12.6 years (standard deviation: 4.9 years). Forty-nine patients (48%) were male and 54 (52%) were female. The most common etiology of neurogenic bladder was spinal dysraphism in 78% of patients (80/103) and 89% (92/103) performed CIC. Indications for treatment were urinary incontinence in 72% of cases (114/158) and bladder hostility in 54% (85/158) (Table 1). Bladder risk was categorized as low in 10% (15/158), intermediate in 33% (49/158), hostile/high risk in 57% (85/158) and unknown in 15% (9/158).

Eighteen patients (11%; 18/158) had a preoperative urinalysis or urine culture performed an average of 7.9 days (range: 2—14 days) prior to surgery. Six patients (33%; 6/18) were asymptomatic and had urine testing performed in anticipation of their upcoming procedure. Four patients (22%; 4/18) were asymptomatic and had urine testing performed at the time of urodynamic testing. Eight patients (44%; 8/18) had urine testing performed by a non-urologic provider to evaluate for possible UTI. Asymptomatic bacteriuria was found in 47% (7/15) of all preoperative urine cultures. When asymptomatic bacteriuria was identified preoperatively, 71% (6/7) were treated with culture-directed antibiotics for an average of 4.5 days prior to onabotulinumtoxinA injection (range: 0—7 days). Urine culture was obtained at the time of cystoscopy in 85% (135/158) of cases. Asymptomatic bacteriuria was found in 77% (104/135) of all intraoperative urine cultures.

A single IV dose of empiric antibiotic was administered for surgical antimicrobial prophylaxis in 94% (148/158) of cases. The most common single antibiotic regimens prescribed were cefazolin (89%; 131/148), clindamycin (3%, 4/148), gentamicin (2%; 3/148), ceftriaxone (1%; 2/148), cefoxitin (1%; 2/148), ampicillin (1%; 1/148) and cefepime (1%; 1/148), respectively. The most common combinations of antibiotics prescribed were ampicillin with gentamicin (2%; 3/148) and cefazolin with gentamicin (1%; 1/148%). Ten patients (6%, 10/158) received no IV antibiotic prophylaxis prior to onabotulinumtoxinA injection. Twenty-three patients (15%; 23/158) were treated empirically with oral antibiotic therapy for a median of 7 days (range: 2—10 days) around the time of surgery. Of those who received oral antibiotics, 26% (6/23) were treated based on a positive preoperative culture, 61% (14/23) were treated based on a positive intraoperative culture, and 13% (3/23) were treated despite having a negative intraoperative culture. All patients treated empirically were asymptomatic.

The overall incidence of symptomatic postoperative UTI was 3.2% (5/158). Of patients who developed symptomatic UTI following treatment, 80% (4/5) had a positive urine culture at the time of onabotulinumtoxinA injection (Table 2). The incidence of symptomatic postoperative UTI in patients with asymptomatic bacteriuria compared to those with sterile urine was not significantly different (3.8%; 4/104 vs 0%; 0/31,

Table 3 Patient characteristics and relationship to symptomatic postoperative UTI.

	No UTI (N = 153)	Symptomatic UTI (N = 5)	P-value
Age at surgery, median (IQR)	13 (8.5–16.6) yrs	13.3 (11.6–14.9) yrs	0.87
Gender, Female	50% (77/153)	60% (3/5)	0.67
Spina Bifida	60% (92/153)	80% (4/5)	0.37
Urinary incontinence	72% (110/153)	80% (4/5)	0.69
Recurrent UTI	17% (27/153)	40% (2/5)	0.20
Clean intermittent catheterization (CIC)	89% (136/153)	80% (4/5)	0.54
Continuous antibiotic prophylaxis (CAP)	16% (25/153)	0% (0/5)	0.32
History of multi-drug resistant UTI	Yes 21% (15/71) No 79% (56/71) Unknown 54% (82/153)	Yes 60% (3/5) No 40% (2/5)	0.048
Vesicoureteral reflux	Yes 17% (22/127) No 83% (105/127) Unknown 17% (26/153)	Yes 20% (1/5) No 80% (4/5)	0.88
History of prior onabotulinumtoxinA injection	43% (66/153)	80% (4/5)	0.10
Bladder risk categorization	Low 9% (13/144) Intermediate 34% (49/144) Hostile 57% (82/144) Unknown 6% (9/153)	Low 40% (2/5) Hostile 60% (3/5)	0.043
Preoperative urinalysis or urine culture performed	11% (17/153)	20% (1/5)	0.54
Positive preoperative urine culture	43% (6/14)	100% (1/1)	0.27
Positive intraoperative urine culture	Yes 76% (100/131) No 24% (31/131) Unknown 14% (22/153)	Yes 100% (4/4) No 0% (0/4) Unknown 20% (1/5)	0.57
IV antibiotic prophylaxis at time of surgery	95% (145/153)	80% (4/5)	0.16
Empiric treatment with oral antibiotics*	15% (23/153)	0% (0/5)	0.35

* Refers to asymptomatic patients who were treated empirically with a treatment course of antibiotics within 7 days before or after their Botox procedure.

p = 0.57). Performing a preoperative urinalysis or urine culture prior to surgery did not affect the incidence of postoperative UTI (5.6%; 1/18 vs. 2.9%; 4/140, p = 0.54). The incidence of post-operative UTI in those who received empiric IV antibiotic at the time of onabotulinumtoxinA injection was 2.7% (4/149), compared to 11% (1/9) in those who did not receive empiric IV antibiotics at surgery, although this was not statistically significant (p = 0.16). No symptomatic postoperative UTIs were observed in the subset of patients treated empirically with a treatment course of oral antibiotics within 7 days before or after their procedure. Based on our data, the number needed to treat with oral antibiotics to prevent one symptomatic postoperative UTI was 27. Upon excluding those treated empirically with oral antibiotics, subgroup analysis of the remaining patients did not find a difference in the incidence of symptomatic postoperative UTI between those who had a positive and negative intraoperative urine culture at the time of onabotulinumtoxinA injection (4.5%; 4/88 vs 0%; 0/26, p = 0.27).

Patient age, gender, diagnosis, continence status, bladder management with CIC, use of continuous antibiotic prophylaxis, history of recurrent UTI, and presence of VUR were not associated with the risk of symptomatic UTI following treatment with onabotulinumtoxinA (Table 3). In the 41 patients (40%; 41/103) with a history of prior onabotulinumtoxinA injection, the mean number of injections per patient was 2.9 (range 2–7). The incidence of symptomatic postoperative UTI was not significantly higher in patients undergoing repeat injection compared to those with no history of prior injection (5.7%; 4/70 vs 1.1%; 1/88, p = 0.1). With regards to bladder risk categorization, the incidence of symptomatic postoperative UTI was highest in low-risk patients (13%; 2/15), compared to intermediate (0%; 0/49) and hostile/high risk (3.5%; 3/85) patients (p = 0.04).

Eighteen patients (17.5%; 18/103) had a known prior history of multi-drug resistant UTI. Of these patients, 78% (14/18) had MDR UTI within 1 year prior to onabotulinumtoxinA injection and 28% (5/18) had a concurrent diagnosis of recurrent UTI. A history of MDR UTI was found to be a significant risk factor in the development of symptomatic postoperative UTI. In patients with a history of MDR UTI, the incidence of symptomatic postoperative UTI was 17% (3/18), compared to 3.4% (2/58) in those with no history of MDR UTI (p = 0.048). Only 17% (3/18) of patients with a known history of MDR UTI had a preoperative urinalysis or urine culture performed prior to onabotulinumtoxinA injection. For patients with a known history of MDR UTI, the number needed to treat with antibiotics to prevent one symptomatic postoperative UTI was 7.

The incidence of symptomatic postoperative UTI in patients who perform CIC was 2.8% (4/140) compared to 5.5% (1/18) in those who do not self-catheterize (p = 0.54). In the cohort of patients not on CIC at the time of treatment (18/159), seventeen patients were able to spontaneously void and one patient was managed with cutaneous vesicostomy. The only observed symptomatic postoperative UTI in this cohort was in the patient with a vesicostomy. Of patients that voided spontaneously, asymptomatic bacteriuria was found in 57% (8/14) of all intraoperative urine cultures. Fourteen patients (82%; 14/17) received empiric IV antibiotic at the time of onabotulinumtoxinA injection

and three patients (18%; 3/17) were empirically treated with a course of oral antibiotics. There were no symptomatic postoperative UTIs observed in the group of patients who voided spontaneously.

Discussion

Patients with neurogenic bladder are predisposed to asymptomatic bacteriuria, UTI, and colonization by bacteria with antibiotic resistance [12,13]. The susceptibility of this population may be due to risk factors such as routine catheterization, bladder stasis, urinary tract abnormalities, and antibiotic exposure [12]. In pediatric patients with neurogenic bladder, UTI can often lead to irreversible renal scarring. As the use of onabotulinumtoxinA injection for hostile/high-risk neurogenic bladder and neurogenic detrusor overactivity in pediatric patients increases, it is important to recognize that the most common adverse event following treatment is UTI [3].

Several studies in the adult literature report conflicting results regarding the need for antibiotic prophylaxis prior to onabotulinumtoxinA treatment to mitigate the risk of UTI [13—18]. Adult guidelines from the Infectious Disease Society of America recommend treating asymptomatic bacteriuria before procedures in which mucosal bleeding is anticipated [19]. However, the guidelines also recommend *against* treating asymptomatic bacteriuria in patients who are reliant on CIC [19]. Therefore, the adult guidelines are not clear on how to proceed when patients on CIC undergo procedures in which mucosal bleeding is anticipated. For children undergoing onabotulinumtoxinA injection, evidence-based recommendations regarding antibiotic prophylaxis and the need for routine preoperative urine culture prior to treatment do not exist. To our knowledge, this is the first study to assess whether a sterile urinary tract is necessary to reduce the incidence of symptomatic postoperative UTI in pediatric patients undergoing intradetrusor onabotulinumtoxinA injection.

Our results demonstrate that the incidence of symptomatic postoperative UTI in children undergoing treatment with onabotulinumtoxinA is low at only 3.2%. This is similar to the FDA randomized Phase 3 trial investigating onabotulinumtoxinA in children, which reported a 3.5% incidence of UTI within two weeks after treatment [3]. The incidence of UTI increased to 19.5% at 12 weeks after treatment, although this was no different compared to the 6 months before treatment [3]. In an earlier study, Greer et al. [20] suggested the incidence of UTI after onabotulinumtoxinA injection in children is almost 10%. The lower incidence of postoperative UTI in our study may be a result of our stricter definition of UTI, that required a positive urine culture of $\geq 10^3$ CFU/ml in growth of any uropathogenic bacteria and associated urinary symptoms or fever. In addition, a relatively short 14-day postoperative timeframe was chosen to increase our confidence that any recorded UTI was truly associated with the procedure.

Close to 90% of patients were on CIC at the time of onabotulinumtoxinA treatment and it is therefore not surprising that asymptomatic bacteriuria was found in 77% of all intraoperative urine cultures. It is somewhat surprising that asymptomatic bacteriuria was found in only 47% of all preoperative urine cultures, which seems lower than expected. However, only 9.5% of patients (15/158) had a preoperative urine culture and this small sample may not be representative of the entire population. The incidence of symptomatic postoperative UTI in children with asymptomatic bacteriuria was only 3.8%, and there was no significant difference in the risk of UTI between patients with asymptomatic bacteriuria and those with sterile urine. Additionally, the evaluation and treatment of asymptomatic bacteriuria prior to surgery did not significantly decrease the risk of symptomatic postoperative UTI. This suggests that clinicians need not routinely order diagnostic urine cultures prior to onabotulinumtoxinA injection. Furthermore, treatment with oral antibiotics in this setting appears to confer little benefit, as the number needed to treat to prevent one symptomatic postoperative UTI is 27. For reference, a NNT value of 20 or above is generally not considered an efficacious treatment [21]. The administration of treatment antibiotics to all children undergoing intradetrusor onabotulinumtoxinA injections could further predispose this population to colonization by bacteria with antibiotic resistance, which is an increasing clinical concern [22,23].

In this retrospective review we identified possible risk factors associated with symptomatic postoperative UTI following onabotulinumtoxinA injection. These included a history of prior multi-drug resistant UTI and low-risk bladder categorization. Somewhat counterintuitively, the incidence of postoperative UTI was highest in low-risk patients (13%), compared to those with intermediate (0%) and hostile bladders (3.5%). This may have been due to our overall low incidence of UTI and a disproportionally small number of patients with low-risk bladder included in our study. For patients in the low-risk category, the indication for treatment with onabotulinumtoxinA was almost exclusively urinary incontinence (93%). The incidence of VUR and recurrent UTI in this subset of patients was 13% and 20%, respectively, which does little to explain the higher risk of postoperative UTI observed in our low-risk patients. Additionally, 89% of low-risk patients were already managed with CIC prior to treatment with onabotulinumtoxinA. The introduction of CIC has been shown to increase the risk of UTI compared to spontaneous voiding in infants and toddlers with meylomenigocele [24], but this was not the case in our cohort.

Our results also indicate that patients undergoing repeat onabotulinumtoxinA injections appear to have increased risk of symptomatic postoperative UTI. Although not statistically significant, this is arguably clinically significant given the fact that 40% of our cohort underwent an average of 3 distinct treatments over the seven-year study period. Patient age, gender, diagnosis, bladder management, use of continuous antibiotic prophylaxis, VUR and recurrent UTI were not found to be significantly associated with symptomatic postoperative UTI in this cohort. With regards to bladder management, it is notable that 80% of patients who developed postoperative UTI following treatment were performing CIC. We were unable to find a significant association between use of CIC and postoperative UTI risk, but this may be due to a limited sample size of patients not on CIC (only 12% of cohort) and resultant lack of power. Only one postoperative UTI was observed in the subgroup of patients not on CIC, and it was in a patient with a vesicostomy, which precluded any meaningful analysis of this subset of patients.

Limitations

There are several limitations to this single-center retrospective study. There is the possibility that patients developed symptomatic UTI but did not present or communicate their symptoms with a clinician for proper record documentation. However, this possibility is low as a result of our institution's participation in the CDC UMPIRE protocol, since patients are routinely asked during visits if they have been treated for any interim UTIs (including at an outside urgent care) and their responses are well-documented in our electronic medical record. Selection bias is also possible given the retrospective nature of our study. The use of preoperative urine testing, surgical IV antibiotic prophylaxis, and empiric oral antibiotic treatment were not standardized due to significant variability in practice patterns amongst different practitioners.

Another limitation is the overall low incidence of symptomatic post-operative UTI in our cohort (n = 5). The small number of outcome events precluded the use of multivariable analysis, and the results of our univariate analyses should be interpreted as exploratory. We acknowledge that our study is underpowered to detect small differences between the group of patients who developed UTI and those who did not. According to a post hoc sample size calculation using an incidence of 3.5% (as reported in the FDA randomized Phase 3 trial investigating onabotulinumtoxinA in children), a sample size of 434 would be needed to detect small differences between our two groups. Lastly, there may be reduced generalizability of our findings because our cohort consisted of patients treated at an academic tertiary care children's hospital.

Conclusions

The risk of UTI following onabotulinumtoxinA injection in children is low, even in patients with asymptomatic bacteriuria. In our experience, it is not necessary to ensure urine is sterile prior to surgery as this does not significantly affect the risk of post-operative UTI. Routine treatment of asymptomatic bacteriuria prior to onabotulinumtoxinA injection would result in a large number of patients receiving unnecessary antibiotics in order to prevent a single post-operative UTI. As a result, we recommend against preoperative urine testing for most asymptomatic patients. However, select patients with a prior history of multi-drug resistant are at increased risk of post-operative UTI and may benefit from pre-operative urine testing and treatment.

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Ethical approval

The authors have read and complied with the policy of the journal on ethical consent as stated in the Guide to Authors.

Conflicts of interest

CK has served as a consultant and meeting planning director for Intuitive Surgical (Sunnyvale, California). The other authors declare that they have no conflicts of interest.

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