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ORIGINAL ARTICLE

What is the ideal antibiotic prophylaxis for intravesically administered Botox injection? A comparison of two different regimens

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Abstract

Introduction Onabotulinum toxin A (Botox®) administered intravescially is an effective treatment for idiopathic detrusor overactivity, of which urinary tract infections (UTIs) are a common complication. The purpose of this study was to compare two prophylactic antibiotic regimens with the goal of decreasing UTI rates following intravesically administered Botox® injection.

Materials and methods A retrospective review of two groups of patients undergoing intravesically administered Botox® injections was performed—one with idiopathic and one with neurogenic detrusor overactivity. One group received a dose of ceftriaxone intramuscularly (IM) at the time of Botox® injection, and a second group received a 3-day course of a fluoroquinolone orally starting the day before the procedure. The rate of postprocedure UTI was examined using a χ^2 test. A secondary analysis was performed using logistic regression modeling to test the association between clinical characteristics and antibiotic regimen and risk of postprocedure UTIs.

Results Botox® injections were performed on 284 patients: 236 received a single dose of ceftriaxone IM and 48 received 3 days of a fluoroquinolone orally. The UTI rate was significantly lower in the fluoroquinolone group (20.8%) vs. the cephalosporin group (36%), $p = 0.04$. Predictors of postprocedure UTIs included single dose of antibiotics IM [odds ratio (OR 2.80, $p = 0.02$] and a positive preprocedure urine culture (OR 1.31, $p = 0.03$).

Conclusions We found a significantly lower rate of UTIs when patients received a 3-day course of a fluoroquinolone orally as opposed to a single dose of a third-generation cephalosporin IM. Patients with a positive preprocedure culture might benefit from an even longer duration of antibiotics at the time of Botox® injection.

Keywords Overactive bladder · Intravesical · Botox® injection · Urinary tract infection

Introduction

Overactive bladder (OAB) is a debilitating condition that causes significant distress and adversely affects a patient's QoL (QoL) [1]. The International Continence Society defines OAB as symptoms of urgency with or without urgency incontinence, usually associated with frequency and nocturia [2]. Although the etiology of OAB symptoms can be identified in some patients, most patients with OAB have idiopathic detrusor overactivity [3]. According to the most recent guidelines from the American Urological Association and the Society of Urodynamics, Female Pelvic Medicine, and Urogenital Reconstruction (AUA/SUFU), first-line management of OAB consists of behavioral therapy [4]. If symptoms are not resolved with first-line therapy, the recommended second-line therapy is pharmacologic management, mainly consisting of anti-muscarinics or β3-adrenoreceptor agonists per os. In addition to a certain number of patients with an inability to tolerate medication because of side effects, up to 33% of patients do not have adequate response to medication [5]. For those patients in whom first- and second-line therapies for OAB are unsuccessful, sacral or posterior tibial neuromodulation or intravesically administered onabotulinumtoxinA (Botox®) are recommended.

Dmochowski et al. demonstrated that 100–200 U of Botox® resulted in statistically significant reductions in

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urinary incontinence (UI) events, micturition, frequency, urgency, and nocturia, resulting in a statistically significant improvement in QoL over a 12-week period ($p < 0.05$). The most common adverse event noted in the Botox® group was UTI, which occurred in ~40% of patients in a phase 2 clinical trial [6]. In a 12-week study, Chapple et al. reported that the main adverse event associated with Botox® was UTI, with ~20% of patients developing postinjection UTIs [7]. Furthermore, Werner et al. highlighted the benefits of Botox® in patients with neurogenic detrusor overactivity, finding that at 12-weeks postinjection, complete continence was achieved in 96% of patients [8]. Botox® has been shown to improve the QoL in patients with neurogenic detrusor overactivity [9].

Despite the high rate of UTIs following Botox® injection, there is a lack of literature regarding preprocedure antibiotic prophylaxis. The UTI rates reported in the literature represent a varied and heterogeneous population, with no standardized antibiotic prophylaxis or preprocedure or postprocedure urine testing. We previously reported a UTI rate of 35.1% in patients who received a single dose of a third-generation cephalosporin (ceftriaxone) IM at the time of Botox® injection [10]. Given this high UTI rate, we changed our management procedure, with patients receiving a single IM dose serving as historical control group. We sought to determine whether a longer course of prophylactic antibiotics per os would decrease the rate of UTIs following Botox® injection. In addition, we sought to identify possible risk factors for postprocedure UTIs.

Materials and methods

The Cedars-Sinai Institutional Review Board approved this retrospective study (IRB #00040762). A review of the electronic medical records was performed for both male and female patients with neurogenic bladders who received intravesically administered Botox® injections from May 2012 to November 2016 by two urologists in a tertiary female pelvic medicine and reconstructive surgery practice. All injections were performed in the office setting. Patients received either 100 or 200 U of Botox®. Data abstracted included age, body mass index (BMI), history of diabetes, and pre- and postprocedure urine culture results. Preprocedure cultures were obtained for all patients. Patients in the group with a negative preprocedure urine culture were given ceftriaxone IM at the time of Botox® injection. This group formed the historical control group. A second group of patients, also with a negative preprocedure culture, received a 3-day course of 250 mg ciprofloxacin per os daily) starting the day before Botox® injection. Patients with allergies to either cephalosporins or fluoroquinolones were excluded. All patients who had a positive preprocedure culture were treated orally with appropriate antibiotics based on cultures prior to Botox® injection and were included in the study after a negative preprocedure urine culture. All patients were seen at 2 weeks postprocedure, at which time urine cultures were performed. UTI detection was allowed for 30 days postprocedure.

The primary outcome was UTIs following Botox® injection. Postprocedure UTIs were defined as worsening or new-onset lower urinary tract symptoms (urgency, frequency, dysuria) or postprocedure urine culture with >100 K CFU/ml. UTI rate was determined using a χ^2 test. A secondary analysis was performed using multivariate logistic regression analysis to determine the association between clinical characteristics and antibiotic regimen and risk of postprocedure UTIs. Clinical characteristics used were age, BMI, diabetes, and preprocedure urine cultures.

Results

From May 2012 to November 2016, 284 Botox® injections were performed. Two hundred and thirty-six patients received a single dose of ceftriaxone IM and 48 received 3 days of a fluoroquinolone per os. There was no difference in baseline age, BMI, diabetes, or rate of preprocedure positive culture between groups. Overall, 59 (20.8%) patients in the fluoroquinolone group developed a symptomatic UTI, while 102 (36%) patients in the cephalosporin group developed a UTI, $p = 0.04$ (Fig. 1).

On multivariate logistic regression analysis, predictors of postprocedure UTIs included single dose of antibiotic prophylaxis IM [odds ratio (OR) 2.80, 95% confidence interval (CI) 1.2–6.5, $p = 0.02$] and a positive preprocedure urine culture (OR 1.31, 95% CI 1.03–1.66, $p = 0.03$). Age, BMI and diabetes were not associated with postprocedure UTIs.

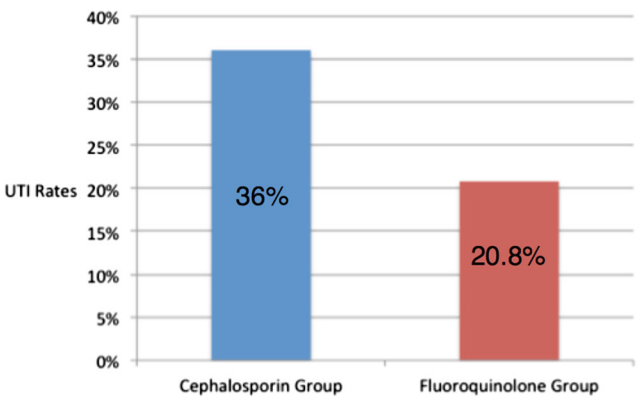

Fig. 1 Urinary tract infection rates were significantly lower in the fluoroquinolone (20.8%) versus the cephalosporin (36%) group, $p = 0.04$

Discussion

With OAB symptom improvement rates reported as high as 69% and incontinence improvement rates up to 58%, intravesically administered Botox® is a highly effective treatment option for many patients [11]. However, a commonly reported complication of Botox® is postprocedure UTIs. We previously reported a 35.1% UTI rate in patients who received a single dose of a third-generation cephalosporin IM at the time of Botox® injection, which substantiates previously published literature highlighting UTI rates after Botox® injections. This rate correlates with previously published UTI rates in neurogenic detrusor overactivity patients that range from 21 to 58% [12, 13]. However, this rate is slightly higher than UTI rates in idiopathic OAB patients, which range from 14 to 26% [14, 15].

Currently, there are few, if any, guidelines regarding preprocedure antibiotic prophylaxis for Botox® injections [4]. Randomized controlled trials show varying UTI rates depending on whether prophylactic antibiotics were given. Nonetheless, there is no consensus on prophylactic antibiotic use for Botox® injections. These antibiotics are not without side effects, as fluoroquinolones are associated with headaches, dizziness, and tendon swelling and tendon. Cephalosporins are associated with nausea, vomiting, thrush, and rash. Based on our previously reported UTI rate of 35.1% when a single dose of a third-generation cephalosporin was administered IM, we sought to determine if a 3-day course of antibiotics could decrease that rate. We chose this regimen based on the literature for transrectal prostate biopsy prophylaxis [16]. We found that patients had a decreased rate of postprocedure UTIs with a 3-day course of a fluoroquinolone. Furthermore, patients with a positive preprocedure urine culture could benefit from an even longer course of antibiotic prophylaxis prior to the Botox® injection.

Although this study has useful clinical implications, we recognize it is not without limitations, the primary one being its retrospective nature. Although we had two independent treatment groups standardized for age, BMI, history of diabetes, and pre- and postprocedure urine cultures, these different treatment regimens were not randomized but represent a change in our practice pattern from a single dose of cephalosporin IM to a 3-day course of a fluoroquinolone. Furthermore, we did not standardize the injection technique between the two urologists who performed them, and there may be a technical factor that could affect UTI rates. Lastly, we only studied a prolonged course of fluoroquinolones. A 3-day course of a cephalosporin per os may have yielded similar results. Of note, we performed this study before the US Food and Drug Administration (FDA) Drug Safety Communication advising of the risks associated with fluoroquinolone used to treat uncomplicated UTIs. Considerations for future studies could include a randomized controlled trial comparing multiple treatment regimens.

Conclusions

In our series, comparing two different antibiotic prophylaxis regimens for intravesically administered Botox® injection, we found a significantly lower rate of UTIs when patients received a 3-day course of a fluoroquinolone per os versus a single dose of a third-generation cephalosporin IM. Patients with a positive preprocedure culture may benefit from a 3-day course of prophylactic antibiotics.

Compliance with ethical standards

Conflicts of interest All authors have no financial disclosures or conflicts of interest to report.

All authors made significant contributions to the final manuscript, and all authors have approved the final submission.

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