Botulinum toxin for treatment of overactive bladder: Injection and complications

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INTRODUCTION

Botulinum toxin (BoNT) is a potent neurotoxin that is used for a variety of therapeutic indications (eg, dystonia, achalasia). Injections of BoNT into the detrusor muscle of the bladder are used to treat patients with bladder dysfunction related to both neurologic disorders and idiopathic causes. BoNT injection is most commonly used for symptoms of overactive bladder syndrome refractory to first-line therapies, including urgency urinary incontinence and detrusor overactivity.

This topic will review the procedure and adverse events associated with intravesical injection of BoNT for treatment of non-neurogenic/idiopathic lower urinary tract dysfunction. The terminology, indications, and clinical evaluation of lower urinary tract conditions are reviewed in a related topic. (See "Botulinum toxin for treatment of lower urinary tract conditions: Indications and clinical evaluation".)

In this topic, when discussing study results, we will use the terms "woman/en" or "patient(s)" as they are used in the studies presented. However, we encourage the reader to consider the specific counseling and treatment needs of transgender and gender expansive individuals.

MECHANISM OF ACTION AND FORMULATIONS

Briefly, BoNT is a neurotoxin that is produced by *Clostridium botulinum*. Two serotypes are commonly available for clinical applications: botulinum toxin type A (BoNT-A) and botulinum

toxin type B (BoNT-B). BoNT-A is most commonly used when treating lower urinary tract dysfunction. Common formulations of BoNT-A include onabotulinumtoxinA (onabotA, available in North America) and abobotulinumtoxinA (abobotA, available in Europe). Other available forms of botulinum toxin not commonly used in the bladder include incobotulinumtoxinA and rimabotulinumtoxinB.

An overview of the pharmacology of BoNT and the available formulations is presented in detail separately.

- (See "Botulinum toxin for treatment of lower urinary tract conditions: Indications and clinical evaluation", section on 'Formulations'.)
- (See "Overview of botulinum toxin for cosmetic indications", section on 'Mechanism of action'.)
- (See "Overview of botulinum toxin for cosmetic indications", section on 'Formulations'.)

CLINICIAN TRAINING

Basic cystoscopy skills are required for the injection of intradetrusor BoNT. Residency or fellowship training is sufficient for most providers to learn the procedure. Additionally, some manufacturers can organize one-on-one educational opportunities with experienced injectors in their area for providers new to intradetrusor BoNT injection. No formal certification is required to perform this procedure, but a certain number of proctored cases or demonstrations of training may be required for hospital credentialing purposes. There is no consensus standard for the minimum number of supervised cases for hospital credentialing.

PROCEDURE FOR ADMINISTRATION

Procedure video — (movie 1)

Patient preparation

Informed consent — In addition to reviewing routine procedure risks and anticipated benefits, we discuss the risks of urinary retention, urinary tract infection (UTI), and systemic absorption resulting in muscle weakness or respiratory collapse with all patients planning BoNT injection. This discussion should be documented on the consent form and in the medical record.

Catheterization training — Given the risk of urinary retention, all patients in our practice who are receiving intradetrusor BoNT injection for overactive bladder (OAB) symptoms are

counseled regarding the risk of requiring intermittent self-catheterization (or an indwelling catheter if preferred) for up to several weeks to months after the procedure. At least one guideline advises that only patients who are able and willing to perform self-catheterization be considered for BoNT injections [1]. The author's practice does not train patients on intermittent catheterization prior to the procedure since the majority of patients will not require it and it can be scary for many patients. Instead, the author discusses the up to 6.5 percent risk of temporary urinary retention after the procedure and options for management [2]. Those who are noted to have retention after the procedure can be instructed on the performance of intermittent catheterization and given the necessary supplies, as needed. However, one limitation to this approach is that not all patients who think they can learn self-catheterization may be able to do so. (See "Placement and management of urinary bladder catheters in adults", section on 'Clean intermittent catheterization'.)

Urinary tract infection detection, treatment, and prevention — All patients should be evaluated for UTI on the day of treatment prior to being anesthetized for the procedure [1]. While prophylactic antibiotics have been associated with reduced rates of UTI [3], the optimal regimen has not been established. Antibiotic options generally include nitrofurantoin or sulfamethoxazole-trimethoprim; selection is based on patient allergies, availability, and local resistance patterns. One study comparing rates of UTI between ciprofloxacin, starting one day prior to treatment continued for three days after, and a single intramuscular dose of ceftriaxone at the time of injection reported significantly lower rates of UTI with the three day oral regimen [3]. The author prescribes oral nitrofurantoin 100 mg twice daily for three days prior and three days after treatment for a total of six days of therapy, although other approaches may be used and this regimen is not universal. (See "Sampling and evaluation of voided urine in the diagnosis of urinary tract infection in adults".)

Patients noted to have a UTI prior to injection should be treated appropriately. One study reported that having had a UTI treated within 30 days of the procedure did not increase the risk of a posttreatment UTI. Available data suggest it is not necessary to delay BoNT treatment after treatment of an acute UTI [4]. (See "Acute simple cystitis in females".)

Anticoagulant therapy — While the approach needs to consider the risk of thromboembolism and bleeding for each patient, the author does typically stop antiplatelet and anticoagulation therapy for 24 hours prior to intradetrusor BoNT injections. Patients may restart their recommended therapy the evening of their procedure but should be counseled that they may note some hematuria for two to three days after the procedure. The approach to the perioperative management of patients receiving anticoagulants is presented in detail elsewhere. (See "Perioperative management of patients receiving anticoagulants".)

Analgesia — Both intravesical or oral medications are used for pain management prior to intradetrusor BoNT injections. Postoperatively, no additional pain medications are typically required but phenazopyridine may be taken as needed for bladder discomfort.

- **Intravesical** – Intravesical analgesia should be placed at least 20 minutes prior to the procedure. Many clinicians use a prefilled syringe of 10 mL of 2% lidocaine HCl injected into the bladder via the external urethral orifice. Some clinicians instill 20 to 30 mL of 1% lidocaine liquid into the bladder via a straight catheter. Both are reasonable; selection is determined by product availability and clinical preference.

- **Oral** – Oral phenazopyridine 200 mg can be given one to two hours prior to the procedure. In a trial of 111 participants comparing preoperative oral phenazopyridine with intravesical lidocaine (50 mL of 2% lidocaine), >90 percent of patients in both groups reported the pain as tolerable [5].

Administration

Drug preparation and dose — BoNT-A is supplied either as a liquid or as a powder that must be reconstituted in normal saline (0.9% sodium chloride) for injection [6]. Both the drug dose and administration site varies according to the lower urinary tract indication and neurologic status of the bladder (neurogenic or non-neurogenic). Typical injection doses for OAB range from 100 to 200 units [7]. For onabotulinumtoxinA (onabotA), the manufacturer advises against using more than 400 units in a three month interval [8]. The lethal dose of onabotA in humans is estimated to be 2800 units for a 70 kg person [9].

In our practice, we utilize onabotA; in the United States, onabotA is the primary form of the toxin utilized. In Europe, abobotulinumtoxinA is commonly available. Doses of the different forms of botulinum toxin A or B serotypes are **not** interchangeable, and care should be taken to insure that the appropriate dose is being used for the specific form of the toxin being used.

- (See "Botulinum toxin for treatment of lower urinary tract conditions: Indications and clinical evaluation".)

Detrusor injection — Intradetrusor injection of BoNT-A through a cystoscope is the most common injection approach for treatment of OAB. The toxin is injected into 4 to 20 sites throughout the detrusor muscle (figure 1).

- **Original injection template –** The template used in the original studies instructed the clinician to inject onabotA 200 units into 20 sites with 1 mL per site; this approach has become the technique advised by the manufacturer [2,10]. Subsequent studies demonstrated that the 100 unit dose provides significant efficacy with lower rates of urinary retention compared with 200 unit dosing [11,12]. The reconstituted 100 units of

onabotA can be injected into 10 locations with 1 mL per site. Based on patient symptoms, the dose can be escalated from 100 to 150 units to even 200 units, if needed. Dose increases are done with caution because of concern for possible increased incidence of antibody formation with higher amounts [2]. (See 'Development of resistance' below.)

- **Our approach** – We limit injections to five sites with 2.5 mL per site to minimize patient discomfort with fewer needle insertions. The first injection is in the midline just above trigone and two to the left and two to the right, similar to the video but with fewer total injections. A final injection of 1 to 2 mL of saline flush (to clear any toxin left in the needle) may be performed at the final injection site or into the trigone. This approach is based only on the author's anecdotal experience that patients experience less discomfort with fewer injection sites. Many providers still utilize the 20 injection technique with 0.5 mL per site with excellent treatment success.

- **Cystoscope options** – Injection with either a rigid or flexible cystoscope has been described, and the author uses both interchangeably [13-15]. Techniques to prevent backflow during injection of BoNT include filling the bladder to near capacity or use of ultrafine needles [16-18]. Precautions should be taken to avoid systemic injection (eg, withdrawing the needle first to confirm an absence of blood before injecting). The general technique for cystoscopy is described separately. (See "Diagnostic cystourethroscopy (cystoscopy) for gynecologic conditions".)

- **Role of trigone injection** – The optimal intravesical anatomic location and number of injections for BoNT-A remain unclear in part because multiple injection patterns have been evaluated in studies with small numbers of patients [19,20]. The concern is that injections into the trigone could cause vesicoureteric reflux (VUR) as a result of inhibition of the active trigonal anti-reflux mechanism [21,22]. In a meta-analysis of five trials that compared intra- and extra-trigone injection of BoNT-A in patients with detrusor overactivity, patients receiving intra-trigone injection had improved overall symptom scores (standardized mean difference -0.53, 95% CI -1.04 to -0.02), higher complete dryness rates (odds ratio 2.19, 95% CI 1.32-3.63), and lower frequency of incontinence episodes (weighted mean difference -0.85 per day, 95% CI -1.55 to -0.16) [23]. However, limitations of the included trials were small total number of patients (n = 334), a mix of male and female patients, high heterogeneity scores, and mixed etiologies of detrusor overactivity (both neurogenic and idiopathic). Rates of VUR were not reported. However, other adverse events were similar between groups (hematuria, bladder discomfort, elevated postvoid residual, general weakness, or UTI). A meta-analysis of eight studies (total of 419 patients) demonstrated significant improvement in symptom scores, higher complete dryness rates, and lower frequency of incontinence episodes in patients who underwent detrusor and trigone injection of

BoNT-A [23]. Additionally, there was no difference in efficacy or safety (ie, ureteral reflux) when comparing depth of BoNT-A injection, specifically intradetrusor (5 mm) versus suburothelial (3 mm) depth [23]. In our practice, we routinely inject the last flush injection into the trigone based on anecdotal improved outcomes.

- **Suburothelial injection** – Suburothelial administration alters sensory afferent transmission rather than causing motor-end plate paralysis but does not appear to more effectively improve urodynamic test measurements in patients with OAB. In a meta-analysis of three studies including a total of 85 patients, the mean differences in detrusor pressure at maximum flow rate and maximum cystometric capacity were not statistically different between women receiving intradetrusor and suburothelial injections, although the trend favored intradetrusor injection [23]. The previously mentioned meta-analysis including 419 patients examined the impact of injection depth on outcomes. Efficacy and safety (ie, ureteral reflux) were similar between intradetrusor (5 to 7 mm) versus suburothelial (3 mm) injection depths [23]. The author uses an injection depth of 3 mm while other experts prefer 5 mm.

Postinjection care — For postinjection care, we provide patients with a handout that includes the following information:

- All patients are reminded to complete their three days of twice daily antibiotics after the procedure.
- The treatment generally takes 7 to 10 days to take effect.
- Anticoagulation or antiplatelet therapy can be restarted the evening of the treatment.
- There are no restrictions on activities.
- No pain medicines are required, but phenazopyridine may be taken as needed for bladder discomfort.
- Patients are warned that they may have some blood in their urine or dysuria for one to two days after the procedure.
- Should patients have worsening of their bladder symptoms (ie, worse leakage, frequency) or burning when they urinate, they are encouraged to call the office. These patients may have a UTI or may be in acute retention, which can both be easily managed when recognized.
- Rates of urinary retention after intradetrusor BoNT injection range from 2 to 6 percent.
- Any patient who comes in saying "my leakage got worse after treatment" likely is in retention and should be evaluated for excessive postvoid residual by either ultrasound

or catheterization. If an elevated residual is confirmed, the patient should be taught intermittent self-catheterization. Temporary placement of an indwelling bladder catheter is done only if the patient is unable to perform self-catheterization.

ADVERSE EFFECTS AND PRECAUTIONS

Systemic absorption

Presentation — Although rare in patients undergoing bladder injections, all patients planning to receive BoNT injection should be warned of, and observed for, potential muscle weakness and pulmonary collapse [24]. Symptoms in adult patients can include dysphagia, ptosis, difficulty holding up the head, and leg weakness and numbness and are thought to occur due to spread of BoNT beyond the injection site [25]. Symptom onset has been reported from hours to weeks after injection of onabotulinumtoxinA (onabotA) [7]. BoNT-A injections should be used with caution in patients with neuromuscular disorders like myasthenia gravis, as the clinical effects may be exacerbated. Caution should also be observed with the use of concomitant aminoglycosides, agents interfering with neuromuscular transmission (curare-like agents), or muscle relaxants, as these substances have the possibility of potentiating the effect of BoNT-A. (See "Botulism", section on 'Clinical manifestations'.)

Systemic effects are rarely observed with lower urinary tract injection of BoNT. Weakness has been reported in 2 to 6 percent of patients treated with 1000 unit abobotulinumtoxinA (abobotA), as well as in some patients treated with 750 units abobotA or 300 units onabotA [6,16]. The reported duration of such symptoms varies from two weeks to three months [26].

Reversal — An antidote is available for overdoses but is only useful if given acutely and will not help long-lasting symptoms of muscle paralysis. With the small amounts of BoNT used for treatment of urinary tract disorders, it is not generally advised that clinicians administering BoNT have the antitoxin on hand. However, adequate supportive care facilities (ie, intensive care unit) and a local health department that has a supply of antitoxin should be accessible on the very rare chance that an overdose occurs. In children undergoing BoNT-A injections for otolaryngologic indications, symptom reversal with pyridostigmine has been reported [27]. (See "Botulism", section on 'Antitoxin therapies'.)

Antitoxin should be reserved for patients who demonstrate significant cardiopulmonary compromise thought to be secondary to BoNT toxin overdose. Administration of antitoxin should be performed in an acute care setting.

Urinary retention — Urinary retention is an established side effect of intradetrusor injection of BoNT-A [28]. Trials have reported an elevated postvoid residual (PVR) in 26 to 43 percent of

patients, 25 percent of whom were symptomatic and required self-catheterization [10,29,30]. In general, up to 6.5 percent is the quoted rate of urinary retention after intradetrusor injection of 100 units of BoNT-A [31]. A case series of 187 injections reported an overall urinary retention rate of 1.6 percent among a group of experienced clinicians [32]. In this study, urinary retention was defined as a PVR ≥350 mL and any patient with subjective voiding difficulty with a PVR or acute retention. In our practice, we utilize a similar definition of retention: any patient with a PVR >400 mL even if they are without symptoms, any patient with subjective complaints of voiding dysfunction with a PVR between 200 to 400 mL, or complete inability to void. The risk of posttreatment urinary retention does exhibit a positive dose-response relationship with the amount of BoNT administered [11,33-35]. Rates of urinary retention are dose related. In a placebo-controlled trial evaluating PVR incidence after injection across five different BoNT doses (range 50 to 300 U), PVR >200 mL occurred in nearly twice the number of patients receiving 200 units compared with 100 units (28.8 versus 14.5 percent, respectively [12]).

Symptoms of urinary retention usually begin approximately two weeks after treatment as it generally takes 7 to 10 days for the BoNT-A to take effect [36]. Other symptoms may include complaints of worsening urinary frequency, worse urinary incontinence, and urinary hesitancy. Symptoms of urinary retention and/or elevated PVR usually resolve in most patients within 9 to 12 weeks.

In our practice, all patients are seen at two to four weeks postinjection for urinary tract infection (UTI) testing with a dipstick and PVR. All patients are given written information at the time of their injection to contact us sooner should they have any acute worsening of their bladder symptoms before their scheduled follow-up appointment. At their follow-up appointment, those patients found to have urinary retention are offered instruction on intermittent self-catheterization or an indwelling Foley catheter. In our experience, older patients tend to choose an indwelling Foley catheter due to its ease of use and the temporary nature of this treatment. Patients who do require posttreatment catheterization are usually seen back in two to three weeks for a voiding trial or to review their intermittent self-catheterization PVR log. All catheterized patients are given a prophylactic antibiotic daily (nitrofurantoin 100 mg) to prevent UTI development while undergoing catheterization of any type.

We also routinely schedule all patients for repeat BoNT injection in six months at the time of treatment or at their two to four week follow-up visit. If retreatment is not required in six months, it can be deferred. We have found that by scheduling set follow-up treatments, we have significantly fewer patients lost to follow-up or encountering difficulty obtaining a timely appointment once their symptoms return.

Management of urinary retention is discussed separately. (See "Acute urinary retention".)

Urinary tract infection — UTIs are prevalent after BoNT-A injection, with rates ranging from 21 to 35 percent in the first year after initial injection, even with periprocedural antibiotic prophylaxis [33,37]. Being of female sex is associated with having post-procedure UTI rates in the upper range (33 to 35 percent) [11,33]. The increase in UTI risk applies to both acute and recurrent infections [38]. For comparison, UTIs occur in 5 to 15 percent of urologic patients receiving placebo injections of saline [38,39].

- **Comparison with sacral neuromodulation –** In a trial comparing BoNT-A injection with sacral neuromodulation for women with urgency urinary incontinence, in those women without a history of recurrent UTI at baseline, recurrent UTIs developed in 24 percent of the BoNT-A group compared with 10 percent of the sacral neuromodulation group [40].

- **Impact of BoNT dose –** Higher rates of UTI have been reported with increasing BoNT doses, which may reflect increasing use of catheterization in patients receiving higher doses. In a dose-ranging trial including 313 patients, those receiving 200 units versus 100 units of BoNT-A had higher rates of PVR >200 mL, higher rates of catheterization, and increased rates of subsequent UTI [12].

Development of resistance — A small number of patients undergoing repeat treatments with BoNT-A will develop antibody-mediated resistance to the clostridial proteins present in commercial preparations. The risk may increase with more frequent treatment intervals or higher drug doses [2]. One study reported that 4 to 10 percent of patients had detectable antibodies to the toxin after repeated treatment for cervical dystonia [41,42]. Risk factors for antibody development include a history of shorter dosing intervals, increasing number of booster doses (multiple doses given at short intervals), and higher overall treatment doses [42]. Precautions to reduce the risk of antibody formation include using the lowest dose of toxin required to achieve clinical effect and waiting at least eight weeks between treatments [9].

The presence of antibodies has been linked to reduced treatment efficacy. Pediatric studies have reported a correlation between treatment failure with intradetrusor BoNT-A and the presence of antibodies to the toxin. Of 17 pediatric patients who underwent multiple intradetrusor BoNT-A injection for neurogenic detrusor overactivity, all six of the nonresponders (35 percent overall) were noted to have clinically significant or borderline levels of BoNT antibodies [43]. The development of BoNT antibodies appears to be more common after multiple treatments, but a case of antibody formation after only one intradetrusor injection has been documented [44].

Hypersensitivity and other adverse effects — This is a rare adverse event overall. We do not routinely test for hypersensitivity prior to administering BoNT-A injections. However, if a patient has a known history of hypersensitivity, BoNT-A should be avoided.

Some patients have complained of transient constipation following BoNT treatment, particularly with BoNT-B [16]. Other mild symptoms associated with BoNT injection include flu-like symptoms, dry mouth, and malaise.

Blood product concerns — Onabotulinumtoxin contains human albumin as an ingredient. As a result, there is a very remote risk of transmission of a viral illness from the drug, although no cases have ever been reported. Additionally, the presence of a human blood product may be concerning to some patients for religious reasons [2].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Urinary incontinence in adults".)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Treatments for urgency incontinence in females (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **Mechanism and formulations –** Botulinum toxin (BoNT) is a neurotoxin that is produced by *Clostridium botulinum*. Two serotypes are commonly available for clinical applications: botulinum toxin type A (BoNT-A) and botulinum toxin type B (BoNT-B). BoNT-A is most commonly used for the treatment of overactive bladder. (See 'Mechanism of action and formulations' above.)

- **Pretreatment counseling –** Pretreatment patient preparation includes discussion of risks specific to the procedure, particularly urinary retention, urinary tract infection

(UTI), and systemic absorption. At least one guideline advises that only patients who are able and willing to perform self-catheterization be considered for BoNT injections in case urinary retention develops. The author does not advise teaching all patients the technique for self-catheterization prior to the procedure as it can provoke unnecessary anxiety. Patients should, however, be clearly counseled about the up to 6.5 percent risk that they might require temporary catheterization (indwelling or by self) for up to several months after treatment. (See 'Patient preparation' above.)

- **Drug preparation and dose** – BoNT-A is supplied either as a liquid or as a powder that must be reconstituted in normal saline (0.9% sodium chloride) for injection. The lethal dose of onabotulinumtoxinA in humans is estimated to be 2800 units for a 70 kg person. (See 'Drug preparation and dose' above.)

- **Injection** – Using a cystoscope, BoNT-A is injected into 4 to 20 sites throughout the detrusor muscle (figure 1). Precautions should be taken to avoid systemic injection (eg, withdrawing the needle first to confirm an absence of blood before injecting). (See 'Detrusor injection' above.)

- **Systemic effects** – Systemic effects of lower urinary tract injection of BoNT are rare, but muscle weakness and, rarely, respiratory depression can occur. Clinicians who administer this agent should counsel patients about these risks and monitor for systemic symptoms. (See 'Systemic absorption' above.)

- **Postinjection care** – Typical postinjection care includes three days of oral antibiotics, phenazopyridine as needed for bladder discomfort, and resumption of usual activities. Alarm findings include persistent gross hematuria, inability to void, dysuria, urinary urgency or frequency, and acute worsening of leakage. (See 'Postinjection care' above.)

- **Adverse outcomes** – Urinary retention and UTIs are the most common adverse events associated with BoNT injections into the bladder. While urinary retention can require a period of self-catheterization, it usually resolves by three months after injection. (See 'Urinary retention' above and 'Urinary tract infection' above.)

REFERENCES

1. Lightner DJ, Gomelsky A, Souter L, Vasavada SP. Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline Amendment 2019. J Urol 2019; 202:558.
2. Botox- onabotulinumtoxina injection, powder, lyophilized, for solution. US Food and Dru g Administration (FDA) approved product information. Revised June 2019. US National Li

brary of Medicine. www.dailymed.nlm.nih.gov (Accessed on August 30, 2019).

3. Houman J, Moradzadeh A, Patel DN, et al. What is the ideal antibiotic prophylaxis for intravesically administered Botox injection? A comparison of two different regimens. Int Urogynecol J 2019; 30:701.
4. Bickhaus JA, Bradley MS, Amundsen CL, et al. Does a Recent Urinary Tract Infection Increase the Risk of Postprocedure Urinary Tract Infection After Onabotulinum Toxin A? Female Pelvic Med Reconstr Surg 2021; 27:121.
5. Stewart LE, Siddique M, Jacobs KM, et al. Oral Phenazopyridine vs Intravesical Lidocaine for Bladder OnabotulinumtoxinA Analgesia: A Rancomized Controlled Trial (OPIL). Am J Obstet Gynecol 2022.
6. Smith CP, Chancellor MB. Emerging role of botulinum toxin in the management of voiding dysfunction. J Urol 2004; 171:2128.
7. Botox- onabotulinumtoxina injection, powder, lyophilized, for solution. US Food and Dru g Administration (FDA) approved product information. Revised September, 2019. US Nati onal Library of Medicine. www.dailymed.nlm.nih.gov (Accessed on June 07, 2019).
8. Botox- onabotulinumtoxina injection. US Food and Drug Administration (FDA) approved product information. Revised 9/2018. US National Library of Medicine. www.dailymed.nl m.nih.gov (Accessed on June 06, 2019).
9. Brin MF. Botulinum toxin: chemistry, pharmacology, toxicity, and immunology. Muscle Nerve Suppl 1997; 6:S146.
10. Brubaker L, Richter HE, Visco A, et al. Refractory idiopathic urge urinary incontinence and botulinum A injection. J Urol 2008; 180:217.
11. Visco AG, Brubaker L, Richter HE, et al. Anticholinergic therapy vs. onabotulinumtoxina for urgency urinary incontinence. N Engl J Med 2012; 367:1803.
12. Dmochowski R, Chapple C, Nitti VW, et al. Efficacy and safety of onabotulinumtoxinA for idiopathic overactive bladder: a double-blind, placebo controlled, randomized, dose ranging trial. J Urol 2010; 184:2416.
13. Schurch B, Stöhrer M, Kramer G, et al. Botulinum-A toxin for treating detrusor hyperreflexia in spinal cord injured patients: a new alternative to anticholinergic drugs? Preliminary results. J Urol 2000; 164:692.
14. Harper M, Popat RB, Dasgupta R, et al. A minimally invasive technique for outpatient local anaesthetic administration of intradetrusor botulinum toxin in intractable detrusor overactivity. BJU Int 2003; 92:325.
15. Kuo HC. Urodynamic evidence of effectiveness of botulinum A toxin injection in treatment of detrusor overactivity refractory to anticholinergic agents. Urology 2004; 63:868.

16. Apostolidis A, Dasgupta P, Denys P, et al. Recommendations on the use of botulinum toxin in the treatment of lower urinary tract disorders and pelvic floor dysfunctions: a European consensus report. Eur Urol 2009; 55:100.
17. Schulte-Baukloh H, Knispel HH. A minimally invasive technique for outpatient local anaesthetic administration of intradetrusor botulinum toxin in intractable detrusor overactivity. BJU Int 2005; 95:454.
18. Apostolidis A, Dasgupta R, Fowler CJ, Dasgupta P. A minimally invasive technique for outpatient local anaesthetic administration of intradetrusor botulinum toxin in intractable detrusor overactivity. BJU Int 2005; 96:917.
19. Emami M, Shadpour P, Kashi AH, et al. Abobotulinum - a toxin injection in patients with refractory idiopathic detrusor overactivity: injections in detrusor, trigone and bladder neck or prostatic urethra, versus detrusor - only injections. Int Braz J Urol 2017; 43:1122.
20. Avallone MA, Sack BS, El-Arabi A, et al. Less is more-A pilot study evaluating one to three intradetrusor sites for injection of OnabotulinumtoxinA for neurogenic and idiopathic detrusor overactivity. Neurourol Urodyn 2017; 36:1104.
21. Karsenty G, Elzayat E, Delapparent T, et al. Botulinum toxin type a injections into the trigone to treat idiopathic overactive bladder do not induce vesicoureteral reflux. J Urol 2007; 177:1011.
22. Schurch B, Schmid DM, Stöhrer M. Treatment of neurogenic incontinence with botulinum toxin A. N Engl J Med 2000; 342:665.
23. Jo JK, Kim KN, Kim DW, et al. The effect of onabotulinumtoxinA according to site of injection in patients with overactive bladder: a systematic review and meta-analysis. World J Urol 2018; 36:305.
24. Tincello DG, Kenyon S, Abrams KR, et al. Botulinum toxin a versus placebo for refractory detrusor overactivity in women: a randomised blinded placebo-controlled trial of 240 women (the RELAX study). Eur Urol 2012; 62:507.
25. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm175011.htm (Accessed on March 17, 2010).
26. Del Popolo G. Botulinum-A toxin in the treatment of detrusor hyperreflexia. Neurourol Urodyn 2001; 20:522.
27. Boerner RM, Young DL, Gnagi SH, et al. Pyridostigmine for the Reversal of Severe Adverse Reactions to Botulinum Toxin in Children. J Pediatr 2018; 194:241.
28. Malde S, Apostilidis A, Selai C, et al. Botulinum toxin A for refractory OAB and idiopathic urinary retention: Can phenotyping improve outcome for patients: ICI-RS 2019? Neurourol Urodyn 2020; 39 Suppl 3:S104.
29. Flynn MK, Amundsen CL, Perevich M, et al. Outcome of a randomized, double-blind, placebo controlled trial of botulinum A toxin for refractory overactive bladder. J Urol

2009; 181:2608.

30. Sahai A, Khan MS, Dasgupta P. Efficacy of botulinum toxin-A for treating idiopathic detrusor overactivity: results from a single center, randomized, double-blind, placebo controlled trial. J Urol 2007; 177:2231.
31. Botox package insert https://www.allergan.com/assets/pdf/botox_pi.pdf (Accessed on July 24, 2019).
32. Patel DN, Jamnagerwalla J, Houman J, et al. What is the true catheterization rate after intravesical onabotulinumtoxinA injection? Int Urogynecol J 2018; 29:1005.
33. Amundsen CL, Richter HE, Menefee SA, et al. OnabotulinumtoxinA vs Sacral Neuromodulation on Refractory Urgency Urinary Incontinence in Women: A Randomized Clinical Trial. JAMA 2016; 316:1366.
34. Chapple C, Sievert KD, MacDiarmid S, et al. OnabotulinumtoxinA 100 U significantly improves all idiopathic overactive bladder symptoms and quality of life in patients with overactive bladder and urinary incontinence: a randomised, double-blind, placebo-controlled trial. Eur Urol 2013; 64:249.
35. Nitti VW, Dmochowski R, Herschorn S, et al. OnabotulinumtoxinA for the treatment of patients with overactive bladder and urinary incontinence: results of a phase 3, randomized, placebo controlled trial. J Urol 2013; 189:2186.
36. Miotla P, Cartwright R, Skorupska K, et al. Urinary retention in female OAB after intravesical Botox injection: who is really at risk? Int Urogynecol J 2017; 28:845.
37. Dowson C, Watkins J, Khan MS, et al. Repeated botulinum toxin type A injections for refractory overactive bladder: medium-term outcomes, safety profile, and discontinuation rates. Eur Urol 2012; 61:834.
38. López Ramos H, Torres Castellanos L, Ponce Esparza I, et al. Management of Overactive Bladder With OnabotulinumtoxinA: Systematic Review and Meta-analysis. Urology 2017; 100:53.
39. Cox L, Cameron AP. OnabotulinumtoxinA for the treatment of overactive bladder. Res Rep Urol 2014; 6:79.
40. Amundsen CL, Komesu YM, Chermansky C, et al. Two-Year Outcomes of Sacral Neuromodulation Versus OnabotulinumtoxinA for Refractory Urgency Urinary Incontinence: A Randomized Trial. Eur Urol 2018; 74:66.
41. Greene P, Fahn S. Development on antibodies to botulinum toxin type A in patients with torticollis treated with injections of botulinum toxin type A. In: Botulinum and tetanus neurotoxins: Neurotransmission and biomedical aspects, DasGupta B (Ed), Plenum Press, New York 1993.
42. Greene P, Fahn S, Diamond B. Development of resistance to botulinum toxin type A in patients with torticollis. Mov Disord 1994; 9:213.

43. Schulte-Baukloh H, Herholz J, Bigalke H, et al. Results of a BoNT/A antibody study in children and adolescents after onabotulinumtoxin A (Botox®) detrusor injection. Urol Int 2011; 87:434.

44. Schulte-Baukloh H, Bigalke H, Heine G, et al. Antibodies against botulinum neurotoxin type A as a cause of treatment failure after the first detrusor injection. Urology 2007; 69:575.e13.

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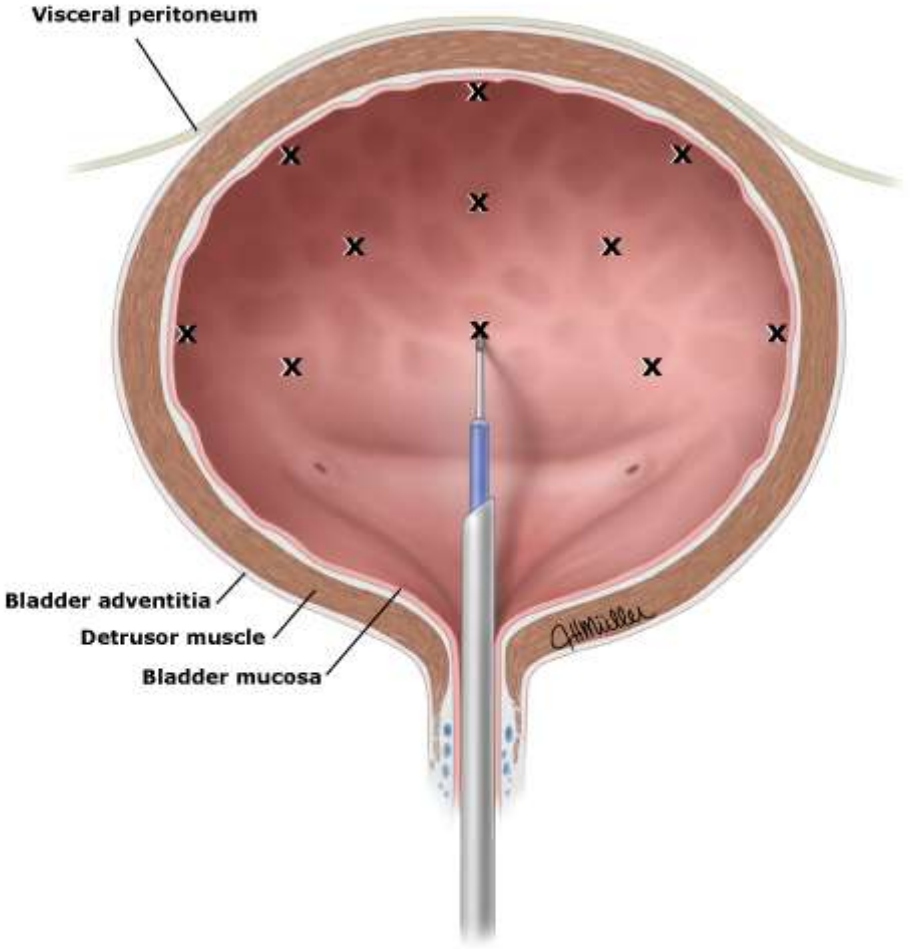
GRAPHICS

Botulinum toxin detrusor injection



Graphic 64588 Version 3.0

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