ORIGINAL RESEARCH

The intravesical injection of highly purified botulinum toxin for the treatment of neurogenic detrusor overactivity

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Abstract

Introduction: We aimed to assess safety and efficacy of incobotulinumtoxinA for the treatment of neurogenic detrusor overactivity (NDO).

Methods: We identified patients with NDO confirmed on urodynamics (UDS) and reported urgency incontinence (UI) in those who received intravesical incobotulinumtoxin A injection for neurogenic bladder between November 2013 and May 2017. Parameters studied were daytime frequency, daily incontinence episodes, daily pad use, clean intermittent catheterization (CIC) volumes, symptom scores (UDI6, IIQ7, PGII), and complications.

Results: We examined 17 male patients who met inclusion criteria and underwent incobotulinumtoxinA injection. Mean age was 61.2 ± 15.4 years. Fourteen patients (82%) were taking oral antimuscarinics prior to the incobotulinumtoxin A injection. There were improvements in the following parameters: average daily pads (4.5 to 3.3, p=0.465), daily urinary frequency (9.4 to 4.6, p=0.048), daily incontinent episodes (2.5 to 0.4, p=0.033), CIC volumes (400 to 550 mL, p=0.356), hours in between CIC (3.6 to 5.2, p=0.127), and the validated questionnaires UDI6 (30.6 to 7.4, p=0.543) and IIQ7 (52.4 to 6.8, p=0.029). There were no documented symptomatic urinary tract infections (UTIs) within 30 days of injection or reports of de novo urinary retention. Nine of 17 patients (53%) reported being dry at their first postoperative visit.

Conclusions: In this preliminary pilot study of a small cohort of males with NDO and UI, significant improvements were seen following incobotulinumtoxinA injection in daily frequency, incontinence episodes, hours in between CIC, and quality of life. Larger-scale and long-term studies are required to confirm these results, but initial findings are promising for wider use of this formulation.

Introduction

Intradetrusor injection of botulinum toxin type A is an effective treatment for overactive bladder (OAB) and neurogenic detrusor overactivity (NDO).[1] Botulinum toxin A is one of seven serotypes of toxins produced by Clostridium botulinum. There are several commercial forms of botulinum toxin A, all with similar toxin structures, but with slightly different protein modifications.[2] One commercial form of botulinumtoxinA, onabotulinumtoxin A or Botox®, is FDA-approved for urinary incontinence (UI) and overactive bladder (OAB) symptoms.[3] Multiple pivotal studies have shown the effectiveness of onabotulinumtoxinA in idiopathic OAB syndrome.[4,5] In patients with NDO, multiple trials have also demonstrated effectiveness of onabotulinumtoxinA for UI. In a phase 3, double-blind, randomized, multicenter, placebo-controlled trial by Ginsberg et al, 416 patients with spinal cord injuries or multiple sclerosis (MS) were randomized to either onabotulinumtoxinA or placebo.[6] OnabotulinumtoxinA significantly reduced UI episodes/week and improved urodynamic parameters and quality of life compared to placebo in patients with NDO.[6] In an extension study, benefit was still seen at four years, with repeat treatments as needed.[7] AbobotulinumtoxinA (Dysport®) and rimabotulinumtoxinB (NeuroBloc®) are other neurotoxin forms available in the U.S. that have been studied for use in the bladder. In a prospective study of 207 patients with idiopathic OAB by Ravindra et al, abobotulinumtoxinA was found to be inferior to onabotulinumtoxinA for the treatment of idiopathic OAB, as it had twice the rate of symptomatic urinary retention requiring clean intermittent catheterization (CIC).[8] It was shown these toxins were not interchangeable at equal doses.[8] Peyronnet et al reported on the efficacy and safety of intradetrusor injection of abobotulinumtoxinA 750 U in patients with NDO.[9] The success rate, which was a composite parameter including continence, number of catheterizations, and lack of DO, was 64.2. In 2007, Hirst et al studied the effect of intradetrusor rimabotulinumtoxinB in a non-randomized study including 25 patients with both

idiopathic and neurogenic detrusor activity (five with NDO due to transverse myelitis and MS). Subjective improvements were seen in a small portion of the idiopathic detrusor activity patients, with two NDO patients reporting no improvement.[10] This study showed a short duration of action of rimabotulinumtoxinB, with effects wearing off by 10 weeks in most of their patients.[10]

IncobotulinumtoxinA, commercially known as Xeomin®, is another commercially available form of botulinumtoxinA and was approved by the FDA in 2011 for cervical dystonia and blepharospasm.[11] It is a highly purified form of this toxin with no complexing proteins.[11] It has been postulated that given its purity, there is less immunogenicity in patients. Potentially decreased immunogenicity of this botulinumtoxinA may be particularly advantageous in the neurogenic population, who often receive injections in multiple different organs. However, it is unclear if the differences in immunogenicity are clinically relevant in this setting. There are no maximum dosing ranges published by the manufacturer for the intravesical administration of incobotulinumtoxin. For limb spasticity, incobotulinum toxin has shown to be as effective as onabotulinumtoxinA, with a comparable adverse event profile when a clinical conversion ratio of 1:1 was used.[12] In limb spasticity, dosage of up to 800 U have been used without compromising safety or tolerability.[13]

In contrast to onabotulinumtoxin, incobotulinumtoxin can be stored at room temperature for ≤36 months before reconstitution. There is also evidence that equal product efficacy with 25 °C storage (room temperature) can be maintained one week post-reconstitution.[14] IncobotulinumtoxinA and onabotulinutoxinaA were found to have comparable effects on DO and similar adverse event profiles, with an almost 1:1 conversion ratio.[15,16] Most studies on NDO outcomes have involved Dysport® and Botox®.[17] Dosing differences and interchangeability between toxin types in terms of clinical impact remains an important area of future research.[17]

Additionally, incobotulinumtoxinA is generally less expensive than onabotulinumtoxinA, making this an attractive and more cost-effective alternative for OAB patients with UI. Tilden et al showed that incobotulinumtoxinA was more cost-effective compared to onabotulinumtoxinA in patients with blepharospasm and cervical dystonia in the Australian healthcare system.[18] They found an incremental cost/quality-adjusted life year gained of $25 588 in incobotulinumtoxinA and $23 794 in onabotulinumtoxinA.[18] The effectiveness of this more purified, less immunogenic incobotulinumtoxinA for NDO with UI has not yet been well-studied.

In 2015, incobotulinumtoxinA was approved in the U.S. for upper limb spasticity in adults. Other non-FDA indications include chronic sialorrhea and temporary improvement in the appearance of moderate to severe glabellar lines with corrugator and/or procerus muscle activity.[19] Some benefits of incobotulinumtoxinA vs. placebo for upper limb spasticity

were shown in the post-stroke population by Kanovsky et al in a prospective, non-randomized study of 148 people completed in 23 European sites.[20] IncobotulinumtoxinA injections resulted in significant and sustained improvements in muscle tone and disability in this patient population.[20]

To date, this formulation has not yet been well-studied for use in the bladder. In a study by Conte et al, the objective was to investigate whether bladder dysfunction in MS patients depends on suprapontine or spinal lesions. Twenty-five MS patients who were spontaneously voiding and had low postvoid residual (PVR) underwent intradetrusor injection with 100 U incobotulinumtoxinA.[21] No significant differences were seen in the Hoffman reflex after injection. However, there were improvements in volumes at first, normal, strong desire, dyssynergic activity, and voiding diary parameters.[21]

The primary objective of this study was to assess the safety and effectiveness of incobotulinumtoxinA in patients with NDO and UI.

Methods

Study design and participants

After institutional review board approval, patients with neurogenic bladder who had undergone intradetrusor incobotulinumtoxinA injections between November 2013 and May 2017 were identified in a retrospective manner at a single Veteran's Affairs Medical Center (VAMC). All patients had previously failed antimuscarinic therapy and had NDO and UI. There was no strict definition used to define antimuscarinic failure. It was assumed that patients who had persistent bothersome voiding symptoms while on the medical therapy were refractory.

All patients underwent detailed history, physical examination, urinalysis, urine culture, and video urodynamics (UDS) prior to injection.

Video UDS were done according to International Continence Society (ICS) standards, with fluid-filled system and external transducers at the reference level of the upper edge of the symphysis pubis using Medtronic® UDS equipment.[22] The baseline bladder capacities of all patients were determined from the most recent UDS preceding the first injection of incobotulinumtoxinA.

Patients with injections of onabotulinumtoxinA within one year of incobotulinumtoxinA treatment were excluded. Of note, patients with prior onabotulinumtoxinA injections were receiving incobotulinumtoxinA due to the new hospital standard of administering this less expensive formulation. However, there were varying levels of efficacy and satisfaction with the onabotulinumtoxinA among the patients. We recorded demographic patient information and baseline clinical data. Additionally, the patients were assessed for

average voiding parameters at home, including daily pad use, frequency, incontinence episodes, and CIC volumes. Patient responses to the following validated questionnaires were also recorded: Incontinence Impact Questionnaire (IIQ-7), Urogenital Distress Inventory (UDI-6), and Patient Global Improvement of Incontinence (PGI-I). The averages of the IIQ-7 and UDI-6 surveys were converted to a 100-point scale. While there are no globally accepted cutoffs, higher scores on the 100-point scale represent higher impact and distress scores.[23] Patients returned for a followup visit within 2–4 weeks following the incobotulinumtoxinA injection and all patients were evaluated. Complications within 30 days of incobotulinumtoxinA injection and de novo urinary retention were recorded.

Statistical analyses

Chi-squared and Fisher's exact test was used for categorical variables and the Mann-Whitney U-test for continuous variables. All data analyses were done using IBM SPSS software, Version 23 (IBM Corporation, Armonk, NY, U.S.). Multivariate analysis was attempted but limited due to the small sample size. Statistical analysis was done with SPSS Statistics 23.0.

Procedure technique

Patients with positive urine cultures were treated with appropriate antibiotics prior to injection. Patients were placed in the dorsal lithotomy position and administered either local anesthesia or conscious sedation, depending on patient anxiety level and/or history of autonomic dysreflexia from other local procedures. Incobotulinumtoxin was diluted in normal saline, with 200 U diluted in 20 mL and 300 U diluted in 30 mL. Given this was a retrospective study with a heterogeneous group of urologists, the amount of incobotulinumtoxin administered was at the discretion of the respective providers. A rigid cystoscope was inserted through the urethra under direct vision and 1 mL injections were distributed throughout the bladder wall, including at the trigone.

Results

Patient demographics and baseline characteristics

A total of 17 participants with NDO (confirmed on UDS) and refractory UI were included in this study. All participants were male with mean age of 61.2±15.4 years. Prior to incobotulinumtoxin injection, six (35%) patients had indwelling Foley catheter, six (35%) were voiding on their own, and five (30%) were doing CIC. Eleven patients had spinal cord injury (SCI): four thoracic spine injuries and seven cervical

spinal cord injuries. One patient had a primary diagnosis of MS with a history of stroke. Two patients had diagnoses of Parkinson's disease (one with a concurrent thoracic SCI) and four had a history of stroke (with one also having MS). Five (29%) patients overall had a concurrent diagnosis of severe traumatic brain injury (TBI).

Two (12%) patients had diabetes mellitus (DM) and three (18%) patients had a history of chronic kidney disease (CKD). Table 1 summarizes baseline characteristics of the participants. Comorbidities were captured with the Charlson age comorbidity indices, reported in Table 1. In terms of previous conservative management, 82% of the participants had been using oral antimuscarinics regularly for at least one month prior to their first incobotulinumtoxinA injection.

Eight (47%) participants had undergone previous injections with onobotulinumtoxinA (greater than one year before incobotulinumtoxinA injection). Nine (53%) patients had repeat injections of incobotulinumtoxinA after their initial injection in the study period. Seven (41%) participants had injections with 300 units and 10 patients (59%) received 200 units.

Overall, 100% of patients underwent repeat intradetrusor incobotulinumtoxin within one year of the initial procedure. Median time to first repeat injection was 34 weeks (inter-

Table 1. Patient demographics	
Total patients	17 (all male)
Age	61.2±15.4 (2181)
Race, n (%)	
White	14 (82%)
African American	3 (18%)
Voiding status, n (%)	
Voiding	6 (35%)
Chronic in-dwelling tube	6 (35%)
CIC	5 (30%)
Neurological diagnosis, n (%)	
SCI	11 (65%)
Cervical SCI	7 (41%)
Thoracic SCI	4 (24%)
MS	1 (6%)
Parkinson's disease	2 (12%)
Stroke	4 (24%)
TBI	5 (29%)
Bladder capacity (mL), median (IQR)	215 (200–462.5)
Baseline creatinine (mg/dL), median (IQR)	0.8 (0.6–1.2)
Charlson age comorbidity index	4.3 ± 2.3 (median 4, IQR 2–6.5)
Incobotulinumtoxin A injection history, n (%)	
Prior onobotulinumtoxin or incobotulinumtoxin injections before study period	8 (47%)

CIC: clean intermittent catheterization; IQR: interquartile range; MS: multiple sclerosis; SCI: spinal cord injury; TBI: traumatic brain injury.

quartile range [IQR] 29–64). Twenty-four percent of patients underwent more than one repeat injection within one year of the initial study injection.

Clinical outcomes

Postoperative data was obtained from two weeks to one month after the patients' first incobotulinumtoxinA injection. Table 2 illustrates outcomes following incobotulinumtoxinA injection in patients who were already on a CIC regimen. Following treatment, the median for daily pads was stable at 0. The median number of incontinent episodes decreased from two to zero after treatment. Median volumes with CIC improved, from 400 to 550, as well as median number of hours between CIC, from four to six, pre- and post-treatment. Average scores for the UDI6 and IIQ7 surveys also improved pre- and post-treatment. All patients in this group were dry following their initial injection, with no one requiring pads after treatment.

Table 3 outlines similar outcomes in patients who were voiding prior to this study. Following treatment, the median for daily pads was 12 from 7.5. The median number of incontinent episodes decreased from 2.5 to one after treatment. Average scores for the UDI6 and IIQ7 surveys also improved pre- and post-treatment. Two patients vs. none were dry after treatment. All patients in this group were dry following their initial injection, with no one requiring pads after treatment.

Finally, Table 4 summarizes results for the subgroup with chronic Foley catheters and suprapubic tubes. Creatinine levels remained stable over time. Average IIQ7 and UDI-6 survey scores were also markedly improved in this group. All patients were dry after an initial course of treatment.

Ten participants overall completed PGI-I surveys postoperatively and results are shown in Fig. 1. In the non-voiding group, three participants completed the survey. One participant each (33%) endorsed feeling a little better, much better, and very much better, totaling approximately 33% for each response. In the voiding group, four participants (66.6%) endorsed feeling very much better after their initial incobotulinumtoxinA injection. One participant each (16.7%) endorsed feeling a little better and much better. Of note, no participants reported no improvement or feeling worse after treatment. Nine of the seventeen patients (53%) reported being dry at their first postoperative visit. One patient who initially had an indwelling Foley prior to incobotulinumtoxinA treatment was able to successfully initiate and perform CIC following intravesical treatment. This was a patient with bilateral Grade 4 vesicoureteral reflux and a small bladder capacity of about 215 mL on UDS. Of note, this patient had resolution of hydronephrosis on renal ultrasound following intravesical treatment with incobotulinumtoxin.

No patients had documented symptomatic urinary tract infections (UTIs) or other adverse effects in the 30 days following treatment.

Discussion

In this cohort of patients with neurogenic bladder and NDO, there were clinically significant improvements in frequency and daily incontinent episodes after an initial injection with incobotulinumtoxinA. Additionally, in patients doing CIC, significant improvements were seen in time between catheterization. Furthermore, significant improvements were seen in quality of life scores. All patients, whether voiding or not, reported global impression of improvement following treatment. The initial results of this pilot study provide promising evidence that incobotulinumtoxinA can be a reasonable

Table 2. Outcomes following incobotulinumtoxin A injection in CIC patients

	Pre-incobotulinumtoxinA Median (IQR)	Post-incobotulinumtoxinA Median (IQR)
Daily pads	0 (0–6)	0 (0–0)
# incontinent episodes daily	2 (1–3)	0 (0–0.25)
Creatinine (mg/dL)	0.7 (0.6–0.8)	0.5 (0.4–0.75)
CIC volumes (mL)	400 (300–500)	550 (400–700)
Hours in between CIC	4 (3–4)	6 (4–6)
UDI6 scores (mean ± SD)	31.5±27.4	8.9±11.5
IIQ7 scores (mean ± AD)	64.3±33.3	9.5±11.2
Patients requiring pads, n (%)	3 (60%)	0 (0%)
Dry patients, n (%)	0 (0%)	5 (0%)

CIC: clean intermittent catheterization; IQR: interquartile range; SD: standard deviation.

Table 3. Outcomes following incobotulinumtoxinA injection in voiding patients

	Pre-incobotulinumtoxinA Median (IQR)	Post-incobotulinumtoxinA Median (IQR)
Daily pads	7.5 (0.75–16.5)	12 (0–18)
Daily frequency	11 (8.5–18)	4 (2–10)
# incontinent episodes daily	2.5 (1–5.5)	1 (0–2)
Creatinine	1.75 (1.2–1.9)	1.7 (1.1–1.9)
UDI-6 scores (mean ± SD)	36.1±43.1	35.1±56.2
IIQ7 scores (mean ± SD)	52.4±40.4	33.3±57.7
Patients requiring pads, n (%)	3 (50%)	2 (33%)
Dry patients, n (%)	0 (0%)	2 (33%)

CIC: clean intermittent catheterization; IQR: interquartile range; SD: standard deviation.

Table 4. Pre and post-incobotulinumtoxinA injection outcomes in patients with chronic indwelling tube (Foley catheters and suprapubic catheters)

	Pre-incobotulinumtoxinA Median (IQR)	Post-incobotulinumtoxinA Median (IQR)
Creatinine mg/dL	0.9 (0.5–1.1)	0.9 (0.6–1)
IIQ7 mean scores (mean ± SD)	39.3±27.8	1.6±2.8
UDI-6 mean scores (mean ± SD)	25±27.4	8.4±11.8
Patients requiring pads, n (%)	1 (17%)	1 (17%)
Dry patients, n (%)	0 (0%)	2 (33%)

CIC: clean intermittent catheterization; IQR: interquartile range; SD: standard deviation.

alternative to onabotulinumtoxinA in patients with UI and other OAB symptoms.

To our knowledge, this is the first study of its kind to examine the effects of incobotulinumtoxinA on bladder diary, urodynamic parameters, and quality of life measures in a range of patients with NDO, both voiding and not voiding. Only one other study has examined the effect of intradetrusor injection of incobotulinumtoxinA. Conte et al completed a study investigating the neurophysiological effects of 100 U incobotulinumtoxinA in patients with NDO due to MS who were spontaneously voiding with low PVR.[21] The primary aim of the study was to investigate whether in MS bladder dysfunction is due to suprapontine or spinal lesions, by examining change in the soleus Hoffman reflex. This study showed improvements in first, normal, and strong desire during UDS, with no change in the Hoffman reflex.[21] This population of neurogenic bladder patients was very differ-

ent from our patient population, comprised mostly of SCI patients, of which only 35% were voiding spontaneously. Furthermore, the dosage of medication used was different.

Our results are very similar to those observed in patients with NDO who have undergone intradetrusor injection of onabotulinumtoxinA. Cruz et al randomized patients with MS (n=154) or SCI (n=121) to placebo, 200 U onabotulinumtoxinA, or 300 U onabotulinumtoxinA. At week six, significant improvements were seen compared to placebo in incontinence episodes per week, urodynamics parameters, and quality of life.[24]

This is the first paper to look at voiding parameters after any botulinumtoxin formulation in the bladder of TBI patients, despite neurogenic bladders being common sequelae of TBI. Prior literature has studied outcomes of botulinumtoxinA injection in these patients but in upper and lower limb spasticities. Fock et al did a prospective, non-randomized study in seven patients with a history of TBI secondary to motor vehicle trauma and suffering from spastic equinus.[25] Patients were injected with onabotulinumtoxinA into the heads of the gastrocnemius and soleus muscles only, totaling 300 U, and six of the seven patients showed significant improvements in walking speed and stride length at 12 weeks.[25] In this study, significant improvements were seen in quality of life following intradetrusor injection of incobotulinumtoxinA; 90% of patients who completed the PGI-I postoperatively noted some degree of improvement within the month after their injections. These findings are in keeping with other studies examining the effects of intradetrusor injection of botulinum toxin. Ginsberg et al showed a significant improvement in impact on quality of life in neurogenic bladder patients, which was not impacted by
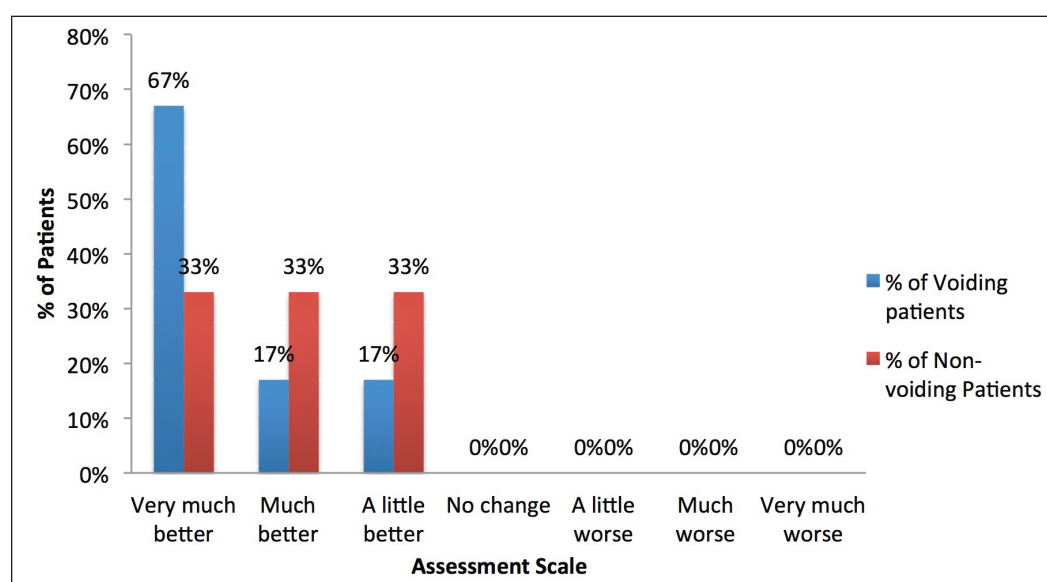
Fig. 1. Patient Global Impression of Improvement Scores, voiding vs. non-voiding patients.

the initiation of CIC.[6] Similarly, Nitti et al showed that in idiopathic OAB patients, there were significant improvement in patients' quality of life even as early as two weeks postoperatively.[5] Finally, Chapple et al described significant improvements in the impact on quality of life survey and the King's Health Questionnaire within 12 weeks of treatment in idiopathic DO patients in a randomized trial.[26] These significant changes in quality of life are important factors to consider, especially with neurogenic patients who are often managing multiple medical conditions. Perceived effects of treatments by the patients enhance the therapeutic benefits. This positive feedback is encouraging, as we seek to expand the use of incobotulinumtoxinA for OAB and UI.

Well-established side effects after intradetrusor botulinumtoxinA injections include urinary retention, UTI, dysuria, and bacteriuria. Less frequent side effects include hematuria and pyrexia.

In the first 12 weeks following treatment, Ginsberg et al described UTI incidence of 28% in both treatment groups (200 U and 300 U), with hematuria and pyrexia occurring in 5% or less in both treatment groups.[6] Nitti et al also described adverse events in the first 12 weeks following injection, showing an incidence of 15.5%.[5] No patients reported adverse effects in our study. This may partly be due to small sample size and short duration of followup. However, it is also our practice to treat bacteriuria prior to intradetrusor injection of incobotulinumtoxinA, which may limit the incidence of symptomatic UTI. Overall, the procedure was well-tolerated.

Limitations

One limitation in this study includes the fact that it was retrospective. This pilot study has a small sample size and would need to be powered appropriately on a larger scale to draw firmer conclusions. The study population was limited to men because of the site location (VAMC), so generalizability to women should be further explored in larger studies. Future larger, placebo-controlled, longer-term studies are needed and other populations that should be studied include patients with idiopathic OAB. Other limitations include variations in followup times from 2–4 weeks. Additionally, no post-injection UDS data was obtained in patients with NDO.

Conclusions

In this preliminary pilot study of a small cohort of males with NDO and UI, significant improvements were seen in daily frequency, number of incontinence episodes, hours in between CIC, and quality of life scores following incobotulinumtoxinA injection. Larger-scale and long-term studies are required to confirm these results, but initial findings are promising for wider use of this formulation.

References

1. Nambiar A, Lucas M. Chapter 4: Guidelines for the diagnosis and treatment of overactive bladder (OAB) and neurogenic detrusor overactivity (NDO). *Neurourol Urodyn* 2014;33Suppl3:S21. https://doi.org/10.1002/nau.22631
2. Santos-Silva A, da Silva CM, Cruz F. Botulinum toxin treatment for bladder dysfunction. *Int J Urol* 2013;20:956. https://doi.org/10.1111/iju.12188
3. Mangera A, Andersson KE, Apostolidis A, et al. Contemporary management of lower urinary tract disease with botulinum toxin A: A systematic review of Botox (onabotulinumtoxinA) and Dysport (abobotulinumtoxinA). *Eur Urol* 2011;60:784. https://doi.org/10.1016/j.eururo.2011.07.001
4. Mangera A, Apostolidis A, Andersson KE, et al. An updated systematic review and statistical comparison of standardized mean outcomes for the use of botulinum toxin in the management of lower urinary tract disorders. *Eur Urol* 2014;65:981. https://doi.org/10.1016/j.eururo.2013.10.033
5. 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. https://doi.org/10.1016/j.juro.2012.12.022
6. Ginsberg D, Gousse A, Keppenne V, et al. Phase 3 efficacy and tolerability study of onabotulinumtoxinA for urinary incontinence from neurogenic detrusor overactivity. *J Urol* 2012;187:2131. https://doi.org/10.1016/j.juro.2012.01.125
7. Kennelly M, Dmochowski R, Schulte-Baukloh H, et al. Efficacy and safety of onabotulinumtoxinA therapy are sustained over 4 years of treatment in patients with neurogenic detrusor overactivity: Final results of a long-term extension study. *Neurourol Urodyn* 2017;36:368. https://doi.org/10.1002/nau.22934
8. Ravindra P, Jackson BL, Parkinson RJ. Botulinum toxin type A for the treatment of non-neurogenic overactive bladder: Does using onabotulinumtoxinA (Botox®) or abobotulinumtoxinA (Dysport®) make a difference? *BJU Int* 2013;112:94. https://doi.org/10.1111/bju.12028
9. Peyronnet B, Roumiguie M, Castel-Lacanal E, et al. Efficacy and safety of the first and repeated intradetrusor injections of abobotulinum toxin A 750 U for treating neurological detrusor overactivity. *World J Urol* 2016;34:755. https://doi.org/10.1007/s00345-015-1666-5
10. Hirst GR, Watkins AJ, Guerrero K, et al. Botulinum toxin B is not an effective treatment of refractory overactive bladder. *Urology* 2007;69:69. https://doi.org/10.1016/j.urology.2006.09.005
11. Walker TJ, Dayan SH. Comparison and overview of currently available neurotoxins. *J Clin Aesthet Dermatol* 2014;7:31.
12. Scaglione F. Conversion ration between Botox®, Dysport®, and Xeomin® in clinical practice. *Toxins (Basel)* 2016;8:65. https://doi.org/10.3390/toxins8030065
13. Wissel J, Bensmail D, Ferreira J, et al. Safety and efficacy of incobotulinumA doses up to 800 U in limb spasticity the Tower study. *Neurolofy* 2017;88:1321. https://doi.org/10.1212/WNL.0000000000003789
14. Soares DJ, Dejoseph LM, Zuliani GF, et al. Impact of post-reconstitution room temperature storage on the efficacy of incobotulinumtoxinA treatment of dynamic lateral canthus lines. *Dermatol Surg* 2015;41:712. https://doi.org/10.1097/DSS.0000000000000365
15. Jost WH, Kohl A, Brinkmann S, et al. Efficacy and tolerability of a botulinum toxin type A free of complexing proteins (NT 201) compared with commercially available botulinum toxin type A (BOTOX) in healthy volunteers. *J Neural Transm (Vienna)* 2005;112:905. https://doi.org/10.1007/s00702-004-0234-8
16. Scaglione F. Conversion ratio between Botox®, Dysport®, and Xeomin® in clinical practice. *Toxins (Basel)* 2016;8. https://doi.org/10.3390/toxins8030065
17. Linsenmeyer TA. Use of botulinum toxin in individuals with neurogenic detrusor overactivity: State-of-the-art review. *J Spinal Cord Med* 2013;36:402. https://doi.org/10.1179/2045772313Y.0000000116
18. Tilden D, Guarnieri C. Cost-effectiveness of incobotulinumtoxinA with flexible treatment intervals compared to onabotulinumtoxinA in the management of blepharospasm and cervical dystonia. *Value Health* 2016;19:145. https://doi.org/10.1016/j.jval.2015.11.009
19. Merz Pharmaceuticals. Prescribing information for XEOMIN, 2018. Available at: http://www.xeomin.com/wp-content/uploads/xeomin-full-prescribing-information.pdf. Accessed May 12, 2020.
20. Kanovsky P, Slawek J, Denes Z, et al. Efficacy and safety of treatment with incobotulinumtoxinA (botulinum neurotoxin type A free from complexing proteins; NT 201) in post-stroke upper limb spasticity. *J Rehabil Med* 2011;43:486. https://doi.org/10.2340/16501977-0796

21. Conte A, Giannantoni A, Gubbiotti M, et al. Intradetrusorial botulinum toxin in patients with multiple sclerosis: A neurophysiological study. *Toxins (Basel)* 2015;7:3424. https://doi.org/10.3390/toxins7093424

22. Rosier P, Schaefer W, Lose G, et al. International Continence Society good urodynamic practices and terms 2016: Urodynamics, uroflowmetry, cystometry, and pressure-flow study. *Neurourol Urodyn* 2017;36:1243. https://doi.org/10.1002/nau.23124

23. Shumaker SA, Wyman JF, Uebersax JS, et al. Health-related quality of life measures for women with urinary incontinence: The Incontinence Impact Questionnaire and the Urogenital Distress Inventory. Continence Program in Women (CPW) Research Group. *Qual Life Res* 1994;3:291. https://doi.org/10.1007/BF00451721

24. Cruz F, Herschorn S, Aliotta P, et al. Efficacy and safety of onabotulinumtoxinA in patients with urinary incontinence due to neurogenic detrusor overactivity: A randomized, double-blind, placebo-controlled trial. *Eur Urol* 2011;60:742-50. https://10.1016/j.eururo.2011.07.002

25. Fock J, Galea MP, Stillman BC, et al. Functional outcome following Botulinum toxin A injection to reduce spastic equinus in adults with traumatic brain injury. *Brain Inj* 2004;18:57. https://doi.org/10.1080/0269905031000149498

26. 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 randomized, double-blind, placebo-controlled trial. *Eur Urol* 2013;64:249. https://doi.org/10.1016/j.eururo.2013.04.001

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