Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2017, 7, 915-921
http://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

Very Low, Real-Time Rate of Urinary Retention after Intradetrusor Botox® for Non-Neurogenic Overactive Bladder

Kirin K. Syed[1], Christopher S. Gomez[2], Angelo E. Gousse[1*]

[1]Bladder Health and Reconstructive Urology Institute, Miramar, FL, USA
[2]Female Urology, Neurourology, Voiding Dysfunction and Reconstruction, Department of Urology, University of Miami, Miami, FL, USA
Email: *a.gousse@miami.edu

How to cite this paper: Syed, K.K., Gomez, C.S. and Gousse, A.E. (2017) Very Low Real Time Rate of Urinary Retention after Intradetrusor Botox for Non-Neurogenic Overactive Bladder. *Open Journal of Obstetrics and Gynecology*, **7**, 915-921.
https://doi.org/10.4236/ojog.2017.78092

Received: December 10, 2016
Accepted: August 18, 2017
Published: August 21, 2017

Abstract

Introduction: According to the most recent AUA/SUFU guidelines, intradetrusor onabotulinumtoxinA (BTN/A) is a standard, evidence strength grade B, third line treatment option for refractory non-neurogenic overactive bladder (OAB). Urinary retention is the most common clinically significant reported side effect ranging from 5.4% to 43% in previous studies. The aim of this study was to investigate the real-time rate of urinary retention in patients treated with BTN/A for refractory non-neurogenic OAB in a multi-institutional study. **Methods:** Retrospective chart review identified 71 patients who were treated with 100U BTN/A for refractory non-neurogenic OAB from August 2011 to July 2015 at two institutions. Using a flexible cystoscope, 100U Botox® reconstituted with 10 ml normal saline was administered. Injections of 1 ml (10 units/mL) were administered in 10 evenly distributed sites sparing the trigone. Pre and post BTN/A post-void residuals (PVR) were reviewed. Urinary retention was defined as PVR > 200 mL requiring clean intermittent catheterization (CIC). **Results:** After exclusion, the study group consisted of 66 patients with a mean age of 67 years and 30% were men. Mean pre and post-procedural PVR were 14.06 mL and 69.21 mL. Eight patients (12.12%) were noted to have elevated PVR > 200 mL post injection however only one patient (female) required initiation of CIC. The rate of urinary retention was 1.5% (N = 1). There was no correlation with age, history of previous radiation, diabetes or prior use of a neuromodulator device. **Conclusions:** To the best of our knowledge, this is the first study to demonstrate a very low risk of *real-time* urinary retention rates in appropriately selected patients treated with BTN/A for refractory non-neurogenic OAB outside of a clinical trial setting.

Keywords

Intradetrusor OnabotulinumtoxinA, Refractory Non-Neurogenic Overactive Bladder, Urinary Retention, OAB, Urinary Retention Rate, Botox®

1. Introduction

Non-neurogenic or idiopathic overactive bladder (OAB) is a symptom complex, which is defined by the International Continence Society (ICS) standardization committee as urgency, with or without urgency incontinence, usually with frequency and nocturia, in the absence of proven infection or other obvious pathology [1]. Although non-life threatening, it is a chronic, costly and debilitating disorder and can have a significant impact on quality of life.

While no standard definition exists for "refractory OAB", it is a term often used to describe patients who have either failed or were unable to tolerate conservative therapy and/or anticholinergic/beta 3 agonist therapy. Available third line options now include pharmacologic use of intradetrusor onabotulinumtoxinA [Botox®, Allergan, Inc., Irvine, CA, USA/(BTN/A)].

Safety, efficacy and durability of BTN/A have been demonstrated in previously published randomized controlled trials [2] [3] [4]. However, one of the most common side effects of therapy is urinary retention. In previously published literature, urinary retention was reported to occur in 5% - 43% of patients and was shown to be dose-dependent [2]-[7]. The purpose of this study was to assess the real-time rate of urinary retention in clinical practice after administration of BTN/A for refractory non-neurogenic OAB in a multi-institutional clinical setting.

2. Methods

Retrospective chart review identified 71 patients who were treated with 100 units (U) BTN/A for refractory non-neurogenic OAB from August 2011 to July 2015 at two institutions. These institutions included a 178-bed community hospital, part of a large health care network that averaged more than 70,000 admissions in 2016. The second institution is a large 900-bed academic center that averages greater than 25,000 annual admissions.

Given the retrospective nature of the study, along with confidential chart review in accordance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and the use of pre-existing patient data and records, our study met criteria for exemption from further ethical clearance. Therefore approval from institutional review boards was not pursued.

Our technique was in accordance with previously described principles [8] [9] [10]. Using a flexible cystoscope, 100 U of Botox® reconstituted with 10 ml normal saline was administered in an office setting without use of general anesthesia. Local anesthesia using 20 mL of 1% Lidocaine was utilized at one institution. Using a 27 gauge injection needle, aliquots of 1 ml (10 units/mL) were adminis-

tered in 10 evenly distributed sites sparing the trigone. In accordance with previously published randomized control trials [2], pre and post BTN/A post void residuals (PVR) were reviewed at 2 and 6 weeks post treatment or at any other visit depending on clinical need. A PVR ≥ 200 mL was considered elevated. Clean intermittent catheterization (CIC) was initiated at PVR ≥ 200 ml with associated symptoms or PVR ≥ 350 mL regardless of symptoms. Urinary retention was defined as any PVR of ≥200 mL that required CIC in accordance with previously published methodology in the phase 3 randomized controlled trail by Nitti *et al.* [2].

Secondary variables assessed included age, history of previous radiation, diabetes, and prior use of a neuromodulator device [Interstim™ neuromodulator (Medtronic, Minneapolis, MN, USA) or peripheral tibial nerve stimulation].

Exclusion criteria included elevated pre-procedural PVR ≥ 100 mL, history of recurrent urinary tract infections (UTIs), predominant stress incontinence symptoms, lack of follow up, patients who were unable or unwilling to perform CIC, patient's with neurogenic bladder and/or any nervous system pathology that may induce lower urinary tract symptoms such as Parkinson's disease, Alzheimer's disease, cerebrovascular accidents, spinal cord injuries etc.

3. Results

After exclusion, the study group consisted of 66 patients with a mean age of 67 years ± 1.61 years. Of the 66 patients, 46 (69.7%) were female and 20 (30%) were men. Mean pre and post-procedural PVR was 14.06 mL ± 24.06 mL [95% CI (19.86, 8.26)] and 69.21 mL ± 1.61 mL [95% CI (90.26, 48.16)]. Eight patients (12.1%) were noted to have elevated PVR ≥ 200 mL post injection and all were asymptomatic. Only one patient (female) required initiation of CIC. The rate of urinary retention was 1.5% (N = 1). Demographics of the eight patients with elevated PVRs are listed in Table 1. Data was obtained by detailed and confidential review of retrospective patient records.

Demographics of the single patient who required CIC for elevated PVR are outlined in Table 2. The patient did not have any history of diabetes or radiation.

Table 1. Demographics of the eight patients with elevated PVRs.

Demographics of Patients with Elevated PVRs	
PVR > 200	8 (12.1%)
Male	3 (37%)
Female	5 (62.5%)
Average age	69.88 years ± 4.3 years
Diabetes	1 (12.5%)
Radiation	0
Prior sacral neurostimulator (Interstim™)	3 (37%)
Prior peripheral tibial nerve stimulation	0 (0%)
Avg pre-procedural PVR	26 mL ± 13.14 mL [95% CI (51.75, 0.25)]
Avg post-procedural PVR	249.88 mL ± 22.55 mL [95% CI (294.08, 205.67)]
Use of local anesthesia (Lidocaine)	Per investigator discretion

Table 2. Clinical characteristics of single patient with urinary retention.

Demographics of Single Patient with Urinary Retention	
Female	Yes
Age	83 years
Diabetes	No
Radiation	No
Prior sacral neurostimulator (Interstim™)	Yes
Prior peripheral tibial nerve stimulation	No
Pre-procedural PVR	70 mL
Post-procedural PVR	379 mL
Use of local anesthesia (Lidocaine)	No

However she did fail prior sacral neuromodulation (Interstim™). Her pre-procedural PVR was 70 mL and CIC was initiated for asymptomatic elevated post-procedural PVR of 379 mL. In addition, no local anesthesia was utilized during injection.

Secondary variables assessed included age, history of previous radiation, diabetes and prior use of a neuromodulator device (Interstim™ neuromodulator or peripheral tibial nerve stimulation). Of the 66 patients, 15 (22.7%) were diabetic, 12 (18%) had history of prior radiation, 10 (15%) had prior sacral neuromodulation (Interstim™) and one (0.1%) had previous peripheral tibial nerve stimulation.

4. Discussion

In 2007, OAB was one the most common urologic disorders, accounting for more than 2 million physician office visits in the United States [11]. The negative impact on health-related quality of life (HRQL) has shown to have a considerable social and financial impact.

Less work productivity, higher rates of depressive symptoms, less sexual satisfaction, erectile dysfunction and lower levels of overall health have been shown to be correlated with OAB [12] [13]. In addition, the economic footprint associated with this condition is staggering. Total national cost, including community and institutional costs, was estimated at $65.9 billion in 2007 and is expected to increase to $82.6 billion by 2020 [14].

Finding an ideal treatment for OAB has been a challenge in the realm of voiding dysfunction. While no perfect treatment exists, there are several options available. An algorithm has been set forth by the AUA/SUFU Guidelines [15] [16]. The guidelines state that third line therapies should be pursued if first line (fluid management and behavioral modification) and second line (anticholinergics/beta 3 agonists) are insufficient, unable to be tolerated and/or do not result in acceptable symptom improvement. Third line treatment options include neuromodulation and chemical denervation. Chemodenervation with pharmacologic use of onabotulinumtoxinA (Botox®, BTN/A) was approved by the FDA

in 2013 for use in patients with OAB who did not adequately respond to oral medications. It was recently upgraded and received the stronger rating of "standard" (strength of evidence grade B) by the amended 2014 AUA/SUFU guidelines [15] [16].

Our study evaluated the real-time rate of urinary retention in clinical practice outside of a regimented clinical study. We demonstrate that the real-time rate of urinary retention in clinical practice is far less than previously reported. Another unique aspect of our study is that 30% of the study population was male, which is significantly higher than the 8% - 10% previously reported [2] [6].

Osborn et al [5] recently reported an overall urinary retention rate of 35% in a clinical study consisting of patients with non-neurogenic OAB that were treated with 100 - 200 U of BTN/A. They defined urinary retention as any patient who was started on daily intermittent catheterization or had an indwelling catheter placed. Bladder drainage with CIC or indwelling catheter was recommended based on the patient's urinary complaints and PVR or on clinical judgment of asymptomatic urinary retention based on PVR alone. In that study, 23% of patients were noted to have post-procedure PVRs between 100 and 200 mL and 92% of the patients with a PVR of >200 ml were started on CIC. Demographic review of the patient population in the study revealed that 24% of the patient population was male, 26% underwent BTN/A under local anesthesia, 63% received 100 U and 37% received 200 U. Further subgroup analysis revealed a 21% rate of urinary retention in patients who received 100 U and had a preoperative PVR of <100 mL. The authors further concluded "going forward the true rate of urinary retention in clinical practice will likely exceed the rates demonstrated in the recent clinical trials".

However our study does not support these findings. Despite having a high number of male patients (30%), only one patient in our study group required initiation of CIC yielding a urinary retention rate of 1.5%. This is significantly lower than any previously reported studies. In addition, there was no correlation with age, history of previous radiation, diabetes or prior use of neuromodulation.

We hypothesize that our favorable rate of urinary retention may differ from previous studies due to differences in technique, inclusion of patients who received >100 units of BTN/A for refractory non-neurogenic OAB in prior studies, difference in threshold to initiate CIC, definition of urinary retention and patient selection.

Some limitations of our study include the retrospective nature and small patient cohort. Although our study population is small, we feel that there is a paucity of information on real-time adverse effects of BTN/A in actual clinical practice. Therefore we believe that our data is still interesting and highlights the importance of patient selection. We believe that careful patient selectivity plays a major role in dramatically diminishing the chances of urinary retention.

Further evaluation in a prospective fashion with a large cohort of patients should be undertaken to verify our results.

5. Conclusion

To the best of our knowledge, ours is the first study to demonstrate an extremely low rate of *real-time* urinary retention in patients treated with BTN/A for refractory non-neurogenic OAB outside of a clinical trial setting. We hypothesize that our favorable rate of urinary retention may differ from previous studies due to differences in technique, inclusion of patients who received >100 units of BTN/A for refractory non-neurogenic OAB in prior studies, difference in threshold to initiate CIC, definition of urinary retention and patient selection.

References

[1] Haylen, B.T., de Ridder, D., Freeman, R.M., *et al.* (2010) An International Urogynecological Association (IUGA)/International Continence Society (ICS) Joint Report on the Terminology for Female Pelvic Floor Dysfunction. *Neurourology and Urodynamics*, **29**, 4. https://doi.org/10.3109/9781439807217-111

[2] Nitti, V.W., Dmochowski, R., Herschorn, S., *et al.* (2012) OnabotulinumtoxinA for the Treatment of Patients with Overactive Bladder and Urinary Incontinence: Results of a Phase 3, Randomized, Placebo Controlled Trial. *Journal of Urology*, **189**, 2186-2193.

[3] Chapple, C., Sievert, K.-D., Macdiarmid, S., *et al.* (2013) 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. *European Urology*, **64**, 249-256.

[4] Chartier-Kastler, E., Nitti, V., De Ridder, D., Sussman, D., Sand, P., Sievert, K., Chapple, C., Charmaine, J., Magyar, A. and Radomski, S. (2015) Durable Improvements in Urinary Incontinence and Positive Treatment Response in Patients with Idiopathic Overactive Bladder Syndrome Following Long-Term OnabotulinumtoxinA Treatment: Final Results of 3.5-Year Study. *Progrès en Urologie*, **25**, 739.

[5] Osborn, D.J., Kaufman, M.R., Mock, S., Guan, M.J., Dmochowski, R.R. and Reynolds, W.S. (2015) Urinary Retention Rates after Intravesical OnabotulinumtoxinA Injection for Idiopathic Overactive Bladder in Clinical Practice and Predictors of This Outcome. *Neurourology and Urodynamics*, **34**, 675-678. https://doi.org/10.1002/nau.22642

[6] Dmochowski, R., Chapple, C., Nitti, V.W., *et al.* (2010) Efficacy and Safety of onabotulinumtoxinA for Idiopathic Overactive Bladder: A Double-Blind, Placebo Controlled, Randomized, Dose Ranging Trial. *Journal of Urology*, **184**, 2416-2422.

[7] Brubaker, L., Richter, H.E., Visco, A., *et al.* (2008) Refractory Idiopathic Urge Urinary Incontinence and Botulinum a Injection. *Journal of Urology*, **180**, 217-222.

[8] Shenot, P.J. and Mark, J.R. (2013) Intradetrusor onabotulinumtoxinA Injection: How I Do It. *The Canadian Journal of Urology*, **20**, 6649-6655.

[9] BOTOX Clinical Data Overview. https://www.botoxforincontinence.com/assets/pdf/Clinical_Data_Overview.pdf

[10] Cox, L. and Cameron, A.P. (2014) OnabotulinumtoxinA for the Treatment of Overactive Bladder. *Research and Reports in Urology*, **6**, 79-89.

[11] Litwin, M.S. and Saigal, C.S. (2012) Urologic Diseases in America. US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, US Government Printing Office, NIH Publication No. 12-7865, Washington DC.

[12] Coyne, K.S., Sexton, C.C., Irwin, D.E., *et al.* (2008) The Impact of Overactive Bladder, Incontinence and Other Lower Urinary Tract Symptoms on Quality of Life, Work Productivity, Sexuality and Emotional Wellbeing in Men and Women: Results from the EPIC Study. *BJU International*, **101**, 1388-1395. https://doi.org/10.1111/j.1464-410X.2008.07601.x

[13] Coyne, K.S., Sexton, C.C., Thompson, C.L., *et al.* (2012) Impact of Overactive Bladder on Work Productivity. *Urology*, **80**, 97-103.

[14] Ganz, M.L., Smalarz, A.M., Krupski, T.L., *et al.* (2010) Economic Costs of Overactive Bladder in the United States. *Urology*, **75**, 526-532.

[15] Gormley, E.A., Lightner, D.J., Burgio, K.L., Chai, T.C., Clemens, J.Q., Culkin, D.J., *et al.* (2012) Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline. http://www.auanet.org/guidelines/overactive-bladder-(oab)-(aua/sufu-guideline-2012-amended-2014)

[16] Gormley, E.A., Lightner, D.J., Burgio, K.L., Chai, T.C., Clemens, J.Q., Culkin, D.J., *et al.* (2012) Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline. *Journal of Urology*, **188**, 2455-2463.