

Promoting patient followup treatment with intra-detrusor onabotulinumtoxinA for overactive bladder

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Abstract

Introduction: We aimed to characterize patient-related factors that promote followup of repeat onabotulinumtoxinA treatments for overactive bladder via a mixed-methods approach.

Methods: A retrospective chart review was conducted for patients who received intra-detrusor injection of onabotulinumtoxinA at our institution from 2011–2018, who were then surveyed to evaluate their experience, knowledge, and perceptions regarding onabotulinumtoxinA treatment and followup. Patients who received one onabotulinumtoxinA treatment and patients who underwent multiple treatments were compared to assess followup rates following initial treatment, group characteristics, patient comfort, and patient knowledge of needed retreatment.

Results: A total of 29.3% of patients received a single treatment and 70.7% of patients received multiple treatments. There was no difference in clinical, demographic, or intake variables between groups. Patients receiving multiple treatments reported having their first procedure in the operating room and reported greater improvement in symptoms and procedure comfort. This group was also more likely to understand that repeat treatments are necessary than those undergoing one treatment.

Conclusions: No research to date has systematically explored patient-reported factors that promote retreatment of onabotulinumtoxinA for overactive bladder. This novel, mixed-methods approach indicates that patient comfort and patient knowledge were the strongest predictors of previous retreatment and anticipated retreatment, suggesting concrete avenues for improved peri-procedural patient counselling and education.

Introduction

Overactive bladder (OAB) is a clinical syndrome characterized by urinary urgency with or without urinary frequency, nocturia, or urge incontinence. It is common, with an international prevalence of approximately 11–25%.^{1–4} Anticholinergic medications and beta-3 agonists are usually employed as oral pharmacological therapy when first-line treatments of behavioral modification and pelvic floor exercises fail.⁵ However, many patients fail medical therapy due to symptom recurrence, intolerable side effects, and poor efficacy.^{6–8} Intra-detrusor injection of onabotulinumtoxinA is recommended by the American Urological Association and European Association of Urology as third-line therapy for refractory OAB.^{5,9} The average length of symptom improvement is 7–9 months.^{8,10,11} Therefore, patients require repeat treatments to achieve sustained benefit.

Studies examining long-term outcomes of intra-detrusor onabotulinumtoxinA treatments are limited; however, failure to return for repeat treatments seems to be consistently seen. Prospective studies with followup periods of four years show as many as 39–49% of patients fail to return for additional management.^{10,11} One retrospective review evaluated the 10-year discontinuation rate for patients receiving bladder onabotulinumtoxinA for neurogenic bladder and found a discontinuation rate of 50.9%.¹² It has been found that a high proportion of patients who stop treatments do so very early in the treatment course. Dropout rates in two retrospective studies ranged from 24–67% after a single injection.^{13,14}

Although some studies do cite adverse events, intolerance, and lack of efficacy as primary reasons for dropout,^{12–14} high dropout rates are not completely explained by these factors: reported rates of dropout for adverse events and lack of efficacy in two large, prospective studies were low, specifically between 3–5% and 2–6%, respectively.^{10,11} Other reasons for dropout cited in the literature are often vague and include categories such as “personal reasons,”

“personal convenience,” “non-compliance,” “patient decision,” or “other.”^{10-12,15} These “other” reasons for dropout have not been well-characterized, and it is often unclear how these reasons for dropout were elicited.

One retrospective study attempted to analyze factors associated with discontinuing onabotulinumtoxinA treatments and found that young age (<50 years) and baseline incontinence (compared with being “dry” before therapy) were associated with discontinuation of onabotulinumtoxinA treatment.¹³ However, this retrospective chart review did not include critical and relevant patient-reported factors, which are essential to understanding why a patient may stop treatments for “personal reasons” or “non-compliance.”

In our study, we sought to better characterize what patient-related factors may promote followup for repeat onabotulinumtoxinA treatments, which has previously been understudied. The primary objective of this study was to investigate what factors promote patient followup for repeat therapy after a single onabotulinumtoxinA treatment. We used a novel, mixed-method approach, using both survey data to obtain patient-reported perceptions and outcomes, as well as a clinical chart review to obtain relevant clinical factors. We examined several potentially critical variables that have not yet been holistically evaluated in the current literature: patient demographics, relevant urological history, travel, cost/insurance, patient comfort during the procedure, patient pain and relevant procedure outcomes, and patient knowledge that repeated treatment is needed for sustained effects.

Methods

This study was approved by the institutional review board at our institution. We used a mixed methods approach; the authors first performed a retrospective chart review of the electronic medical records of patients treated at the authors' institution who underwent intra-detrusor onabotulinumtoxinA injections between 2011 and 2018 (n=174 patients eligible for inclusion). Basic demographic information was extracted (i.e., age), as was urological diagnosis and presence of neurological condition/s. Information about the onabotulinumtoxinA injection treatment was also collected, including date of first onabotulinumtoxinA treatment, number (if any) of repeat treatments, date(s) of followup and re-treatment, dosage(s), and postvoid residual (PVR) at first post-procedure visit.

Fig. 1 shows a flowchart of participant recruitment, consent, and inclusion. Attempts to contact all 174 eligible patients were made via mail and phone. Of these, 98 were reached via phone or mail. Of those, 65 consented to complete the survey portion of this study, 19 were reached but declined to participate, and 14 were reached and consented to participate, but were not included in the final analyses

(i.e., missing data, did not remember receiving onabotulinumtoxinA injection treatments, had a single treatment but were scheduled for retreatment.) Thus, data from 65 patients was included in the final analyses (66.3% response rate of those reached, 37.4% of all eligible patients). There were no differences in demographic or outcome variables for those that were reached or not reached (except for n=11 deceased), or for those who consented to participate vs. did not provide consent (all $p>0.1$).

Patients at our institution had their first injection done in the clinic unless there were concerns regarding: 1) blood pressure; 2) presence of neurogenic bladder; or 3) the patient requested injection be done in the operating room due to pain issues. In clinic, only local anesthesia for the injections was used. Operating room anesthesia varied but was typically monitored by anesthesia care and primarily consisted of local anesthesia. The education given by providers to patients consisted of verbal education at the time of counselling during the study period.

Participants were asked to complete a short, internally developed survey* assessing variables that might promote or reduce rates of followup. This survey asked participants to provide: demographic variables (gender, ethnicity, English language status, education, income), knowledge that repeat treatment was needed, and information regarding their previous visit(s) (i.e., location: operating room vs. clinic, insurance coverage, travel time). They were also asked to rate their levels of pain (on a scale of 1–10) during the procedure, after the procedure, and in terms of improvement of symptoms (how long did symptoms last after treatment). Duration of response (in months) and prevalence of adverse events (urinary tract infection within one week after procedure, inability to urinate requiring use of a catheter to drain the bladder, blood in the urine, pain with urination, fatigue, other), and plans for re-treatment were also collected. All data analysis was performed using SPSS Statistics software (IBM SPSS Statistics for Windows, version 26.0. Armonk, NY, U.S.; IBM Corp). Data are presented as group means or proportions (percentages). Per study objectives, analyses were performed comparing group differences (those who had repeated treatments vs. those who had a single treatment) via Chi-squared tests for categorical variables or t-tests for independent group comparisons of continuous variables. Statistical analyses were performed to assess the following: 1) followup rates after first onabotulinumtoxinA treatment at our institution; 2) characteristics of those who received followup injections vs. those who did not; 3) patient comfort

*No validated questionnaire or survey examining the patient-relevant (i.e., non-clinical) factors for seeking onabotulinumtoxinA treatment for OAB currently exists. Thus, project leads, with combined experience in clinical treatment of OAB patients, knowledge of relevant patient factors, and experience in clinical research study design, developed the questionnaire used in this study. Although not the objective of this current study, future work could validate this measurement for standardized use in this patient population. Limitations relevant to the use of this type of survey have been included in the Discussion.

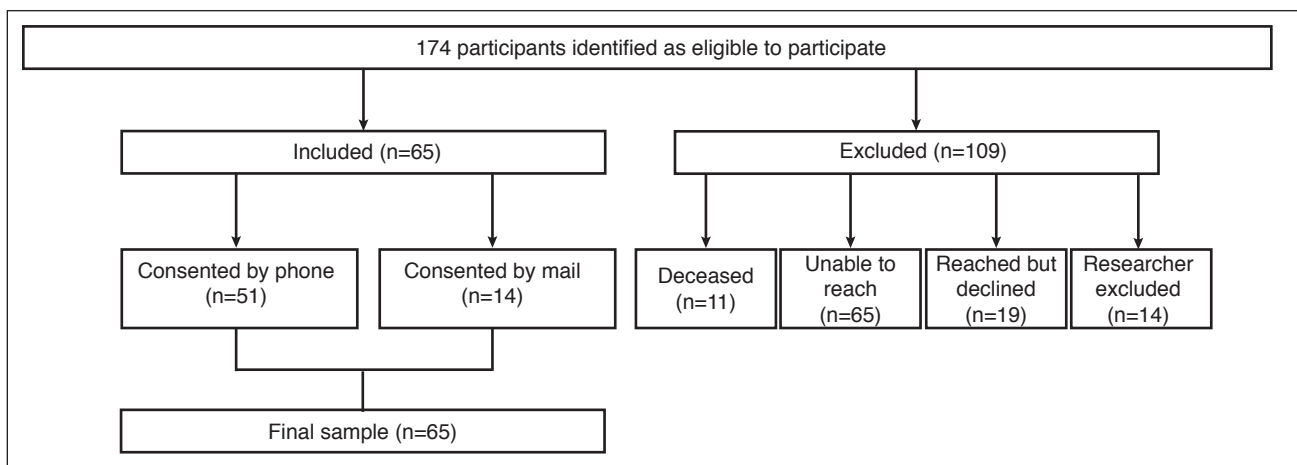


Fig. 1. Breakdown of included and excluded participants. Survey data from 65 patients was included in the final analyses (66.3% response rate of those reached, 37.4% of all eligible patients treated at our institution).

during and after their treatment; and 4) patient knowledge of onabotulinumtoxinA and need for re-treatment and impact on clinical outcomes.

Results

Demographic information for the patients included in this study appear in Table 1. Seventeen (29.3%) patients received a single treatment and 41 patients (70.7%) received more than one treatment (mean 3.7, range 2–10). This initial 70.7% followup (29.3% dropout) after a single treatment falls on the low end of previously reported followup rate ranges of onabotulinumtoxinA injections for OAB.^{13,14} With similar dropout rates for those patients having received a single onabotulinumtoxinA treatment, we then examined what factors impacted patients receiving followup treatments vs. patients who discontinued treatment.

Patient history

Demographic characteristics of the overall sample and categorized by single vs. multiple treatments are summarized in Table 1. There was no difference in demographic variables by repeat treatment: age ($p=0.368$), gender ($p=0.383$), ethnicity ($p=0.643$), English language status ($p>0.9$), education ($p=0.510$), or income ($p=0.539$). There was also no difference in any of the intake or clinical variables as a function of repeat treatments: diagnosis ($p=0.161$), presence of neurological condition ($p=0.620$), insurance coverage of treatment ($p=0.551$), travel time ($p=0.363$), length to followup ($p=0.199$). This indicates that patient characteristics (demographic, clinical/medical) did not impact whether or not patients sought retreatment.

Patient comfort

Table 2 shows a breakdown of outcomes by patient re-treatment. Patients who underwent repeat treatments were significantly more likely to have their first treatment in the operating room compared to patients who underwent a single treatment (44.4% vs. 17.6%, $p=0.02$). Patients who underwent their first treatment in the operating room reportedly experienced less pain during the procedure ($p=0.009$). Patients did not differ in post-procedure pain, improvement in symptoms, or prevalence of adverse events based on location of treatment (all $p>0.09$).

Strikingly, patients who received multiple treatments (re-treatment) reported a greater improvement in their symptoms over time ($p=0.001$), with no difference in rates of adverse events or related urological outcomes (e.g., rates of urinary tract infection, urinary retention, hematuria, dysuria, fatigue, positive urine culture, PVR; all $p>0.09$), nor duration of response ($p=0.934$).

Patient knowledge

Patients who received multiple treatments were more likely to understand that repeat treatments were necessary ($p=0.002$); 97.4% of patients who received multiple treatments answered affirmatively that repeat onabotulinumtoxinA treatments were needed to control symptoms, while only 68.8% of the patients in the single treatment group answered affirmatively ($p=0.002$). There were no significant differences in demographic or medical history between patients who did and did not understand that repeat onabotulinumtoxinA treatments are needed (all $p>0.5$).

Table 3 depicts a breakdown of outcomes by knowledge of necessary re-treatment. Knowledge of necessary re-treatment impacted several outcome variables of interest: pain after treatment ($p=0.069$), improvements in symptoms

Table 1. Patient demographic characteristics

(%)	All patients	Single treatment	Multiple treatments
Age, mean (SD)	58.2 (14.9)	62.0 (10.7)	58.4 (14.9)
Gender			
Male	9 (17.0%)	4 (23.5%)	5 (13.9%)
Female	44 (83.0%)	5 (13.9%)	31 (86.1%)
Ethnicity			
Caucasian	42 (79.2%)	15 (88.2%)	27 (75.0%)
Hispanic	1 (1.9%)	0	1 (2.8%)
African American	7 (10.8%)	1 (5.9%)	6 (16.7%)
Native American	1 (1.9%)	0	1 (2.8%)
Asian/Pacific Islander	2 (3.8%)	1 (5.9%)	1 (2.8%)
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)
English language status			
English is first language	53 (100.0%)	17 (100%)	36 (100%)
Language other than English is first language	0 (0.0%)	0 (0.0%)	0 (0.0%)
Highest level of education			
No schooling completed	0 (0.0%)	0 (0.0%)	0 (0.0%)
Less than high school degree	2 (3.8%)	1 (5.9%)	1 (2.9%)
High school graduate or degree	16 (30.8%)	4 (23.5%)	12 (34.3%)
Some college, no degree	10 (19.2%)	5 (29.4%)	5 (14.3%)
Associate degree	2 (3.8%)	0	2 (5.7%)
Bachelor degree	16 (30.8%)	4 (23.5%)	12 (34.3%)
Graduate degree	6 (11.5%)	3 (17.6%)	3 (8.6%)
Yearly household income			
Less than \$20 000	15 (28.8%)	4 (23.5%)	11 (31.4%)
\$20 000–34 999	10 (19.2%)	4 (23.5%)	6 (17.1%)
\$35 000–49 999	4 (7.7%)	3 (17.6%)	1 (2.9%)
\$50 000–74 999	11 (21.2%)	2 (11.8%)	9 (25.7%)
\$75 000–99 999	5 (9.6%)	2 (11.8%)	3 (8.6%)
\$100 000–149 999	5 (9.6%)	2 (11.8%)	3 (8.6%)
\$150 000–199 999	1 (1.9%)	0	1 (2.9%)
\$200 000 or more	1 (1.9%)	0	1 (2.9%)

($p=0.023$), duration of response ($p=0.067$), total number of re-treatments received to date ($p=0.009$), and reported plans for future re-treatment ($p=0.032$). Knowledge did not impact pain during or after the procedure, PVR at post-procedure followup, or any adverse effects (all $p>0.2$).

Discussion

This is the first study to examine patient-reported beliefs, perceptions, and knowledge regarding onabotulinumtoxinA treatments for OAB, specifically as it relates to rates of followup and understanding of the need for re-treatment. Previous reports indicate that patients are often lost to followup following their first intradetrusor onabotulinumtoxinA injections at rates of 24–67%.^{13,14} While some work has examined clinical reasons for dropout, such as adverse

events, intolerability, and lack of efficacy,¹² no research to date has systematically explored patient-reported factors that promote retreatment. This study explored demographic, clinical, environmental, and treatment-relevant factors via a mixed-methods model and can therefore comment holistically on patient factors affecting followup and re-treatment. Our findings indicate that patient comfort and knowledge were the strongest predictors of both previous re-treatment and anticipated retreatment, regardless of demographic, clinical, and environmental factors.

Patient comfort was a significant predictor of re-treatment. Results indicated that patients who received multiple treatments were significantly more likely to have received their first treatment in the operating room. Although periprocedural pain ratings did not significantly differ between patients who received multiple as compared to a single treatment, patients who had their first treatment in the operating room tended to have lower pain scores than patients who received their first treatment in clinic. This suggests that improving patient comfort around the time of the procedure may positively influence followup rates. Physicians may want to maximize periprocedural pain control if offering a first onabotulinumtoxinA treatment in clinic in order to improve compliance with followup. This finding has implications for urology practice and for onabotulinumtoxinA usage across other procedures.

Our results also indicate that patients' knowledge regarding the necessity for repeat treatments influenced whether a patient returned for further treatments. Although this may sound intuitive, we found that patients who received only one onabotulinumtoxinA treatment were more likely to not understand that multiple injections were necessary to maintain therapeutic efficacy, as indicated in both their lack of followup after a single treatment, as well as their lower reported likelihood for retreatment (97.8% vs. 64.7%). This suggests that inadequate periprocedural counselling may play a role. Although this topic has been vastly understudied in the literature, one particular qualitative study interviewed patients with OAB to determine barriers to receiving third-line therapies, and identified two key barriers: lack of education about the therapies and lack of resources.¹⁶

Poor health literacy may represent another barrier that impairs physicians' ability to foster valuable communication, and has been associated with worsened outcomes in chronic diseases.¹⁷ Low socioeconomic status, non-native English-speaking status, chronic disease, and lack of education have all been found to be associated with low health literacy.¹⁸ However, there were no significant differences in these variables between patients who did and did not understand that repeat onabotulinumtoxinA treatments are necessary, nor those who said they were planning to receive retreatment, suggesting that these particular patient characteristics are not indicative of loss to followup.

Table 2. Outcome variables of interest are displayed by whether or not patients had received single vs. multiple treatment/s of onabotulinumtoxinA to date

n (mean/%)	n	Single treatment	Multiple treatments	p
Group means				
Pain during treatment (out of 10)	53	17 (M=3.24)	36 (M=1.97)	0.099
Pain after treatment (out of 10)	52	17 (M=1.71)	35 (M=0.97)	0.166
Improvement in symptoms (out of 10)	51	17 (M=4.35)	34 (M=7.71)	0.001
Duration of response (months)	58	17 (M=2.88)	41 (M=2.85)	0.934
PVR at first post-procedure visit	31	10 (M=363.6)	21 (M=175.6)	0.040
Proportion of adverse events				
UTI within 1 week	58	3 (17.6%)	2 (4.9%)	0.115
Use of catheter to urinate	58	3 (17.6%)	5 (12.2%)	0.584
Blood in the urine	58	0	4 (9.8%)	0.182
Pain with urination	58	0	4 (9.8%)	0.182
Fatigue	58	0	3 (7.3%)	0.252
Other adverse events	58	8 (47.1%)	11 (26.8%)	0.135

PVR: postvoid residual; UTI: urinary tract infection.

Instead, the authors suggest that the use of physician-tailored and standardized education could increase patient comprehension of their need for re-treatment following onabotulinumtoxinA injections. This type of patient education (e.g., standardized videos, scripts, pamphlets) has been shown to increase patient knowledge. For example, in pediatric urology, educational videos led to improved short-term knowledge and increased long-term retention of proper antibiotic use.¹⁹ In another example, improved patient comprehension about prostate cancer and quality of clinical encounters was reported with the use of videos in conjunction with in-person cancer consultations.²⁰ Limited prospective education for OAB (e.g., use of online self-management program, internet-based demonstration of relevant exercises) suggests that patient-directed education would specifically benefit treatment for this condition;²¹⁻²³

however, standardized education via a universally available platform or system has not yet been described. Overall, these studies suggest that a standardized and accessible platform, such as educational videos relevant to patients' condition(s), could enhance provider-patient relationships and patient knowledge of their specific condition.

Critically, results indicate that knowledge for the need for repeat treatments had a positive impact on clinical outcomes. Patients' knowledge was associated with improved pain after treatment, greater improvement in symptoms, longer duration of response, and higher total number of retreatments received to date (p=0.009). Thus, the suggestion to improve patient education is likely to have a positive effect on clinical outcomes and warrants future study.

The current study contains several limitations. Our findings are limited by small sample size; however, we report a

Table 3. Outcome variables of interest are displayed by whether or not participants knew that onabotulinumtoxinA treatments need to be repeated

n (mean/%)	n	Knowledge=Yes	Knowledge=No	p
Group means				
Pain during treatment	51	45 (M=2.20)	6 (M=3.83)	0.156
Pain after treatment	50	44 (M=1.07)	6 (M=2.50)	0.069
Improvement in symptoms	50	44 (M=6.98)	6 (M=3.50)	0.023
Duration of response	57	50 (M=2.90)	7 (M=2.00)	0.067
PVR at first post-procedure visit	28	24 (M=224.5)	4 (M=404.3)	0.194
Total number of retreatments	57	50 (M=3.16)	7 (M=1.14)	0.009
Proportion of adverse events				
UTI within 1 week	57	5 (10%)	0	0.381
Use of catheter to urinate	57	8 (16.0%)	0	0.254
Blood in the urine	57	4 (8.0%)	0	0.438
Pain with urination	57	4 (8.0%)	0	0.438
Fatigue	57	3 (6.0%)	0	0.506
Other adverse events	57	15 (30.0%)	3 (42.9%)	0.493

PVR: postvoid residual; UTI: urinary tract infection.

66.3% patient response rate, which is comparable to similarly published clinical survey studies (72%).²⁴ In fact, our comparable response rate is impressive, given the fact that low response rates are often seen at large public institutions,²⁵ in cases where incentives are not offered,^{26,27} and when surveys are conducted via mail.²⁷ Due to the nature of survey studies, findings may also have been subject to response bias and recall bias. Some patients were contacted many months to years after their initial treatment, which may have influenced survey response. This range varies based on contact method and number of contact attempts made, but author records indicate a range of one month to two years. Adverse events were also primarily patient-reported, while objective data (urine cultures and PVR) was limited. Although not the primary objectives of interest, the authors note that Interstim is offered at our institution and is available as a next-line option should onabotulinumtoxinA treatments fail. In addition, this study may not have adequately assessed other clinical factors or additional aspects of medical history that might have contributed to loss of followup or decision not to undergo repeat injections.

Conclusions

This novel, mixed-methods study demonstrates that knowledge of the need for repeat onabotulinumtoxinA treatments is associated with return for additional treatments, as well as improved clinical outcomes, including greater improvement in symptoms and a longer duration of response. Our study also suggests that periprocedural comfort may play a role influencing a patient's compliance with repeat onabotulinumtoxinA treatments, and that initial treatment in the operating room may lead to better rates of followup for re-treatment. Future research should prospectively investigate targeted interventions to improve periprocedural counselling to patients considering intradetrusor onabotulinumtoxinA treatment for OAB, which may improve clinical outcomes.

Competing interests: The authors do not report any competing personal or financial interests related to this work.

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