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RESEARCH ARTICLE

Variability of urodynamic parameters in patients with idiopathic overactive bladder before intradetrusor botulinum toxin injections

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Short title: *The impact of urodynamics on management the overactive bladder*

What is not known yet, about the topic

No predictive parameters are established for urodynamic variables used in diagnosis of detrusor overactivity before surgical treatment with botulinum toxin A intradetrusor injections.

Research hypothesis

There are scientific controversies regarding the necessity of preoperative urodynamic investigation, which may allow the evaluation of effectiveness of botulinum toxin A injections.

The novelty brought to the scientific literature

Urodynamic tests have the potential for being used as a biomarker to provide a rapid assessment of effectiveness of botulinum toxin injections and being an early indicator of severity of idiopathic overactive bladder symptoms.

Abstract

Introduction. The aim of study was to establish if the treatment of overactive bladder in women and its result reported by patients were different depending on the findings of urodynamics, performed before botulinum toxin injection. We obtained clinical data based on the necessity and importance of performing urodynamic tests up to surgical treatment with botulinum toxin A injection in detrusor muscle, at patients diagnosed with idiopathic overactive bladder and detrusor overactivity, offering a guarantee of an effective and long-lasting treatment and assure with predictive parameters for some postoperative complications.

Material and methods. The research was carried out at the Department of Urology and Surgical Nephrology, during the years 2019 – 2022. After applying the inclusion and exclusion criteria, 36 women diagnosed with overactive bladder were enrolled in the prospective pilot study, aged between 18 and 70 years, refractory to drug treatment and investigated urodynamic by excluding/including the presence of detrusor overactivity and clinically using voiding diary/24h, bladder symptoms and Quality of Life questionnaires before and after botulinum toxin A injection. The primary data were analyzed and presented as a mean and standard deviation.

Results. All women involved in the study were diagnosed clinically and urodynamic with overactive bladder, of which 55.5% of cases were associated with detrusor overactivity and subsequently received BTX-A injectable surgical treatment with a dose of 100U. At urodynamics, the low values of the indices obtained at cystometry were established: first sensation of bladder filling (79.8 ± 56.3 ml), first desire to void (117.8 ± 103.2 ml), strong desire to void (162 ± 125 ml) and maximal cystometric capacity (183.4 ± 139.8 ml), which correlated in 100% cases with OAB symptoms (urinary urgency, frequency and nocturia) from the OABSS validated questionnaire. The capacity of the bladder at each sensation was lower, being inversely proportional to the detrusor overactivity present in women with OAB. Based on UDS data, the diagnosis of OABi with detrusor overactivity was confirmed by establishing the presence of phasic detrusor contractions (3.9 ± 1.1), increased values of detrusor pressure (45.9 ± 23.9 cmH2O) and the presence of bladder hypocompliance (10.6 ± 11.5 ml/cmH2O), these data in 100% of cases predicted an effective BTX-A injection. Daily activity and psychosocial behavior improved after intradetrusor botulinum injections toxin was influenced by reducing daytime urination from 28% to 40% and urinary urgency from 30 to 69%.

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Conclusions. This study identified a number of statistically significant urodynamic variables associated with objective clinical data, which confirm the impact of severity of idiopathic overactive bladder symptoms and the subsequent effect of botulinum toxin type A injections in case of urodynamic confirmation of detrusor overactivity presence.

Key words: idiopathic overactive bladder, detrusor overactivity, botulinum toxin, intravesical injections, lower urinary tract.

Introduction

Urodynamics (UDS) is considered an important test in case of lower urinary tract symptoms (LUTS). The *International Continence Society* (ICS) states that the goal of urodynamic studies is to reproduce the patient's symptoms while performing measurements that aim to determine the underlying cause of LUTS and assess the associated pathophysiological processes [1].

UDS is the „gold standard" for assessing the bladder and sphincter function, used as an objective parameter to the administered treatment. A superior advantage of UDS over urinary diary used to evaluate the drug at an early stage is that UDS has the potential to capture a physiological response without waiting for the patient's behavior (urination habit) in response to physiological improvement [2].

Idiopathic overactive bladder (OABi) is a clinical syndrome characterized by urinary urgency, usually associated with frequency and nocturia, with or without urinary urge incontinence, in the absence of urinary tract infection (UTI) or other pathologies. Idiopathic overactive bladder symptoms affect approximately 17% of women, and its prevalence increases with patient's age, reaching up to 30.9% cases [3, 4].

OABi denotes a syndrome with unknown etiology, detrusor overactivity (DO) considered being a major cause of basic OAB pathophysiology. UDS is a sensitive investigation for detection DO in up to 70% of women with OAB [5, 6].

Idiopathic DO is an objective finding based on urodynamics, characterized by contractions of detrusor during filling phase and is associated with the urgency urinary sensation. Urgency, frequency and urinary urge incontinence have been shown to be the most sensitive factors for predicting DO (61.0%) in women. In a study by Khan *et al.* (2009) was established that urinary incontinence and nocturia were associated with DO in approximately 65.9% of patients with OAB, the authors also showed involuntary contraction of detrusor at urodynamics during cystometry at low volume of infusing the bladder [5, 7].

Some researchers believe that UDS is mandatory for diagnosis and treatment among women with symptoms of OAB, otherwise determining the diagnosis only on the basis of urinary symptoms would lead to underdiagnosis of detrusor overactivity. Some studies may be needed to diagnose female urinary disorders, which are represented by post-urinary symptoms that coexist with storage symptoms. Symptoms of OAB was present in 90% of women with infravesical obstruction [8]. Thus, the role of performing UDS at early stages in diagnosis the OAB in women is essential.

Many clinicians use UDS to diagnose DO before detrusor injection treatment. According to the recommendations of the NICE Guide (National Institute for Excellence in Health and Care) it is mandatory to investigate „urodynamics" to confirm the diagnosis of detrusor overactivity before performing minimally invasive treatment such as botulinum toxin type A (BTX-A) injections [1, 9, 10].

ICS defines detrusor overactivity as involuntary contractions of the detrusor during the filling phase, which can be spontaneous or induced, further classifying into two distinct subgroups: neurogenic and idiopathic. The clinical symptoms of idiopathic DO are associated with involuntary phasic contractions of the detrusor muscle, which prevent the storage of urine, manifested by urinary urgency and/or urge urinary incontinence. These phasic contractions can be diagnosed only based on urodynamic investigation at cystometry. Urodynamics is a diagnostic test that involves inserting a catheter into the bladder and one into the vagina or rectum, reproducing urinary symptoms and identifying the underlying pathology [10-12].

ICS states that „the clinical purpose of urodynamics is to reproduce symptoms while is performing accurate measurements to identify the underlying causes of symptoms and to quantify the link to pathophysiological processes". Studies about pathophysiological mechanisms underlying the occurrence of OAB are usually based on urodynamic findings [9].

It is widely accepted that urodynamics is not indicated to all women with bladder disorders, and practical guidelines recommend urodynamic testing when the diagnosis remains uncertain after clinical evaluation, when symptoms do not correlate with objective physical findings or in case that patient is refractory to drug treatment [13].

The clinical research done by Brubaker *et al.* established that in patients with refractory OAB diagnosed by urodynamics with DO and subsequently undergoing BTX-A injections surgery, approximately 60% of cases had a positive clinical response. However, there are many scientific studies that appears to be contradictory about urodynamic confirmation of detrusor overactivity before treatment, that may not be predictive in determining treatment success. Cystometry, most important part of urodynamic study, is an essential part in the diagnosis of pathology and the evaluation of treatment of OAB, acting as a diagnostic test to identify etiology, such as involuntary phasic contractions of detrusor or low bladder compliance [10, 14].

The NICE Institute UK, the American Association of Urology (AUA) and the European Association of Urology (EAU) recommend injecting BTX-A bladder detrusor muscle at women with refractory OABi and associated DO who are willing and able for self-catheterization [4].

BTX-A leads to selective paralysis of small-amplitude detrusor muscle contractions in time of strong contractions during urination, by influencing the afferent and efferent

pathways of detrusor control during filling and urination. At least two mechanisms of action of BTX-A are assumed: efferent modulation (reducing the acetylcholine release) and the ability to reduce the related urinary reflex transmission. In addition, this neurotoxin reduces the level of nerve growth factor [16, 17].

Multiple clinical trials have reported results about BTX-A injection therapy for patients with idiopathic DO, for evaluating and establishing a necessary dose for improving present urinary symptoms. An improvement in urodynamic parameters was established from a dose of 100U. At this dose, urinary urgency symptoms, frequency and urinary incontinence urge decreased sharply, and bladder capacity, evacuation pressure, and quality of life were improved significantly, with a successful rate of 73.3%. The side effects were less common at this dose than at 150 or 200U. According to these findings, 100U of BTX-A has become a standard dose for idiopathic DO and has shown a good outcome. Contradictory, Sahai *et al.* (2020), in an analysis of urodynamic data from their randomized clinical trial, reported that the maximum detrusor pressure was very high (>110 cmH_2O), which may predict a poor response to treatment with 200U of BTX-A, indicating that that higher doses may be required at these patients. The effectiveness of BTX-A injections in patients with low bladder compliance has a shorter duration of action (12-24 weeks) than in those with normal compliance. Preoperative bladder compliance was significantly lower in patients who did not respond to BTX-A injections [14, 15].

The AUA and EAU currently recommend a dose of 100U BTX-A as the starting dose in the treatment of refractory OAB. BTX-A detrusor muscle injection is a relatively minimally invasive procedure compared to alternative surgical treatment and is usually performed as outpatient surgery. The success rate of BTX-A injections varies between 60-80% [4, 16].

The clinical results of an individual treatment with BTX-A are expressed in 1-3 weeks and can last up to 9-12 months, patients usually requiring repeated treatments. Repeated BTX-A injections in the treatment of lower urinary tract disorders and pelvic floor dysfunction is recommended by the EAU Guideline. The reinjection period should not be less than 3 months and a range of 6 to 9 months is recommended to prevent the production of circulating antibodies, which could induce a decrease in post-injection therapeutic effect with BTX-A.

Side effects after BTX-A injections of the detrusor muscle at patients with OAB can lead to develop a high volume of post-void residual urine volume (PVR) in the first month after injection, acute urinary retention, ranging from 6-45% and requiring intermittent self-catheterization (11%), occurrence of UTI with a reported incidence rate between 0-45% and/or poor treatment efficacy (13%) [4, 15, 17].

Material and methods

A prospective clinical study was performed and a post-hoc analysis of data based on the results of urodynamic parameters before injection with botulinum toxin type A intradetrusor at patients with OABi. This study provided a unique opportunity to describe the variability of the results after botulinum toxin injections of detrusor muscle, performed after the urodynamic investigation per patient over a period of 3 years.

This research included 36 women diagnosed clinical and urodynamic with OAB, aged between 18 and 70 years from a single clinic, refractory to drug treatment and treated with botulinum toxin type A injections, during the years 2019 – 2022, at the Department of Urology and Surgical Nephrology, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova. In this study, fundamental ethical principles of research have been respected. All patients gave informed consent for study entry. The study protocol was endorsed positively by *Nicolae Testemitanu* SUMPh Research Ethics Committee (Minutes №. 24, 05.03.2021). Patients who underwent the surgical procedure, were asked to indicate that they understood the nature of the surgical procedure for being informed and after they gave the permission for operation by signing the informed consent.

Study procedure

This analysis was performed as part of a prospective pilot study to evaluate the clinical and urodynamic parameters of detrusor muscle contractility before botulinum toxin type A injections in patients with overactive bladder associated with idiopathic detrusor overactivity.

Inclusion criteria were women (>18 years age) diagnosed with idiopathic OAB, refractory to anticholinergic therapy for more than 6 weeks, due to ineffectiveness or tolerability, DO confirmed by urodynamic test with or without urge urinary incontinence and completed the voiding diary/24h and valid questionnaires before and after injections.

The exclusion criteria were – neurogenic urinary bladder, bladder pain syndrome/interstitial cystitis, infravesical obstruction diagnosed on urodynamics, UTI, lithiasis/bladder tumors.

Before and after botulinum toxin injection, all patients completed voiding diary/24h, the OAB validated urinary symptoms questionnaire (OABSS), and the health-related quality of life questionnaire (OABq-HRQoL). Patients underwent ultrasound investigation to establish PVR and preoperative UDS (uroflowmetry, cystometry and voiding pressure study).

Study equipment

The detailed medical history of the patients was analyzed (assessment of urinary symptoms, filling and incontinence, previous investigations and/or conservative, pharmacological and/or surgical treatments for OAB and relevant surgical medical history). Clinical examination was performed, including assessment of stress urinary incontinence, prolapse of pelvic organs, tumor masses or other pelvic pathologies.

The collected information included patient demographic factors, medical history (history of recurrent UTI, history of pelvic floor surgery, presence/absence of prolapse, menopause).

Voiding diary was completed for at least 24 hours as a valid journal prior to the urodynamic investigation. All patients were asked to complete the OABSS and OABq-HRQoL questionnaires before and after injections. LUTS/OAB symptoms assessed by validated OABSS developed by Blaivas *et al.* (2007) and Man *et al.* (2006), was completed by all women before the intravesical botulinum toxin type A injection and during a post-injection follow-up.

The minimally invasive (urodynamic) and noninvasive clinical evaluation of women with urinary OAB symptoms that were performed in the study included: cystometry, free uroflowmetry ± pressure flow study, bladder ultrasound for determine the presence/absence of PVR and urinalysis with urine culture to exclude the presence of UTI.

UDS investigation

Urodynamic studies were performed for the diagnosis of OAB and DO using urodynamic equipment Medica SpA Memphis Division (Medolla-Italy). Women with infravesical obstruction, detrusor underactivity, and detrusor overactivity with inadequate contractility were excluded from this study.

The evaluated urodynamic parameters were PVR assessed by ultrasound, maximum cystometric capacity (MCC), maximum detrusor pressure (MDP), maximum urinary flow pressure (PdetQmax), maximum urinary flow rate (Qmax) and bladder compliance (BC). BC was calculated using the ratio urine volume/detrusor pressure, being considered low when $\Delta V/\Delta Pdet$ was ≤ 30-40 ml/cmH_2O, despite not well-established and insufficient data regarding the normal values.

The actual procedure was explained to all patients in a clear manner by providing a scenario, instructions on how to report the 4 sensations during the cystometry. Patients signed the informed consent before the procedure.

Rectal urodynamic catheter was inserted ~10 cm, after that the urethra was catheterized using a 7Fr double lumen urodynamic catheter. The bladder was emptied after confirmation of the lack of residual urine based on the urodynamic investigation. Patients placed in a sitting position after the filler wires have been connected. The transducers were placed at reference heights according to ICS standards with the respective calibration of atmospheric pressures. The working of transducers was confirmed asking patients to cough and the filling of the bladder was performed with saline solution prepared at room temperature (filling speed 20 ml/min). The filling was stopped once the patient reached the maximum cystometric capacity, then the patient urinated.

BTX-A injection procedure

Surgical treatment was performed under intravenous anesthesia. All patients received antibiotic prophylaxis (Ciprofloxacin 500mg, KRKA, Slovenia). The used dose was 100U of BTX-A (Neuronox®, Medytox Inc., Korea). The dose was diluted with 10 ml of 0.9% saline solution. Under the guidance of the Karl Storz 19Fr rigid cystoscope, the bladder was dilated by infusing ~200 ml of 0.9% saline solution. Using a rigid injection needle with a diameter of 5Fr, 4mm long, inserted ~2-3mm into the detrusor supratrigonal muscle, BTX-A was injected, 10 units/mL in 20 separate places at a distance of ~1 cm, using 0.5 ml for each injection site. The trigone, the ventral wall and dome of the bladder were avoided due to its close relationship with the peritoneal cavity. The bladder was emptied after the injection.

Statistical analysis

Statistical data analysis was performed using unifactorial dispersion analysis designed in Microsoft Excel 2019 software and IBM SPSS Statistics 22, using the standard and paired t-tests, with a significance level of 0,05. The categorical data were presented as absolute and relative values and the continuous data – in the form of mean and standard error, or as a percentage of results, comparing results before and after procedure.

Results

There were analyzed data from 36 women, with clinical and urodynamic diagnosis of overactive bladder associated with detrusor overactivity in 55.5% of cases who received 100U of BTX-A injectable surgical treatment, between January 2019 and January 2022.

Table 1. *Demographic data of patients with idiopathic overactive bladder.*

Demographic data	(N = 36)
Age (years)	40.7 ± 13.64
Reproductive period (18 - 44 years)	21 (58.3%)
Pre-menopausal (45 - 55 years)	6 (16.6%)
Menopause (56 - 65 years)	8 (22.2%)
Post-menopausal (> 65 years)	1 (2.7%)
Disease outcome (years)	5.61 ± 3.9
Body mass index	24.5 ± 2.5
Symptoms	
Urinary frequency	36 (100%)
Urinary urgency	36 (100%)
Nocturia	36 (100%)
Urge urinary incontinence	2 (5.5%)
Natural births	20 (55.5%)
DOi	20 (55.5%)
Conservative previous treatment	36 (100%)
Anticholinergic preparations (Solifenacin, Trospium Chlorid, Tolterodine)	23 (63.8%)
Selective β3-adrenoceptor agonists (Mirabegron)	13 (36.1%)
Behavioral treatment	36 (100%)
Nr. of repeated injections	1 (5%)

Note: DOi - idiopathic detrusor overactivity.

The mean age of women included in this study was 41 years (18-67 years), which corresponds to the reproductive period; the duration of OAB symptoms was ~6 years (Table 1). Before the injection, the period of drug treatment was 3 months by administration of combined anticholinergic medicine (63.% of cases) and selective β3-adrenoceptor agonists (36.1% of cases), without improvement of LUTS/OAB. In 100% of cases, patients had urinary symptoms like urinary frequency, urgency, and nocturia.

Urodynamic data was obtained before injection in 36 patients, from which in 20 patients (55.5% of cases) were confirmed the presence of DO. The bladder contractility index (CI) was found to be within the normal range in 100% of cases in patients investigated urodynamic and diagnosed with DO (Table 2). In 100% of cases the PVR was measured before surgery, averaging 4.9 ml (between 0-10 ml).

Table 2. *Urodynamic parameters in patients with idiopathic overactive bladder before botulinum toxin type A injection treatment.*

Urodynamic parameters		BTX-A pre-injection (n = 36)	Normal values
Uroflowmetry	Maximum voided volume (ml)	132.7 ± 136.7	150-500
	Qmax (ml/s)	9.8 ± 4.1	17.04
	Qave (ml/s)	2.2 ± 1.6	13.2
Cystometry	FS (ml)	79.8 ± 56.3	170-250
	FDV (ml)	117.8 ± 103.2	250-330
	SDV (ml)	162 ± 125	350-560
	MCC (ml)	183.4 ± 139.8	450-550
	MDP (cmH_2O)	45.9 ± 23.9	25-60
	Nr. of contractions	3.9 ± 1.1	1 before void contraction
BC (ml/cm H_2O)		10.6 ± 11,5	>30-40
CI		124.6 ± 39,4	100-150
PVR (ml)		4.9 (0-10)	0-7

Note: Qmax - maximum flow rate; Qave - average flow rate; FS -first sensation of bladder filling; FDV - first desire to void; SDV - strong desire to void; MCC - maximum cytometric bladder capacity; MDP - maximum detrusor pressure; BC - bladder compliance; CI - index of detrusor contractility; PVR - post-void residual urine volume; BTX-A - botulinum toxin type A.

Based on UDS data, the diagnosis of OABi with DO was confirmed by establishing the presence of phasic contractions of the detrusor muscle (3.9±1.1), increased values of detrusor pressure (45.9 ± 23.9 cmH_2O) and the presence of bladder hypocompliance (10.6 ± 11.5 ml/cmH_2O), these data in 100% of cases predicted an effective BTX-A injection.

Urodynamic parameters, such as bladder capacity at each sensation and detrusor pressure were affected by the presence of DO in women with OAB. Low values of indices obtained at cystometry: first sensation of bladder filling (79.8±56.3 ml), first desire to void (117.8±103.2ml), strong desire to void (162±125 ml) and maximal cystometric capacity (183.4±139.8 ml) were 100% correlated with OAB symptoms (urgency, frequency and nocturia) from the OABSS validated questionnaire. We showed that the capacity of the bladder at each sensation was lower, being inversely proportional to the detrusor overactivity in women with OAB.

PVR values ($\bar{x}$ = 4.9 ml) did not correlate with the occurrence of acute urinary retention or the need for intermittent post-injection self-catheterization, as well as the low value of urinary flow rate (9.8 ± 4.1ml/s).

The urinary symptoms were evaluated before BTX-A injection – urinary frequency (100%), urinary urgency (100%), nocturia (100%) and urge urinary incontinence (10%). Our observations were the same as results of botulinum toxin type A therapy in OAB from other international studies. Which has shown that botulinum toxin influence on urination (daytime urination has been reduced from 28% to 40%), and the urgency urination being reduced from 30% to 69%.

Based on the voiding diary, we analyzed the following indices before and after injection – total voided volume, functional bladder capacity, nocturia index, and nocturia polyuria index, number of daytime voiding and total index of urgency and frequency urination (Table 3).

Table 3. *Primary post-injection efficacy according to voiding diary parameters.*

Voiding diary parameters	BTX-A pre-injection (n = 20)	BTX-A post-injection (after 6 weeks) (n = 20)
TVV / 24h (ml)	1314 ± 645	1565 ± 168
FBC (ml)	163.1 ± 123.9	338 ± 69
IN	2.86	0.7 ± 0.1
IPN (%)	28.7 ± 9.4	15.8 ± 5.1
DV	11.3 ± 1.68	5.1 ± 2
TUFS	31.7 ± 7.8	7.7 ± 3.8

Note: TVV - total voided volume; FBC - functional bladder capacity; IN - index of nocutia; IPN - index of nocturia polyuria; DV - daytime voiding; TUFS - total urgency and frequency score; BTX-A - botulinum toxin type A.

All validated self-report questionnaires quantifying OAB symptoms (daytime urinary frequency, nocturia, urinary urgency and urge urinary incontinence) were completed by all women prior to intravesical BTX-A injection and during a follow-up visit at first and third month after intravesical injections. A significant decrease of negative impact of LUTS/OAB on daily indoor and outdoor activity, physical and social activity was reported by patients following the completion of post-injection quality of life questionnaire (OABq-HRQoL).

From the study group, 19 patients received a single BTX-A injection. One patient (5% of cases) underwent repeated botulinum toxin type A injections, when an insufficient response or recurrence of urinary symptoms was observed after a minimum waiting time of 6 months. All patients were followed-up for at least 3 months after their first BTX-A injection.

Intravesical BTX-A injection has a positive effect on patients' emotions, with each follow-up visit (1st, 3rd and 6th month) an improvement in emotional state was observed. Sleeping difficulties and fatigue were reduced after the first month after the injection. Moreover, a statistically significant reduction in LUTS/OAB severity was observed using the OABSS questionnaire (Table 4).

The OABSS questionnaire indices and their improvements after BTX-A injection are shown in table 5. The results showed improvement of more than 2 points in 65% of treated patients, remained unchanged in 20% and worsened in 14%.

Table 4. *Injection efficacy according to the degree of impairment of symptoms from OABSS questionnaire.*

Severity of OABSS	BTX -A pre-injection (n = 20)	BTX-A post-injection (after 6 weeks) (n = 20)
Absence of symptoms	0	11 (55%)
Mild	8 (40%)	8 (40%)
Severe	12 (60%)	1 (5%)

Note: OABSS - overactive bladder symptoms questionnaire; BTX-A - botulinum toxin type A.

OABSS values improved on average by 35% after treatment, and in 55% of cases improved by 3 or more points. Scores for daytime urinary frequency, nocturia and urinary urgency improved significantly after BTX-A injection by 41.7%, 26.1% and 34.1%, respectively (Table 5).

Table 5. *Post-injection efficacy according to the symptoms from OABSS questionnaire.*

OABSS	BTX-A pre-injection (n = 20)	BTX-A post-injection (after 6 weeks) (n = 20)
Urinary frequency	100%	65.9%
Urinary urgency	100%	58.3%
Nocturia	100%	73.9%
Urge urinary incontinence	10%	0

Note: OABSS - overactive bladder symptoms questionnaire; BTX-A - botulinum toxin type A.

Our results showed that the impact of idiopathic refractory OAB on patients was improved. The overall impact of the bladder problem on quality of life increased slightly at the 6th and 9th month after treatment, compared with the 3rd month (Table 6).

Table 6. *The degree of impairment of quality of life in patients with idiopathic overactive bladder before and after the treatment with botulinum toxin type A injection, based on the OABq-HRQoL questionnaire.*

Degree of impairment on quality of life	BTX-A pre-injection (n = 20)	BTX-A post-injection (after 6 weeks) (n = 20)
OAB-QoL Subscale Symptom-Severity	75%	10%
HRQoL subscales Coping	70%	10%
HRQoL subscales Concern	70%	25%
HRQoL subscales Sleep	95%	25%
HRQoL subscales Social	55%	0
HRQoL total	70%	25%

Note: BTX-A - botulinum toxin type A; OAB-QoL - the quality-of-life questionnaire related to OAB symptoms; HRQoL - health-related quality of life.

Regarding the side effects of intravesical therapy with BTX-A, in the actual group of patients, 7 cases of urinary tract infection were detected (35% of cases), diagnosed by a positive urine culture. None of the patients required clean intermittent self-catheterization (CIC) due to acute urinary retention or increased post-void residual urine volume.

Discussion

Original definition of OAB is based on symptoms that highlight urinary urgency as a cardinal symptom. Although still controversial, it is believed that this urgency stems from an overactive bladder contraction (detrusor overactivity), which causes a "sudden, compelling urge to void" [18].

Urodynamic testing is a useful diagnostic tool and could be of great value in evaluating the efficacy before BTX-A injection. Urodynamic studies will not replace studies using voiding diary and OAB validated questionnaires to confirm symptoms, the outcome, and efficacy of treatment in OAB. However, clinical evidence from concept studies using voiding diary and OAB symptoms questionnaires may take approximately 9-16 months [2].

DO was considered one of the major features typical of OAB and OAB symptoms are thought to be indicative of a subsequent finding of DO on UDS. Digesu *et al.* found that only 54% of women with OAB had DO based on UDS, and 27% of women diagnosed with DO based on UDS had clinical symptoms of OAB. According to the findings, only the symptomatic diagnosis of OAB was not recommended for women with LUTS, especially for BTX-A injection [8].

A significant number of women with symptoms of overactive bladder showed LUTS, but the presence of OAB symptoms alone is not sufficient to predict the diagnosis of OAB with detrusor overactivity and the effectiveness of subsequent treatment.

Maximum cystometric capacity and bladder compliance were the variables with the most statistically significant associations in this study. Capacity is a measure of the potential for retention of bladder volume, smaller volumes being associated with more severe OAB symptoms. Bladder compliance, which is described as the complex interaction of volume and pressure during bladder filling, in the case of low compliance, was a bladder with reduced adaptation mechanisms and therefore associated with the severity of clinical manifestations.

Another important urodynamic parameter was the volume infused at the onset of the first sensation of bladder filling, that appears at smaller volumes were associated with more severe symptoms of urinary urgency. The first sensations of bladder at early stages of the filling phase are expected to be associated with several episodes of urgency.

These variables are also proposed by some authors as potential indicators between idiopathic and neurogenic DO. The value of these parameters has recently been supported by studies that evaluates the effect of OAB treatments based on urodynamic results. The effect of BTX-A in patients with idiopathic DO has been shown to improve bladder compliance and cystometric capacity, increased bladder filling volume, and decreased severity at first sensation of bladder filling [19]. The proven sensitivity of these urodynamic measurements offers good results in further research and in the treatment of patients with OAB.

We demonstrated the presence of a clinically relevant correlation between urodynamic findings and subsequent results of BTX-A injection therapy in patients with OAB.

Although both urodynamics and voiding diary with OABSS questionnaires may influence the clinical decisions of subsequent treatment, our study supports the role of UDS as predictors of outcome in patients with bladder overactivity.

Urodynamics seems to influence treatment decisions made by clinicians in determining treatment pathways in women with OAB. Patients that were diagnosed by UDS before treatment, appears to have greater reductions of symptoms than those who did not perform the investigation [1].

Based on our own study, we presented the short-term results of 36 patients treated with a dose of 100 and 200U with BTX-A in a single institution, urodynamic investigated before injection, with OAB and detrusor overactivity. There are some subjective and objective differences between the effect of BTX-A treatment on women who were diagnosed with DO by urodynamic tests before injection and those who were not, as evidenced by numerous worldwide clinical trials, suggesting that being OAB with DO as a serious disorder of bladder function among women.

International studies have suggested that maximal detrusor pressure, poor compliance, and maximal cystometric capacity were predictors of nonresponse and identified urinary retention and infection as potential side effects, but subsequent studies have refuted these data, but have identified that episodes of urge urinary incontinence and smoking status may be additional predictors of non-response to BTX-A injections in patients with refractory DO [20].

We found that lower Qmax values was predictive for urinary dysfunction requiring intravesical injection, this finding could be the result of weaker detrusor muscle contractility. However, low preoperative PVR values are not correlated with the occurrence of acute post-injection urinary retention or the need for clean intermittent self-catheterization.

In correlation with the results of an international study performed in two medical centers using 200U dose of BTX-A in patients with OABi, we can assume that low Qmax could be predictive of CIC use. The data in the literature contradict this, with some studies suggesting that preoperative PVR is associated with increased CIC and others not. However, in most preoperative studies PVR > 200 ml was an exclusion criterion. Poor contractility of the detrusor, leading to the presence of high post-injection PVR with BTX-A have been associated with the onset of ITU [16].

A significant improvement in LUTS/OAB symptoms was observed in the evaluation of own results. Daily activity and psychosocial behavior have improved due to reduced symptoms of urinary frequency, urge urinary urgency and nocturia, intradetrusor injections with botulinum toxin influence daytime urination, which have been reduced from 28% to 40%, reducing the urinary urgency from 30 to 69%.

A randomized clinical trial by Dmochowski *et al.* (2012) found that doses of 100U and higher provided better efficacy compared to 50U. Another study by Denys *et al.* (2007) showed no significant difference in urgency and incontinence episodes between groups of patients receiving BTX-A injections at doses from 100 and 150U after 3 months of follow-up. It was also shown that a dose of 50U had no benefit, as the results were not significantly different from a placebo injection [16].

In addition to the significantly improved number of daily voids, urgency episodes and nocturia, there was an improvement of quality of life observed in patients bothered especially by urinary urgency.

Surprisingly, in our study we did not report acute urinary retention that requires CIC. Ultrasound did not show any significant post-void residual urine volume. This is probably due to the small research group.

Rates of CIC requirement after BTX-A injection into the bladder are highly variable, ranging from 4% to 45% of cases. In other worldwide clinical trials, the mean CIC rate was approximately 23% of cases [21, 22].

The urodynamic test may be considered a predictive diagnostic method for some postoperative complications of botulinum toxin injection in patients with idiopathic overactive bladder and detrusor overactivity.

BTX-A is generally safe, effective treatment approved in many countries for overactive bladder symptoms. Barriers for using the toxin include meeting the clinical criteria for approved use, access to specialists, and the financial cost of treatment, which can be significant, although subsidized to varying degrees depending on use [23].

Conclusions

Clinical and urodynamic evaluation are essential in preparing for botulinum toxin type A injection in patients with OAB, suggesting a more severe bladder storage disorder when DO is present.

This study identified several urodynamic variables that have statistically significant correlations with objective clinical data, which report an impact on the severity of idiopathic overactive bladder symptoms and on the treatment efficiency with botulinum toxin type A injection in case of urodynamic confirmation of detrusor overactivity presence. Maximum cystometric capacity, bladder compliance, maximum voided volume and severity of first sensations of bladder filling could be considered predictive and useful values for being implemented in routine clinical practice for the diagnosis.

Urodynamic investigation reveals the particular characteristics of the results of the patients, despite the inherent variability of the parameters of urodynamic tests, women diagnosed with detrusor overactivity are significantly affected by their quality of life and have a severe degree of bladder dysfunction.

Declaration of conflicting interests

The author declares the absence of any conflict of interest in the elaboration of this article.

Authors' contribution

Both authors contributed equally to the development of the manuscript and approved its final version.

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