

The use of urodynamic studies for the followup of neurogenic bladders treated with onabotulinumtoxinA

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Abstract

Introduction: Intradetrusor injection of onabotulinumtoxinA (BoNTA) is well-established as treatment for patients with neurogenic bladders. Urodynamics (UDS) is used at regular intervals during followup to monitor intravesical pressure. With regards to the discomfort and risks associated with UDS, our objective was to assess if UDS done at regular intervals in the followup of neurogenic bladders treated with BoNTA had an impact on management. **Methods:** We retrospectively analyzed the medical records of adult patients with neurological disorders treated with BoNTA for either detrusor overactivity or low bladder compliance at the Institut de Réadaptation en Déficience Physique de Québec (IRDPQ). At our centre, UDS was routinely performed at baseline, three months after the first treatment, then three months after every fifth set of injections. **Results:** We identified 57 patients with neurological disorder treated with intravesical BoNTA. Each patient had between one and 19 sets of injections (mean 5.61 injections) and 1–6 followup UDS (mean 2.09). Of the 119 followup UDS reviewed at our centre, three UDS (2.5%) resulted in a modification of the urinary tract management from BoNTA to bladder augmentation. Two regimens were suspended and one was ended due to patient preference. **Conclusions:** Our study showed that UDS at pre-set intervals for followup of patients receiving BoNTA injections were rarely associated with modifications in the treatment course. Therefore, UDS should only be performed in cases where there are changes in the patient's symptoms or if the urologist suspects that the treatment response is suboptimal.

Introduction

Patients with neurological disorders, such as spinal cord injury, spina bifida, and multiple sclerosis, may suffer from neurogenic detrusor overactivity (NDO) or low bladder compliance. The majority of these patients encounter symptoms of discomfort, urgency, and frequency with or without incontinence that can be very bothersome on a daily basis.

Furthermore, patients with neurological disorders also may have asymptomatic high intravesical pressure or secondary hydronephrosis that can lead to damage to the upper urinary tract.¹⁻⁴ The urologist plays a critical role in providing patient care to achieve social continence, minimize symptoms, and protect renal function.

Intra-detrusor injections of onabotulinumtoxinA (BoNTA) has emerged as a safe and effective treatment for NDO.¹⁻⁷ Urodynamics (UDS) is currently used in the followup care of patients that have benefited from BoNTA treatment. At our institution, followup protocol includes UDS performed at diagnosis, prior to BoNTA injection, three months after the first treatment, and then three months after every fifth set of injections. However, in some instances, patients had additional or less UDS studies performed based on their symptoms, clinical evolution, or on the urologist's clinical judgment. Even though this systematic followup has not been documented or proven mandatory in the literature, UDS is used in our protocol at regular intervals to confirm that intravesical pressure and compliance remains under safe thresholds. It also allowed us to manage and adjust further treatments accordingly.

On the other hand, UDS performed at regular intervals entails non-negligible financial and resource burdens for our healthcare system. In fact, it is our duty as physicians to limit the use of unnecessary tests and only order those that are essential to our patients' management in order to keep up with our healthcare system resources. Moreover, aside from the cost associated with repeated UDS, potential risks inherent to the test itself, such as autonomic dysreflexia and severe hypertension, urinary tract infection, hematuria, and pain or muscular weakness, should also be taken into consideration.^{2-4,6-8}

The objective of this study is to assess if the recurrent and pre-set use of UDS has an impact on the outcome and management of patients treated for neurogenic bladder with BoNTA with regards to the risks and the costs that may be associated with UDS.

Methods

All of our patients were selected from the rehabilitation centre. The criteria of inclusion for this study were: adult

patients with neurogenic bladder treated with intradetrusor injections of BoNTA for either NDO or low bladder compliance between 2003 and 2015. A retrospective analysis of the medical records of the 61 eligible patients was done. From all the patients treated with BoNTA at our centre, we excluded four patients who received their first intravesical BoNTA injections, but were not followed with UDS at our centre. Data were collected for the remaining 57 patients with regards to patients' characteristics: neurological disorder, method of bladder management (Credé manoeuvre, clean intermittent catheterization [CIC], indwelling catheter, etc.), use of anticholinergics or beta3-agonists, and BoNTA treatments. Each UDS was analyzed and subsequent modifications in management were recorded. Descriptive data analyses were performed. This study is a qualitative analysis, which did not necessitate elaborate statistical analysis.

Results

Fifty-seven patients were eligible for analysis (34 males, 23 females). Patients were between the ages of 20 and 75 years (median 50). They were affected by a variety of neurological disorders, such as spinal cord injury (SCI), multiple sclerosis (MS), spina bifida, Huntington's disease, cerebral palsy, transverse myelitis, epidural abscess, and sacral agenesis. The most frequent neurological disorder was SCI, observed in 63.2% of our cohort. Out of the 57 patients, 15 (26.3%) had an indwelling urethral catheter, while 42 (73.7%) performed CIC (Table 1). Before initiation of BoNTA, all patients had a trial of at least one anticholinergic medication or mirabegron.

Each patient had between one and 19 injections of intradetrusor BoNTA, with a mean of 5.6 treatments. During BoNTA management, 1–6 followup UDS were performed per patient, with a median of two. Patients received either 200 or 300 units of BoNTA per treatment. Twenty-seven patients (47%) had 200 units of BoNTA injected during the first treatment and most of them progressed to a 300 unit dose. BoNTA was injected under local anesthesia in linear injection of 1 cc aliquots of BoNTA under cystoscopic control. A baseline UDS was performed in order to diagnose NDO, evaluate the indication of BoNTA injections, and analyze bladder function and clinical evolution after BoNTA injections. Reinjection was performed on demand at symptom recurrence. In our cohort, BoNTA efficacy lasted for a median of six months. Complications reported during and after injections were mild hematuria, cystitis, pain, hypertension, and hyper-reflexia. When we compared baseline and followup UDS done three months after BoNTA, the vast majority of patients had an improvement in capacity, uninhibited contractions, compliance, and intravesical pressure.

Of the 119 followup UDS reviewed in our centre, only three (2.5%) resulted in a modification of the urinary tract

Table 1. Patient characteristics

Number of patients	57
Gender, n	
Male	34
Female	23
Age, median (range)	50 years (20–75)
Neurological disorder, n (%)	
Spinal cord injury	36 (63.2)
Paraplegia	21 (36.8)
Tetraplegia	15 (26.3)
Multiple sclerosis	9 (15.8)
Myelitis	3 (5.3)
Familial spastic paraplegia	2 (3.5)
Spina bifida	2 (3.5)
Miller Fisher syndrome	1 (1.8)
Cerebral palsy	1 (1.8)
Huntington's disease	1 (1.8)
Epidural abscess	1 (1.8)
Sacral agenesis	1 (1.8)
Bladder emptying, n (%)	
Indwelling catheter	13 (22.8)
Clean intermittent catheterization (CIC)	40 (70.2)
Spontaneous voiding	2 (3.5)
Combination of CIC and spontaneous voiding	2 (3.5)

management. These three patients experienced persistence/recurrence of symptoms, such as incontinence and high intravesical pressure under BoNTA therapy, and therefore, had their management changed to bladder augmentation after two, six, or 11 BoNTA treatments, respectively. Two patients decided to continue BoNTA injections while awaiting surgery because of the delay for the surgical intervention. One patient postponed surgery and carried on with the BoNTA therapy and, after a few treatments, finally had improvement of both clinical symptoms and UDS parameters. Surgery was, therefore, no longer required in this case. To date, he is still undergoing BoNTA treatment.

During followup, two regimens of treatments were suspended and one was terminated in accordance to the patient's preference (traveling and time constraints, desire to experiment a trial period without BoNTA, refusal of treatment) with no correlation to the UDS results, nor the medical advice of his/her urologist.

Discussion

Reports on BoNTA efficacy for NDO and urinary incontinence are very abundant in the literature.¹⁻⁷ However, to our knowledge, this is the first study performed to evaluate the usefulness of routine followup UDS during BoNTA treatment. Multiple authors have concluded that BoNTA injections decrease urinary incontinence episodes, improve quality of life, and reduce the frequency of CIC.¹⁻⁷ In addition, the majority of studies

used UDS as an indicator of improvement in bladder function for patients undergoing BoNTA therapy. Results showed that BoNTA produced significant improvement in bladder capacity, detrusor mean pressure, and compliance.^{1-4,6,7} Interestingly, some studies performed UDS at regular intervals to evaluate persistence of BoNTA efficacy through time. Those studies reported a sustained improvement in UDS parameters over time for as long as six years.¹ Although they were not designed to address the use of UDS in patient followup, one may extrapolate that if UDS parameters remained stable for the vast majority of patients during those studies, the situation would likely be similar for our patients receiving BoNTA treatments. This is concordant with our observations that as UDS tend to remain stable over time, we rarely see modifications in management based solely on UDS results. Moreover, as we mentioned earlier, the efficacy of BoNTA injections has been well-demonstrated by numerous authors in the past. There seems to be no significant tachyphylaxis over time with repeated injections.^{1,3,4,7} Consequently, it seems even less indicated to do regular UDS in order to assess treatment effectiveness.

It would be reasonable to perform UDS three months after the first set of injections in order to assess BoNTA efficacy and evolution of UDS parameters even though BoNTA is minimally invasive and not without serious complications. If a patient still has high intravesical pressure under BoNTA or if UDS parameters are still abnormal or worrisome in an asymptomatic patient, we would tend to plan closer followup. In all other cases, we suggest performing UDS only when there is a change in patient's symptoms. The three patients (2.5%) who had their management changed to bladder augmentation experienced persistent symptoms, such as incontinence, with high intravesical pressure or uncontrolled uninhibited detrusor contractions on UDS. No worrisome UDS parameters were found without symptoms. We believe that for such cases, i.e., patients with ongoing and unresolved symptoms, we would be more likely to obtain data from UDS that will guide our clinical decisions. Moreover, these three patients had a diagnosis of SCI (one at the level of D3 and two at D8), which could represent a population at higher risk for high intravesical pressure and refractory symptoms. Physicians could consider closer followup or adopt a lower threshold for workup and investigations when these patients are symptomatic or present with abnormal UDS parameters.

There are risks associated with UDS that must be taken into consideration. These risks include hyperreflexia and severe hypertension, urinary tract infection (UTI), hematuria, and pain or muscular weakness. Studies reported UTI incidence of 2–57% following UDS, and a 1.1–5.5% incidence of autonomic dysreflexia in patients suffering from SCI.^{2,4,6-8} Other studies did not reported dysreflexia as an adverse effect, but showed an incidence of 4–21% for symptoms such as headache, nausea, vomiting, sweating, and hypertension.^{2,8} In our study, we recorded a 17.6% incidence

of hyperreflexia and 0.9% incidence of symptomatic infections following BoNTA injections. We hypothesized that the lower incidence of UTI obtained in our study was due to the retrospective nature of our data. In fact, we assumed that not all complications were reported in medical records and patients could have been seen by a physician outside the rehabilitation centre without our knowledge.

Conclusion

Our study showed that UDS at pre-set intervals for the followup of patients receiving BoNTA injections were rarely associated with modifications in treatment course. Therefore, UDS should only be performed after the first injection to validate response to BoNTA treatment and when there are changes in the patient's symptoms or response to the BoNTA injections, or if the urologist suspects that the treatment response is suboptimal.

Competing interests: Dr. Nadeau has attended advisory boards for Allergan, AMD, Astellas, Boston Scientific, Ferring, and Pfizer; has been a speaker at CME conferences for Allergan, Astellas, Ferring, Laborie, and Pfizer; and has participated in clinical trials supported by Astellas. Dr. Moore has attended advisory boards for Astellas and Pfizer; and has participated in clinical trials supported by Astellas and Pfizer. Dr. Bergeron reports no competing personal or financial interests related to this work.

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