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

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Abstract

Introduction: Intradetrusor injections of onabotulinumtoxinA (BoNTA) is well-established as treatment for patients with neurogenic bladders. Urodynamics (UDS) are 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 neurologic 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 were 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 neurologic disorder treated with intravesical BoNTA. Each patient had between 1–19 sets of injections (mean 5.61 injections) and 1–6 followup UDS (mean 2.09 UDS). 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 neurologic 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, frequency with or without incontinence that can be very bothersome on a daily basis. Furthermore, patients with neurologic disorder also may have asymptomatic high intravesical pressure or secondary hydronephrosis that can lead to damage the upper urinary tract.[1,2,5,6] The urologist plays a primordial role in providing patient care to achieve social continence, to minimize symptoms, and to protect renal function.

Intradetrusor injections of OnabotulinumtoxinA (BoNTA) has emerged as a safe and effective treatment for NDO.[1,2,3,4,5,6,8] Urodynamics (UDS) is currently used in the follow-up care of these patients that have benefited from the BoNTA treatment. In our local institutional follow-up protocol, UDS is performed at diagnosis, prior to BoNTA injection, 3 months after the first treatment and then 3 months after every 5th injection after the initial treatment. 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 follow-up 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 remained under safe threshold. 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 resources burden 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, pain or muscular weakness, should also be taken into consideration.[2,4,5,6,7,8]

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 center. The criteria of inclusion for this study were: adult patients with neurogenic bladder treated with intradetrusor injections of BoNTA for either detrusor overactivity 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 in our center, we excluded four patients who received their first intravesical BoNTA injection but were not followed with

UDS in our center. Data were collected for the remaining 57 patients with regards to patients' characteristics: neurologic 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 were analysed 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 (57) patients were eligible for analysis (34 males and 23 females). Patients were between the ages of 20 and 75 (median 50 year-old). They were affected by a variety of neurologic 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 neurologic disorder was spinal cord injury, observed in 63.2% of our cohort. Out of the 57 patients, 15 patients (26.3%) had an indwelling urethral catheter, while 42 (73.7%) performed clean intermittent catheterization (CIC) (Table 1). Before initiation of BoNTA, all patients had a trial of at least one anticholinergic medication or mirabegron.

Each patient had between 1 and 19 injections of intradetrusor BoNTA, with a mean of 5.6 treatments. During BoNTA management, 1 to 6 follow-up UDS were performed per patient with a median of 2. 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 1cc aliquots of BoNTA under cystoscopic control. A baseline UDS was performed in order to diagnose NDO, evaluate the indication of BoNTA injections, analyze bladder function and clinical evolution after BoNTA injections. Reinjection was performed on demand at symptoms recurrence. In our cohort, BoNTA efficacy lasted for a median of 6 months. Complications reported during and after injections were mild hematuria, cystitis, pain, hypertension and hyperreflexia. When we compared baseline and follow-up UDS done 3 months after BoNTA, the vast majority of patients had an improvement in capacity, uninhibited contractions, compliance and intravesical pressure.

Of the 119 follow-up UDS reviewed in our center, only three (2.5%) resulted in a modification of the urinary tract 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 2, 6 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

finally had improvement of both clinical symptoms and UDS parameters, which occurred after a few treatments. Surgery was therefore not required anymore in this case. To this date, he is still undergoing BoNTA treatment.

During follow-up, 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 their urologist.

Discussion

Reports on BoNTA efficacy for neurogenic detrusor overactivity and urinary incontinence are very abundant in the literature.[1,2,3,4,5,6,8] However, to our knowledge this is the first study performed to evaluate the usefulness of routine follow-up UDS during BoNTA treatment. Multiple authors have concluded that BoNTA injections decrease urinary incontinence episodes, improve quality of life and the frequency of intermittent clean catheterizations.[1,2,3,4,5,6,8] In addition, the majority of studies used UDS as an indicator of improvement in bladder function for patients under BoNTA therapy. Results showed that BoNTA produced significant improvement in bladder capacity, detrusor mean pressure and compliance.[1,2,4,5,6,8] 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 6 years.[1] Although they were not designed to address the use of UDS in patients' follow-up, 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 urodynamics' result. Moreover, as we mentioned earlier, the efficacy of BoNTA injections has been well demonstrated by numerous authors in the past years. There seems to be no significant tachyphylaxis over time with repeated injections.[1,5,6,8] 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 but not without serious complications. If 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 follow-up. In all other cases, we would rather suggest to perform 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 spinal cord injury (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 follow-up or adopt a lower threshold for work-up and investigations when these patients are symptomatic or present with abnormal UDS parameters.

In addition, there are risks associated with UDS, such as hyperreflexia and severe hypertension, urinary tract infection (UTI), hematuria, pain or muscular weakness. Studies reported an incidence of 2% to 57% of UTI following UDS and a 1,1% to 5,5% incidence of autonomic dysreflexia in patients suffering from SCI.[2,4,6,7,8] Other studies did not reported dysreflexia as an adverse effect but showed an incidence of 4% to 21% for symptoms such as headache, nausea and vomiting, sweating and hypertension.[2,7] 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 center without our knwoledge.

Conclusion

Our study showed that UDS at pre-set intervals for the follow-up 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 injection or if the urologist suspects that the treatment response is suboptimal.

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Figures and Tables

Table 1. Patient characteristics	
Number of patients	57
Gender, n	
Male Female	34 23
Age, median (range)	50 years (20–75)
Neurologic disorder, n (%)	
Spinal cord injury Paraplegia Tetraplegia	36 (63.2) 21 (36.8) 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)