REVIEW

Injection of botulinum toxin type A in the urethral sphincter to treat lower urinary tract dysfunction: review of indications, techniques and results: 2011 update

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Introduction: *The first application of botulinum toxin type A (BoNT-A) in urology was its injection into the urinary sphincter to treat neurogenic detrusor-sphincter dyssynergia (DSD) in quadriplegic men. Since that first report by Dyskatra et al in 1988, the results of focal BTA injections into the sphincter, the bladder wall and lately into the prostate have raised the interest of the urology community in this promising new therapeutic modality. This is an evidence-based review of the current indications, techniques and outcomes of BTA injections into the urethral sphincter.*

Materials and methods: *The Medline database was searched for the period between 1966 and October 2010, using the keywords "botulinum toxin" and "urethra" or "urethral sphincter". English written articles were selected. A level of evidence according to the Oxford Centre for evidence-based medicine was assigned to each article.*

Conclusion: *Since our first review in 2006, very little has been added to the literature on the use of botulinum toxin injected into the external sphincter. At present, those most likely to benefit from intrasphincteric BTA injection are MS patients suffering the symptoms of DSD and quadriplegic men with DSD unable to perform self-catheterization. Well developed and conducted studies are necessary; these must be done urgently to better define the place and the results of this drug otherwise widely used in other indications in urology.*

Key Words: botulinum toxin, urethral sphincter, detrusor sphincter dyssynergia, multiple sclerosis, spinal cord injury, detrusor hypocontractility

Introduction

The first application of botulinum toxin type A (BoNT-A) in urology was its injection into the urinary sphincter to treat neurogenic detrusor-sphincter dyssynergia (DSD) in quadriplegic men.[1] Since that first report by Dyskatra et al in 1988, the results of focal BTA injections into the sphincter, the bladder wall[2-5] and lately into the prostate[6] have raised the interest of the urology community in this promising new therapeutic modality. In 2006, we published an evidence-based review on the use of BoNT-A in the urethral sphincter.[7] Since this technique is widely used in neurourology practice, we are proposing an updated version of our previous review. It is an evidence-based review of the current indications, techniques and outcomes of BTA injections into the urethral sphincter.

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Methodology

The Medline database was searched for the period between 1966 and October 2010, using the keywords "botulinum toxin" and "urethra" or "urethral sphincter". English written articles were selected. The references cited in these articles were examined, and relevant papers were added to the selection. A level of evidence according to the Oxford Centre for evidence-based medicine was assigned to each article.

Terminology of preparations of botulinum toxin

The botulinum neurotoxins marketed in the United States are now named onabotulinum toxin A (brand name Botox), rimabotulinum toxin B (Myobloc), abobotulinum toxin A (Dysport), and incobotulinum toxin A (Xeomin), which was recently approved in the US market. With this recent entry, 3 type A and 1 type B brands of botulinum neurotoxins are available in the United States. The new generic names have not yet been adopted by other regulatory agencies. For example, the European Medicines Agency retains the official denomination of botulinum toxin for all products of botulinum neurotoxins.[8] We did not use this brand new terminology in our review since none of the referenced articles used it.

Mode of action and indications

The scientific background for the application of BoNT-A in the external urethral sphincter in patients with detrusor-sphincter dyssynergia is based on its known effect of blocking the presynaptic vesicular release of acetylcholine (ACh) at the neuromuscular junction.[9] This leads to temporary reversible chemodenervation of the targeted muscle.

The aim of BoNT-A injection into the urethral striated sphincter (USS) is to induce muscle relaxation. In cases of DSD or USS hypertonia, such relaxation is thought to decrease enough urethral resistance to improve voiding.

Despite clinical evidence from its use in neurologic disorders suggesting an effect of BoNT-A on afferent abnormalities, weakening of striated musculature has remained an appropriate aim in the management of DSD and pelvic-floor disorders characterized by excessive and sometimes painful muscle spasms.[9]

Urethral BoNT-A injection has been used first and mainly to treat neurogenic DSD[1,10-15] related to various neurological conditions, such as traumatic cervical spinal cord injury (SCI) and multiple sclerosis (MS). In these instances, it is used to improve voiding or to help performing clean intermittent catheterization (CIC). The same approach has been applied to treat non-neurogenic obstructive sphincter dysfunctions, such as detrusor-sphincter incoordination, USS hypertonia, or difficulty voiding due to chronic prostatitis.[16] It has been also proposed as an alternative to self-catheterization in urinary retention related to detrusor hypocontractility secondary to post surgical bladder denervation or cauda equina injuries.[17]

Technique

BoNT-A is usually injected into the urinary sphincter under elecromyographic (EMG) or cystoscopic guidance. The EMG-based technique consists of locating the USS with an EMG needle. In males, the needle is usually inserted into the perineal raphe at equal distances from the scrotum and anus. The needle is directed towards the prostatic apex, which is palpated rectally.[15] In females, the technique derives from the urethral sphincter EMG.[18] The same type of needle is inserted, once medially or twice para-medially, into the anterior vaginal wall, underneath the mid-urethra, approximately 2 cm proximal to the meatus.

In both genders, recognition of the typical tonic activity of the USS or reflex activity elicited by glandular or clitoral squeezing (bulbo-cavernous reflex) ensures the correct location of the needle tip within the USS. Injection into the USS under EMG guidance has been shown by MRI studies to accurately and specifically target the USS.[19] No difference has been found between a single median injection and two para-median injections in each hemi-sphincter.[19]

Cystoscopy-guided injection is delivered under visual control, with an endoscopic needle passed through a rigid or flexible endoscope. Two to four injection points are entered at 12, 3, 6 and/or 9 o'clock in the sphincter. The needle has to be inserted deeper (1 cm) than in bulking agent injection, to inject the muscle and not the sub-urothelial space.[20]

BoNT-A doses injected into the USS range from 80 IU to 100 IU of Botox or from 150 IU to 250 IU of Dysport according to indications and authors. The total dose is usually diluted in 2 mL to 4 mL of saline 0.9%. Both techniques are usually performed under local anesthesia (10 mL of lidocaine gel, injected into the urethra, 10 minutes before injection) as an outpatient procedure. Patients with spinal cord injury above T6 need blood pressure monitoring during the procedure because of the risk of autonomic dysreflexia.

The efficacy of both techniques, in terms of USS denervation and quality of bladder emptying, seems to

be comparable.[1,15] The choice of either technique depends on the physician's experience and preferences.

Chen et al[21] reported transrectal ultrasound-guided transperineal BoNT-A injection to the external urethral sphincter for treatment of neurogenic DSD. The patient is placed in the left lateral position, and an ultrasound transrectal 7.5-MHz 3-dimensional multiplanar transducer probe is inserted. The longitudinal scanning plane is used allowing location of a relatively hypoechoic external urethral sphincter distal to the apex of the prostate. The needle is inserted to the level of the external urethral sphincter, which is more clearly demonstrated on the ultrasound monitor by pinching the patient's glans penis to induce the bulbocavernous reflex.

Tsai et al[22] developed a technique for localizing the external sphincter for transperineal injection of BoNT-A. He performs a combined method of fluoroscopic and electromyographic guidance, using a Foley catheter inserted for visualization of vesicourethral junction.

The patient is placed on his back with hips flexed and externally rotated. A 16F or 18F Foley catheter is inserted into the bladder. The catheter balloon is inflated with 10 mL of contrast medium. Then the examiner slowly withdraws the catheter until the balloon is secured at the bladder neck. The contrast-filled catheter channel appears as a small radio opaque line that extended from the balloon distally, lining the urethra along its path. The location of the external urethral sphincter is identified around the membranous urethra. An 8 cm Teflon-coated concentric needle electrode, in connection with a 2-channel Medelec Synergy T2 electromyography machine, is prepared for performing transperineal injection. The advancement of needle electrode is monitored as it approaches the external urethral sphincter, under EMG and fluoroscopic guidance. Less than 30 seconds of fluoroscopy time is generally needed for each patient.

Results

Since Dykstra's first report, BoNT-A was used to treat variety of disorders including neurogenic DSD, non-neurogenic obstructive sphincter dysfunction and hypocontractile bladders.

BoNT-A efficacy in neurogenic DSD was demonstrated in two sets of populations; quadriplegic men unable to perform self-catheterization and MS patients of both genders. Efficacy was evaluated using various parameters: postvoid residual (PVR), maximum flow rate (Qmax), maximum urethral pressure, maximum detrusor pressure, frequency of hyperreflexia episodes, objective USS denervation under EMG and validated questionnaires, Table 1.

Few articles have specifically reported on non-neurogenic DSD. Zermann et al[16] observed that BoNT-A injections improved bladder emptying and pain in patients with chronic prostatitis. In six women with complete or partial urinary retention due to non-relaxing urethral sphincter, Fowler et al[23] found no effect of BoNT-A injection.

Chen et al[24] evaluated BoNT-A injection into the bladder neck and urethra of men with small BPH and LUTS that were refractory to medical treatment. Qmax significantly increased at 1 month and was still improved at 6 months. Bladder capacity increased and PVR decreased at 1 and 3 months but not at 6 months after treatment. QoL index and global satisfaction were improved significantly at all time points after treatment. They suggested that bladder neck and urethral dysfunction may play a role in LUTS in men without BPH.

BoNT-A injection was also evaluated in children with non-neurogenic DSD by many authors. Mokhless et al[25] prospectively evaluated BoNT-A injection into the sphincter in 10 children with nonneurogenic neurogenic bladder. Postoperatively PVR and detrusor leak point pressure decreased significantly and uroflowmetry showed a marked increase in maximum urine flow. Four patients with bilateral hydronephrosis showed regression of hydronephrosis.

Radojicic et al[26] evaluated BoNT-A transperineal pelvic floor/external sphincter injection combined with behavioral therapy and biofeedback in 20 children with voiding dysfunction who had been resistant to previous therapies. Nine patients regained normal voiding and 8 showed improvement. Three did not manifest any significant improvement.

Franco et al[27] evaluated the effects of sphincteric BoNT-A injection in a series of 16 neurologically normal children with evidence of external sphincter dyssynergia with various voiding problems. PVR was decreased significantly, yet uroflow data revealed no difference in flow rates before or after injections.

Petronijevic et al[28] investigated the role of BoNT-A and bladder rehabilitation in the treatment of 9 female children with dysfunctional voiding. BoNT-A in a dose of 500 units was injected transperineally into the external urinary sphincter. Bladder rehabilitation was introduced 2 weeks after injection. The mean voided volume increased significantly and PVR significantly decreased after the injection. Significant differences in other uroflowmetry parameters were not found.

Kuo et al[17,29] studied the effect of BoNT-A injection in 35 patients with detrusor hypocontractility. They concluded that 81% had a prefect result or improvement in bladder emptying. Qmax was increased significantly, and mean voiding pressure and PVR decreased significantly.

TABLE 1. **Efficacy of BTA injection in urethral striated sphincter**

Author, method	Patients	Dose	Results	Duration	Level of evidence
Dykstra et al[1] Case series	11 SCI males	Oculinum 140-240U	USS denervation 11/11; MUP↓-27 cmH_2O; PVR↓-146 mL; no AD	50 days	4
Dykstra and Sidi[11] RCT vs placebo	5 SCI males	Oculinum 20-240U	USS denervation 3 vs 0; MUP↓-25 cmH_2O vs 0; PVR↓-125 mL vs no change	2 months	1c
Schurch et al[15] Case series	24 SCI males	Botox 100U Dysport 250U	↓MUP; ↓duration of DSD episodes; ↓AD; ↓PVR	9-12 months	4
Petit et al[13] Case series	17 SCI males	Dysport 150U	↓MUP-24 cmH_2O; PVR↓-176 mL; ↓MDP -19 cmH_2O	2-3 months	4
Gallien et al[12] Case series	5 SCI males	Botox 100 U	MUP↓; PVR↓; AD↓	3 months	4
Wheeler et al[39] Case series	3 SCI males	Botox 100U	Subjective improvement 2/3; PVR↓	3 months	4
Phelan et al[14] Case series	13 5 SCI males 8 MS 8 (2 post operative retention, 6 perineal hypotonia)	Botox 100U	Catheter removal 11/13; PVR↓-174 mL; subjective improvement 67% Catheter removed in 8/8; PVR↓-174 mL; 67% subjective improvement	-	4
De Seze et al[10] RCT vs lidocaine	13 9 SCI m, 3 MS, 1 P	Botox 100U	MUP↓-32 cmH_2O vs no change; PVR ↓-159 mL vs ↓-60; MDP↓	3 months	1c
Liao and Kuo[33] Case series	200	Botox 50-100 U	PVR↓ by ≥ 50%; 88.5% improvement rate	1 month	4
Kuo[30] Case series	27	Botox 50-100 U	PVR↓-91%	more than 1 year	4
Kuo[31] RCT vs medical treatment	30	Botox 100 U vs medical treatment	PVR↓-44.4%; MVP↓-22%; 80% improvement rate	3-9 months	2a
Smith et al[20] Case series	68 SCI 15 perineal hypotonia	Botox 100-200 U Botox 80-200 U	PVR↓-63%; MVP↓-36%; 83% catheter free Catheter removed 83%; MUP↓-29 cmH_2O; PVR↓-152 mL	6 months	4
Kuo[29] Case series	103	Botox 50-100 U	PVR↓-61%; MVP↓-31%; 85% improvement rate	4 months	4
Kuo[17] Case series	20	Botox 50 U	PVR↓-83%; MVP↓-31%; 90% improvement rate; MUCP↓-24 cmH_2O	3-4 months	4
Fowler et al[23] Case series	6	Dysport 200 U	0% improvement rate	-	4

TABLE 1 (Cont'd). **Efficacy of BTA injection in urethral striated sphincter**

Author, method	Patients	Dose	Results	Duration	Level of evidence
Smith et al[40] Case report	1 (postop retention)	Botox 100 U	Voiding resumed after 72 hrs; Qmax 28 mL/s	-	4
Zermann et al[16] Case series	11 chronic prostatitis	Botox 200 U	Subjective improvement 9/11; pain ↓7.6 to 2.3; ↓MUP and PVR	3 months	4
Petronijevic et al[28] Case series	9	Dysport 500 U (combined with standard/behavioral urotherapy)	PVR ↓-64%; 78% improvement rate	6 months	4
Radojicic et al[26] Case series	20	BoNT-A 50 U or 100 U (brand not mentioned)	PVR ↓-65%; 85% improvement rate	9 months	4
Mokhless et al[25] Case series	10	Botox 50-100 U	PVR↓-77%; DLPP↓-37%; 100% catheter free	6 months	4
Mall et al[41] Case report	1	Botox 40 U	PVR↓-94%	More than 9 weeks	4
Safari et al[32] Case series	60 myelo-meningocele	BTA 10U/kg in detrusor (group A) 8 IU/kg in detrusor and 2 IU/kg in USS (group B)	All patients showed significant improvement in bladder capacity, MDP, and DSD after 3 and 6 months. Significant improvement in PVR only among group B	3 months	4
Chen et al[24] Case Series	30 males	BoNT-A 100U (trigone, bladder neck, proximal urethra, distal urethra and external sphincter)	Qmax significantly increased at 1 month and was still improved at 6 months. Bladder capacity increased and PVR decreased at 1 and 3 months but not at 6 months	6 months	4
Chancellor[42] Case series	68 MS patients with DSD	BoNT-A 200 U	PVR ↓-162 mL, MVP↓-29 cmH_2O; bladder capacity ↑43 mL; retention ↓-80%	6 months	4
Chen et al[43] Case series	20 SCI with DSD	Single injection of botox 100 U	PVR↓-41.2%; static UPP ↓-20.6%; dynamic UPP ↓-17.3%; no change in Pdet.	4 weeks	4
Kuo et al[44] Case series	33 SCI and DSD	Botox 100 U	Satisfaction rate 60.6%; Qmax↑2.6 mL/s; PVR↓-85 mL	3 months	4
Lim al[45] Case series	8 males Bladder neck dyssynergia	BoNT-A 100U	Overall mean reduction was 50%. Frequency decreased by 46% and IPSS & I-QoL scores decreased by 47%	4 weeks	4
Franco et al[27] Case series	16 children	BoNT-A 200-300 U	75% continent from first postop visit; PVR ↓-35 cmH_2O; uroflowmetry didn't show any difference	21 months	4

SCI = spinal cord injury; USS = urethral striated sphincter; MUP = maximum urethral pressure; PVR = postvoid residual; AD = autonomic dysrefelexia; DSD = detrusor sphincter dyssynergia; MS = multiple sclerosis; P = parkinsonism; MDP = maximum detrusor pressure; MVP = maximum voiding pressure; MUCP = maximum urethral closure pressure; Qmax = peak flow rate; DLPP = detrusor leak point pressure; UPP = urethral pressure profilometry; IPSS = international prostate symptom score; I-QoL = incontinence quality of life questionnaire; BoNT-A = botulinum toxin type A

Kuo et al[30] also investigated the recoverability of bladder contractility after urethral BTA injection in patients with idiopathic low detrusor contractility. Recovery of detrusor contractility was defined as an increase in detrusor pressure and maximal flow rate and reduced postvoid residual urine volume. The recovery of detrusor contractility after urethral BTA injection occurred in 13 patients (48%). They concluded that patients with detrusor underactivity with normal bladder sensation combined with a poor relaxation or hyperactive urethral sphincter were significantly more likely to recover normal detrusor function.

BoNT-A has been also used in a group of posthysterectomy women with voiding dysfunction.[31] Both voiding pressure (115.2+/-63.7 mL versus 90.2+/-49.5 mL) and postvoid residual volume (330.9+/-124.9 mL versus 183.9+/-183.4 mL) improved significantly after treatment. The obstructive symptom score was significantly reduced and the QoL index improved postoperatively. The success rate was 80%. The maximal effect appeared about 1 week after treatment. The duration of the therapeutic effect ranged from 3 to 9 months.

In children, Safari et al[32] compared the efficacy of BoNT-A intravesical injections with and without injections in external urethral sphincter in treating bladder hyper-reflexia in patients suffering from myelomeningocele. A total of 60 patients were randomly divided into two groups and were followed up for 6 months. 10 IU/kg of BoNT-A was injected into the detrusor muscle, sparing the trigone and ureteral orifices in group A. Group B received 8 IU/kg of toxin and 2 IU/kg of toxin through four injections in external urethral sphincter. All patients showed significant improvement in bladder capacity, maximal detrusor pressure and detrusor-sphincter dyssynergia after 3 and 6 months of receiving injections. Significant improvement in postvoiding residual volume was observed only among patients of group B. Both methods resulted in a significant reduction in daily incontinence grade, constipation, and vesicoureteral reflux, but comparison between the study groups showed better outcomes for group B in relation to incontinence, constipation, vesicoureteral reflux, and creatinine level. This is nearly the single study which evaluates combined therapy of DSD and detrusor overactivity (DO) with intradetrusor and intrasphincteric injections of BoNT-A.

The duration of the BoNT-A effect ranged from 1 to 4 months after a single injection. According to Schurch et al,[15] it can be increased up to 12 months with two consecutive monthly reinjections after the initial injection.

Kuo et al[33] searched for causes of failed external sphincter injection of BoNT-A in patients with voiding dysfunction who do not benefit from this treatment. A total of 200 patients during a 5 year period were included in this study. Treatment was considered successful when patients were subjectively satisfied with the outcome, patients with chronic urinary retention resumed spontaneous voiding, patients with a large postvoid residual volume had a reduction in postvoid residual of more than 50%, and patients voided with a lower detrusor pressure or lower abdominal pressure to urinate adequately. The overall success rate was 88.5% (177 patients), including 47.5% (95 patients) with an excellent result and 41% (82 patients) with an improved result. The causes of failed treatment in 23 patients were detrusor underactivity with very low abdominal straining pressure in 7, a tight urethral sphincter in 7, bladder neck obstruction in 7, and psychological inhibition of voiding in 2.

De novo stress incontinence after BoNT-A injection into the sphincter was found to occur in 4%-10% of patients with initially normal micturition.[20,29] No severe side effects were encountered after BoNT-A injecton into the USS.[34] Transient upper limb muscle weakness, lasting from 2 weeks up to 2 months was seen in three quadriplegic patients. One case of unexplained fever was reported. It lasted 2 weeks and resolved spontaneously.

Discussion

Neurogenic DSD

All authors concluded that BoNT-A injection was efficient in improving bladder emptying in patients of neurogenic DSD.

Quadriplegic men were the most widely studied population. BoNT-A injection into the USS is proposed to these men as means of chemical sphincterotomy, an alternative to surgical sphincterotomy or stent. Its goal is to obtain autonomic bladder emptying, triggered by uninhibited detrusor contractions. The potential advantages of BoNT-A injections are its relatively limited invasiveness and reversibility. It gives the opportunity to patients who are reluctant to undergo sphincterotomy, to appreciate the results through a reversible intervention. It might be specifically valuable in the early phase of their disability after spinal shock has resolved, while they are still involved in heavy care programs and accept their handicap with difficulty. There are discrepancies in the impact of the treatment on PVR and bladder pressure.

To evaluate BoNT-A injection efficacy, none of the studies used detrusor leak point pressures (DLPP)

as a primary outcome except for a single publication in 2006.[25] This is surprising as we know the value of DLPP as a predictor of upper urinary tract damage.[35] Furthermore, the need for post sphincterotomy adjuvant treatment of bladder neck has to be evaluated.

MS patients represent the main other population that was studied. DSD in MS patients does not usually have the same features and consequences as in spinal cord injured patients. Upper tract involvement as well as complete retention is infrequent. The most common problems related to DSD are recurrent urinary tract infections,[36] which limit immunomodulator treatments of MS, worsen MS symptoms or aggravate overactive bladder symptoms which are frequently present in MS.[36]

The goal of BoNT-A injection into the USS in MS patients is to decrease urethral resistance enough to avoid chronic retention/urinary stasis/PVR elevation but not to the point of inducing stress urinary incontinence. The potential advantage of BoNT-A injections over clean intermittent catheterization in MS patients is that patients' cognitive and visual impairment as well as manual dexterity do not affect their eligibility for treatment. MS patients have not been specifically studied. Because they have different expectations about DSD treatment and their therapy involves different goals compared to quadriplegic men, dedicated studies are warranted.

Non-neurogenic obstructive sphincter dysfunction

Despite previous publications on the efficacy of BoNT-A injection into the USS to improve bladder emptying and obstructive symptoms of various non-neurogenic obstructive sphincter dysfunctions, it is difficult to make clear recommendations or indications. The indications vary widely, from obstructive symptoms and pain associated with prostatitis to pelvic floor hypertonia or uncertain DSD secondary to the presence of a sub-urethral tape.

Moreover, differences in outcome measurements and efficacy criteria preclude any comparative analysis. In addition to its pathophysiology, diagnostic criteria and the clinical relevance of non-neurogenic obstructive sphincter dysfunction remain questionable.

In case of Fowler's syndrome, the inefficacy of BTA to treat retention is thought to be related to the myogenic nature of the sphincter dysfunction in this rare disorder.

Detrusor hypocontractility

Kuo et al[17,29,30] have studied the effect of BoNT-A injections in cases of detrusor hypocontractility in order to avoid self-catheterization.

This approach has raised lot of concerns; Kuo[17] reported a mean detrusor pressure at voiding of 64 cmH_2O after BoNT-A injection, still above the safe limit of 40 cmH_2O stated by McGuire. Above this value, there is a heightened risk of vesicoureteral reflux, which can be further aggravated by voiding in these patients, as it is not active physiological micturition involving the trigonal anti-reflux mechanism.

The safety of micturition by abdominal straining, even with a supposed decrease in urethral resistance, is doubtful. Chronic abdominal straining is known to favor groin hernia and hemorrhoid formation or pelvic organ prolapse in females.

Since the bladder neck in both genders and the prostate in men contribute to urethral resistance and continence, one can wonder by how much an injection of BoNT-A into a normal or hypotonic sphincter can decrease total urethral resistance. And if it does so enough to dramatically reduce the pressure needed to void, why does it not induce stress incontinence? The risk of denovo stress incontinence related to induce sphincter insufficiency has to be evaluated specifically.

Recommendations for future studies

MS patients and quadriplegic men are the two populations mostly benefiting from BoNT-A sphincteric injections. Even MS patients have different expectations and goals about their DSD management compared to quadriplegic men. These two populations need to be studied separately in properly powered randomized, placebo controlled trials.

In quadriplegic men, the primary outcome to evaluate the efficacy of sphincter injection of BTA should be DLPP. In MS patients, the primary outcome should include symptom evaluation, PVR estimation and number of episodes of urinary tract infections. De novo stress incontinence should be assessed and considered as a treatment adverse effect. Possible changes in DO need to be studied since relief of obstruction might relief DO.

All studies, in quadriplegic men as well as in MS patients should include, as secondary outcomes quality of life questionnaires; for example Qualiveen[37] and I-QoL.[38]

Another novel field of research for BTA injection is patients with combined neurological impairment (MS, Parkinsonism or post stroke) and organic bladder outlet obstruction. Prostate surgery in these patients is questionable and has a high failure rate. Due to reversibility of BTA and minimal invasiveness, intra-sphincteric BTA injections may help to distinguish benign prostatic hyperplasia related obstruction from DSD related bladder outlet obstruction. BTA use could be both diagnostic and therapeutic.

There are sparse publications on the non-neurogenic obstructive sphincter dysfunction. Still further studies are required to confirm the early studies, despite the increased number of publications in the last 5 years. The presence of obstruction and urethral sphincter hypertonia or paradoxical contractions during micturition should be among the inclusion criteria and should be confirmed by videourodynamics. BTA injections should be compared to a placebo group (saline injection).

The need for regular re-injections of BTA into the USS to maintain results suggests that cost effectiveness analyses must be conducted with medium and long term projections. These analyses will have to compare BTA treatments to alternative options (sphincterotomy or sphincteric stents in quadriplegic patients and intermittent catheterization in MS or non-neurological patients).

In summary

There is level of evidence 1c for the use of BTA in DSD in neurogenic patients, but the clinical value of this has to be studied further before a recommendation can be made.[9] If injection is done, Botox 100 U in 4 mL should be used (Grade C recommendation).[9] Further studies in adults with voiding dysfunction of non-neurogenic origin are needed, (Grade A recommendation).[9]

Conclusion

Since our first review in 2006, very little has been added to the literature on the use of botulinum toxin injected into the external sphincter. Considering the difficulties that we have to treat the challenging problem of spastic/dyssynergic sphincter, this is very disappointing. Well developed and conducted studies are necessary; these must be done urgently to better define the place and the results of this drug otherwise widely used in other indications in urology.

At present, those most likely to benefit from intrasphincteric BTA injection are MS patients suffering the symptoms of DSD and quadriplegic men with DSD unable to perform self-catheterization. □

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