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BLADDER BASE INJECTION IS AS EFFECTIVE AND SAFE AS BLADDER BODY INJECTION OF BOTULINUM TOXIN A FOR IDIOPATHIC DETRUSOR OVERACTIVITY

Hypothesis / aims of study

Intradetrusor injection of botulinum toxin A (BoNT-A) has been found to modulate the release of neurotransmitters from sensory nerve endings, and effectively modulate the inflammatory process mediated by nociceptive afferent nerve dysfunction [2,3]. Clinical experiences of intravesical BoNT-A injection have achieved satisfactory results in increasing bladder capacity and decrease urgency sensation in patients with neurogenic or idiopathic detrusor overactivity (IDO). However, postvoid residual (PVR) increased significantly and some patients required clean intermittent catheterization (CIC) to evacuate PVR. The purpose of this study is to evaluate and compare the efficacy and safety among bladder body, bladder body and trigone, and bladder base including trigone injections of botulinum A toxin (BoNT-A) for the treatment of idiopathic detrusor overactivity (IDO) refractory to antimuscarinic agents.

Study design, materials and methods

This study is designed as a single-blind, randomized, parallel, active- controlled trial. The urodynamic DO confirmed patients were randomly assigned to receive BoNT-A 100U (BOTOX, Allergan, Irvine, CA, USA) in one of the three: (A) bladder body 100U injections, (B) bladder body 75U plus trigone 25U injections, (C) bladder base 50U and trigonal 50U injections. All treatments were evaluated at baseline and primary end-point at 3 months for symptom score, urodynamic studies, and global satisfaction assessments (GRA). The success rate and the duration of therapeutic effects were compared among three subgroups. Paired Student t-test was used to analyze for paired comparison between baseline and 3 months results within subgroups and an independent t-test was used for the changes after treatment among subgroups. Kaplan-Meier survival analysis was used to compare the cumulative success rate among three subgroups.

Results

A total of 110 patients were screened, 5 rejected treatment after signed informed consent, resulting in 105 patients who were enrolled into this study. After decoding at the end of this study, 37 patients were randomized to subgroup A, 35 subgroup B, and 33 subgroup C injections. A successful result was reported in 76 patients (72%) at 3 months, including 26 (70.3%) of subgroup A, 26 (74.3%) of subgroup B, and 24 (73%) of subgroup C injections. There was no significant difference in the success rate at 3 months among subgroups. The USS and GRA were significantly improved in all subgroups at 3 months, while only patients in subgroup A and B had significant reduction of urgency and UUI episodes. (Table 1) The changes of IPSS subscores and QoL index from baseline to 3 months showed significant improved in the QoL index as well as the storage subscore and no change in the empty subscore in all subgroups at 3 months. Urodynamic parameters showed no significant difference in the changes from baseline to 3 months among all subgroups. (Table 2) Longer therapeutic success rates also showed no significant difference among three subgroups.

Interpretation of results

This study revealed that intravesical BoNT-A injection had a therapeutic effect on OAB patients. About 72% of patients could become dry or OAB symptom improvement. There was no significant difference in the success rate at 3 months or long-term among subgroups with different injection site. However, AUR did not occur in patients receiving bladder base and trigonal injection. Ageing patients with co-morbidity may carry higher risk of large PVR and straining to void. Although the occurrence of AE does not affect the success rate of intravesical BoNT-A injection for OAB, we might consider bladder base and trigone injection for OAB patients who were at higher risk of developing AE. The results of this study revealed that no significant difference in efficacy and safety among subgroups with different injection site. The storage IPSS subscore, urgency/UUI episodes and urgency severity all showed significantly improved after BoNT-A injection, but the IPSS empty subscore did not increase at 3 months. Moreover, patients with bladder base and trigonal injection did not develop AUR after BoNT-A injection, but carry the same risk for large PVR and straining to void, suggesting that blocking sensory nerves from bladder base or bladder body has similar effect on urgency reduction, but less effect on detrusor contractility was noted in patients without bladder body injection

Concluding message

The results revealed that intravesical BoNT-A injection is an effective treatment for IDO irrelevant to injection sites. Bladder base and trigone injection is as effective and safe as bladder body with or without trigonal injection.

Table 1. The changes of urgency and urgency incontinence (UUI) episodes per 7 days from baseline to 3 months (primary end-point)

		(A) Bladder body (n=37)	(B) Bladder body + trigone(n=35)	(C) Bladder base + trigone (n=33)	P value
Urgency	BL	50.6±26.9	58.7±33.1	43.9±33.5	0.184
	3M	53.1±22.9	54.9±22.5	41.0±18.0	0.046
	P value	0.912	0.398	0.702	
UUI	BL	19.3±32.5	15.2±19.8	22.0±29.4	0.375
	3M	7.07±16.2	5.13±14.2	15.8±35.1	0.201
	P value	0.004	0.002	0.518	
Urgency	BL	69.9±27.6	71.6±27.1	66.0±29.2	0.836

and UUI	3M	60.2±23.2	60.1±20.8	56.8±26.0	0.851
	P value	0.020	0.012	0.142	
USS	BL	3.65±0.59	3.60±0.74	3.67±0.65	0.910
	3M	2.42±1.03	2.36±1.14	2.47±1.11	0.932
	P value	0.000	0.000	0.000	
GRA	BL	0.03±0.16	0.03±0.17	0.09±0.38	0.504
	3M	1.85±1.00	1.91±0.88	1.87±0.97	0.966
	P value	0.000	0.000	0.000	

Table 2. The changes of urodynamic parameters from baseline to 3 months

		(A) Bladder body (n=37)	(B) Bladder body + trigone (n=35)	(C) Bladder base + trigone (n=33)	Statistics among subgroups
Qmax	BL	14.4±6.22	14.1±6.88	13.3±5.85	
	3M	13.9±7.64	12.5±6.99	11.1±4.57	
	change	0.56±5.83	-1.26±4.87	-1.99±4.60	0.142
PVR	BL	17.0±37.9	35.6±71.3	42.9±68.5	
	3M	87.2±87.7	110.2±95.3	108±75.8	
	change	68.1±90.1	72.4±105	61.1±86.2	0.895
Capacity	BL	268±121	287±110	244±121	
	3M	323±123	336±129	309±141	
	change	62.7±114	49.6±108	59.8±125	0.898
Pdet	BL	30.1 ± 15.6	27.6 ± 14.5	27. 7± 14.6	
	3M	25.3 ± 15.2	25.7 ± 11.7	23.6 ± 13.6	
	change	-5.35 ± 7.57	-2.1 ± 3.54	-4.1 ± 5.13	0.865
Voiding	BL	93.2±14.1	88.0±17.3	84.5±22.8	
efficiency	3M	75.3±21.6	69.3±24.9	66.8±19.5	
	change	-14.8±23.0	-17.9±24.5	-18.6±22.0	0.798

Specify source of funding or grant	**Buddhist Tzu Chi General Hospital**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
Is this a Randomised Controlled Trial (RCT)?	**Yes**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Institutional Review Board of Buddhist Tzu Chi University and Tzu Chi General Hospital**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**