552

Jhang J[1], Lee C[1], Jiang Y[1], Kuo H[1]
1. *Department of Urology, Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan*

REPEAT ONABOTULINUMTOXINA INJECTIONS PROVIDE BETTER THERAPEUTIC RESULTS THAN SINGLE INJECTION IN TREATMENT OF BLADDER PAIN SYNDROME

Hypothesis / aims of study
Currently treatments for interstitial cystitis (IC) and bladder pain syndrome (BPS) usually cannot completely eradicate bladder pain and increasing bladder capacity. Previous study showed intravesical OnabotulinumtoxinA (BoNT-A) Injections could provide short-term symptomatic relief in treating IC/BPS. However, long-term follow-up does not show successful outcome after single injection. This study is designed to investigate the efficacy and safety of repeated intravesical BoNT-A injections in comparison with a single injection for the treatment of IC/PBS refractory to conventional treatment.

Study design, materials and methods
Intravesical injection of 100 U of BoNT-A was performed in 104 patients every 6 months for up to 4 times. At 6 months after the initial injection, patients could decide whether they wanted to continue BoNT-A injection or not, based on their subjective therapeutic effects.Patients who received single injection served as active controls. Patients were requested to rate bladder symptoms compared with baseline on a 7-point centered scale from markedly, moderately, and slightly worse, no change, to slightly, moderately, and markedly improved. Patients with moderately and markedly improved results were considered to have successful treatment outcomes. Measured parameters included O'Leary-Sant symptom indexes (ICSI) and problem indexes (ICPI), visual analogue score (VAS), voiding diary variables, urodynamic parameters, maximal bladder capacity under anaesthesia, glomerulation grade, and global response assessment (GRA). Multiple measurements and Kaplan-Meier analysis were used for success rates among groups.

Results
Among 104 patients, 15 received single, 25 received two, 19 received three, and 45 received four injections, respectively. The mean (± SD) of ICSI, ICPI, total scores, VAS, functional bladder capacity, and daytime frequency all showed significant improvement after repeated BoNT-A treatment with different injections (Table 1). Significantly better success rates were noted in patients who received four injections and three injections, compared to those who received a single and two injection (Fig. 1). There was no significant difference of long-term success rates among patients who received 3 and 4 injections. Difficult urination was the most common adverse events. Only one episode of acute urinary retention occurred and only one patient needed clean intermittent self-catheterization for 3 months. The occurrence of adverse events did not increase with increasing number of BoNT-A injections (Table 2).

Interpretation of results
The results of this study demonstrated that repeated intravesical injections of BoNT-A increased FBC and provided long-term pain relief in patients with IC/PBS who were refractory to conventional treatment. The long-term success rates of 3 or 4 repeated intravesical
BoNT-A injections were better than a single or two injections. Previous studies showed intravesical injections of BoNT-A have anti-inflammatory effect on IC/BPS, and current study also implies repeat BoNT-A injection might achieve long-term control of bladder inflammation. The incidence of adverse effects did not increase after repeat BoNT-A injections.

Concluding message
Repeated intravesical BoNT-A injections are safe and effective for pain relief and can increase bladder capacity and provide a better long-term success rate than a single injection for treatment of IC/PBS.

Table 1. Changes of baseline parameters before each time-point of BoNT-A injection

	BoNT-A x1 Baseline (N=104)	BoNT-A x2 Baseline (N=89)	BoNT-A x 3 Baseline (N=64)	BoNT-A x 4 Baseline (N=45)	P value
ICSI	12.3±3.5	9.0±4.8	9.1±4.3	7.9±3.9	<0.0001
ICPI	11.4±3.0	8.1±4.6	8.1±4.5	6.2±4.6	<0.0001
OSS	23.7±6.2	17.1±9.1	17.2±8.5	14.1±8.4	<0.0001
VAS	5.2±2.4	3.5±2.4	3.6±2.5	2.7±2.4	<0.0001
Frequency	15.5±8.0	11.2±5.9	11.3±6.0	10.0±5.3	0.001
Nocturia	4.8±4.7	3.6±4.0	3.5±4.0	3.1±2.6	0.081
Qmax	12.5±5.5	12.3±5.7	13.5±6.6	12.4±5.7	0.647
FBC	128.4±74.5	181±89.8	199.5±99.9	229.1±111.4	<0.0001
Volume	239.5±111.9	261±116.6	302.7±136.7	274.5±147.6	0.297
CBC	271.3±111.3	299.4±117.1	343.3±120.8	339.3±160.6	0.004
PVR	38.2±92.9	53.1±98.3	45±84.3	56.5±90.1	0.039
MBC	667.8±216.9	741.9±190.4	734.7±207.4	758.0±199.0	0.030

GRA	0	1.2±1.1	1.5±1.0	1.9±1.1	<0.0001

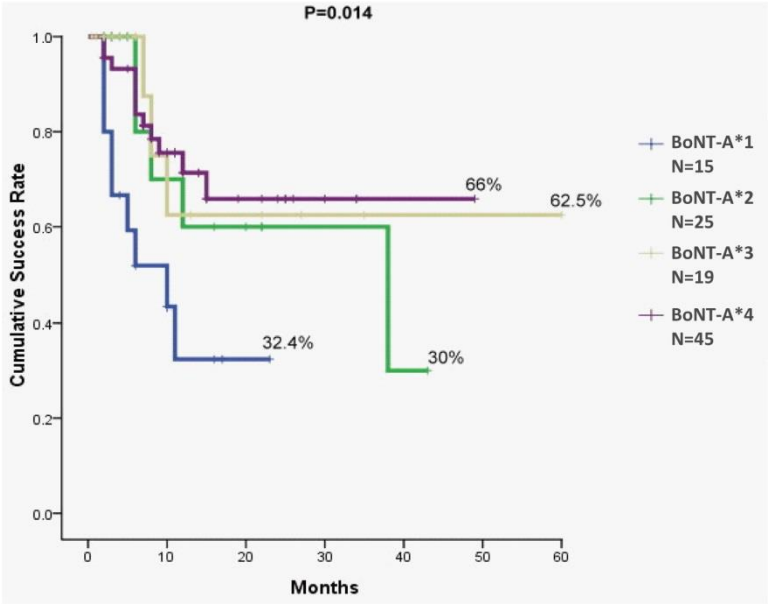
BoNT-A: botulinum toxin type A, CBC: cystometric bladder capacity, FBC: functional bladder capacity, GRA: global response assessment, ICPI: interstitial cystitis problem indexes, ICSI: interstitial cystitis symptom indexes, MBC: maximal bladder capacity, OSS: O'Leary-Sant symptom score, PVR: postvoid residual, Qmax: maximum flow rate, VAS: visual analog scale

Table 2. Adverse events occurred after repeated BoNT-A injections. There was no significant difference among each injection group

	Adverse events						
	None	UTI	Dysuria	CISC	AUR	Hematuria	Total
BoNT-A X 1	64 (61.5%)	6 (5.8%)	32(30.8%)	0	0	2 (1.9%)	104
BoNT-A X 2	49 (55.1%)	7 (7.9%)	31 (34.8%)	0	1 (1.1%)	1 (1.1%)	89
BoNT-A X 3	29 (46%)	10 (15.9%)	23 (36.5%)	1 (1.6%)	0	0	64
BoNT-A X 4	29 (64.4%)	5 (11.1%)	11 (24.4%)	0	0	0	45

AUR: acute urinary retention, CISC: clean intermittent self-catheterization, UTI: urinary tract infection

Fig. 1. The cumulative success rates of the 104 patients receiving single injection or different numbers of repeated onabotulinumtoxin A (BoNT-A) injections.



Disclosures
Funding: None **Clinical Trial:** Yes **Public Registry:** No **RCT:** No **Subjects:** HUMAN **Ethics Committee:** Research Ethics Committee of Buddhist Tzu Chi General Hospital, Hualien, Taiwan **Helsinki:** Yes **Informed Consent:** Yes