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Liao C[1], Jiang Y[2], Kuo H[2]

1. *Department of Urology, Cardinal Tien Hospital and School of Medicine, Fu-Jen Catholic University, New Taipei, Taiwan,* ***2.*** *Department of Urology, Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan*

PROSPECTIVE RANDOMIZED COMPARATIVE STUDY OF INTRAVESICAL ONABOTULINUMTOXIN A INJECTION WITH DIFFERENT INJECTION NUMBER FOR OVERACTIVE BLADDER SYNDROME

Hypothesis / aims of study

Intravesical onabotulinumtoxin A (BoNT-A) injection is effective for detrusor overactivity (DO) or overactive bladder (OAB) refractory to antimuscarinics. However, the high rates of treatment-related adverse events (AEs) prevent its more widespread use. Decreasing the dose of BoNT-A may decrease these AEs, but may also decrease the therapeutic effects concurrently. Adjusting the injection sites and number is another way to minimize the de novo AEs and maintain the therapeutic effects. Therefore, we conducted a prospective randomized comparative trial to compare the therapeutic effects and safety of intravesical BoNT-A injection with different injection number for OAB.

Study design, materials and methods

Patients with urodynamic DO and at least one episode of urgency or urgency incontinence per day as recorded in the 3-day voiding diary were enrolled. All patients had been treated with antimuscarinics for more than 4 weeks and antimuscarinics was discontinued. Patients were randomly assigned to receive intravesical injection of BoNT-A 100 U (Allergan, Irvine, California, USA) in one of the three groups with the following injection number: (A) 100 U in 10ml injections, 1.0ml for each injection, totally 10 injections at bladder body (B) 100 U in 10ml, 0.5ml for each injection, totally 20 injections at bladder body, (C) 100 U in 10ml, 0.25ml for each injection, totally 40 injections at bladder body. Treatment results were assessed by overactive bladder symptom score (OAB-SS), Urgency severity score (USS), Patient Perception of Bladder Condition (PPBC), voiding diary, and urodynamic parameters.

Results

Sixty-seven patients (34 male and 33 female, mean age 65 years) were randomized into 3 groups. The average number of OAB-SS, USS, and PPBC decreased while the average post-void residual urine (PVR) increased in all 3 groups (Table 1). The changes of urodynamic parameters and parameters in void diary were also comparable between groups. The rates of overall adverse effects were also similar between groups. There was no significant difference in the rates of hematuria, dysuria, urinary retention, bladder pain, micturition pain, large PVR and UTI among three groups (Table 2).

Interpretation of results

This is the first prospective randomized comparative trial to compare the therapeutic effects and safety of intravesical BoNT-A injection with different injection number for OAB. It had been reported that single BoNT-A injection spreads the neurotoxin activity to the opposite side of the guinea pig bladder. Our results supported that decreasing injection number may maintain the therapeutic effects. However, the overall AEs were not decreased associated with decreased injection number. The therapeutic effect depends on the dose of BoNT-A, and possibly, the volume of BoNT-A solution which may distribute to the same size of the suburothelial area.

Concluding message

Intravesical BoNT-A injections with different injection number had similar therapeutic effects. The rates of overall adverse effects were also similar between groups. We therefore proposed, based on the results of this study, injection at 10 sites with 1mL (containing 10 U BoNT-A) BoNT-A solution is adequate for an optimal therapeutic effect on OAB.

Table 1. Treatment results

		10 sites (n=24)	20 sites (n=22)	40 sites (n=21)	#P value
OABSS	B	12.61 ± 2.12	12.38 ± 2.09	11.75 ± 2.24	0.627
	1M	10.06 ± 2.86*	9.31 ± 3.16*	8.88 ± 3.81*	
	3M	9.06±3.82*	10.06±3.58*	8.60±3.36*	
USS	B	3.94 ± 0.24	3.88 ± 0.50	3.94 ± 0.25	0.720
	1M	3.61 ± 0.78	3.19 ± 0.91*	2.88 ± 1.20*	
	3M	3.24±1.15*	3.53±1.01	3.27±1.28	
PPBC	B	5.44 ± 1.25	5.00 ± 1.46	4.31 ± 1.82	0.019
	1M	2.83 ± 1.04*	3.13 ± 1.67*	2.06 ± 1.34*	
	3M	2.94±1.52*	3.59±1.66*	2.00±1.07*	
UUI／3D	B	11.82 ± 13.88	5.69 ± 7.64	10.27 ± 12.38	0.493
	1M	6.18 ± 10.48*	5.00 ± 8.33	6.20 ± 9.89	
	3M	8.38±13.62	9.00±20.41	2.00±2.48*	
Urgency／3D	B	32.71 ± 18.38	28.50 ± 13.00	31.33 ± 18.76	0.931
	1M	22.53 ± 16.67*	29.44 ± 30.54	23.47 ± 22.71	
	3M	24.00±17.25	28.38±26.96	30.46±27.67	
Frequency／3D	B	39.71 ± 17.54	37.63 ± 11.01	39.33 ± 18.89	0.963
	1M	34.76 ± 10.55	37.13 ± 27.45	35.07 ± 14.54	
	3M	34.50±10.55	37.00±22.01	40.31±26.54	

	B	291.00 ± 123.07	292.50 ± 110.79	377.33 ± 186.83	
FBC	1M	307.65 ± 143.42	291.88 ± 87.80	300.00 ± 180.95	0.865
	3M	297.81±136.74	291.25±125.43	291.54±150.27	
	B	14.56 ± 11.10	15.71 ± 10.75	14.40 ± 9.64	
Qmax	1M	12.50 ± 7.41	13.76 ± 8.14	13.80 ± 12.85	0.638
	3M	11.88±7.57	17.59±8.68	13.86±10.92	
	B	168.56 ± 86.08	187.18 ± 97.77	226.33 ± 127.69	
Volume	1M	208.89 ± 148.84	181.41 ± 82.35	189.20 ± 101.00	0.995
	3M	200.06±135.35	225.65±97.31*	207.14±173.31	
	B	27.67 ± 29.80	74.76 ± 70.91	25.60 ± 27.82	
PVR	1M	149.00 ± 99.63*	169.76 ± 92.43*	125.47 ± 89.60*	0.070
	3M	110.24±85.53*	151.06±132.24*	91.57±119.43*	

*P< 0.05 comparisons between data at baseline and 1 month or 3 months after treatment
FBC: functional bladder capacity, OAB-SS: overactive bladder symptom score; PPBC: patient perception of bladder condition, PVR: postvoid residual, Qmax: maximal flow rate, USS: urgency severity score, UUI: urgent urinary incontinence.
comparisons of the changes between groups

Table 2. Common AEs after different intravesical BoNT-A injection groups

	10 sites (n=24)	**20 sites (n=22)**	**40 sites (n=21)**	**P value**
Hematuria	4 (16.7%)	6 (27.3%)	3 (14.3%)	0.512
Urinary retention	3 (12.5%)	1 (4.5%)	2 (9.5%)	0.637
Bladder pain	0	1 (4.5%)	2 (9.5%)	0.305
Micturition pain	0	1 (4.5%)	0	0.354
Large PVR (≥200 mL)	14 (58.3%)	17 (77.3%)	11 (52.4%)	0.207
Dysuria	7 (29.2%)	6 (27.3%)	6 (28.6%)	0.990
UTI	4 (16.7%)	8 (36.4%)	2 (9.5%)	0.079

UTI: urinary tract infection

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