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EFFECT OF REPEATED INTRAVESICAL BOTULINUM TOXIN A INJECTIONS ON TREATMENT OF REFRACTORY INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME--- PRELIMINARY RESULTS

Hypothesis / aims of study

Interstitial cystitis/painful bladder syndrome (IC/PBS) is a debilitating chronic disease of unknown aetiology characterized by urgency frequency and suprapubic pain at full bladder. Current treatments are usually unsuccessful in completely eradicating bladder pain and increasing bladder capacity (1). Although botulinum toxin A (BoNT-A) injection seems promising in treating symptoms of IC/PBS, long term results did not provide successful outcome (2). This study valuated the effects of repeated intravesical BoNT-A injections plus hydrodistention on treatment of IC/PBS refractory to conventional treatment.

Study design, materials and methods

A prospective study was performed in a urological referral centre. Patients with IC/PBS who have failed conventional treatments have been enrolled. They received intravesical injection of 100 U of BoNT-A (onabotulinumtoxinA, Allergan, Irvine, CA, USA) immediately followed by cystoscopic hydrodistention under intravenous general anesthesia. Repeated BoNT-A injection and hydrodistention were performed at 6 months after the first treatment if they felt recurrence of baseline symptoms and desired for further treatment. The BoNT-A injection plus hydrodistention was repeated every 6 months up to 4 times or till patients declared their symptoms have relieved. In each time of therapy, O'Leary-Sant symptom and problem indexes (ICSI and ICPI), bladder pain visual analogue scale (VAS), functional bladder capacity (FBC), daily urinary frequency and nocturia were recorded at baseline, 3 months and 6 months after treatment. Urodynamic parameters were measured at baseline and 6 months after treatment. Global response assessment (GRA) was used to evaluate successful treatment response.

Results

From 2005 October till now, 6 men and 65 women aged 44.1±11.5 (31-57) and 47.9±12.6 (21-76) years respectively were enrolled in this study. Among them, 71, 49, 32 and 19 patients completed one, two, three and four times of intravesical BoNT-A injection respectively. As the number of treatment increased from one to four times, the IC/PBS symptom score, pain VAS and daytime frequency significantly decreased. When BoNT-A injection was repeated up to four times, FBC, volume at full sensation and cystometric bladder capacity significantly increased (Table 1). In addition, a successful result (GRA $\geqq$2) at 6 months after the first, second, third and fourth BoNT-A injection was reported in 24 (44%), 15 (44%), 9 (53%) and 7 (54%) patients (Figure 1). The overall incidence of adverse effects including urinary tract infection, dysuria, intermittent catheterization, acute urine retention and hematuria during first, second, third and fourth treatment was 28%, 29%, 45% and 32% respectively (p=0.305).

Interpretation of results

Repeated intravesical BoNT-A injection plus hydrodistention might not only continue decreasing the clinical symptoms (IC/PBS symptom score, pain VAS, daytime frequency and FBC) significantly but also continue improving the urodynamic parameters (volume at full sensation and cystometric bladder capacity) significantly in patients with refractory IC/PBS. Long-term successful result might be achieved. The adverse effects for repeated treatment did not increase significantly than single treatment. The effects of repeated intravesical BoNT-A injections might involve not only inhibiting release of acetylcholine in the neuromuscular junctions of the detrusor but also anti-inflammatory response.

Concluding message

The effect of repeated intravesical BoNT-A injection plus hydrodistention on treatment of refractory IC/PBS is promising and durable with acceptable adverse effects.

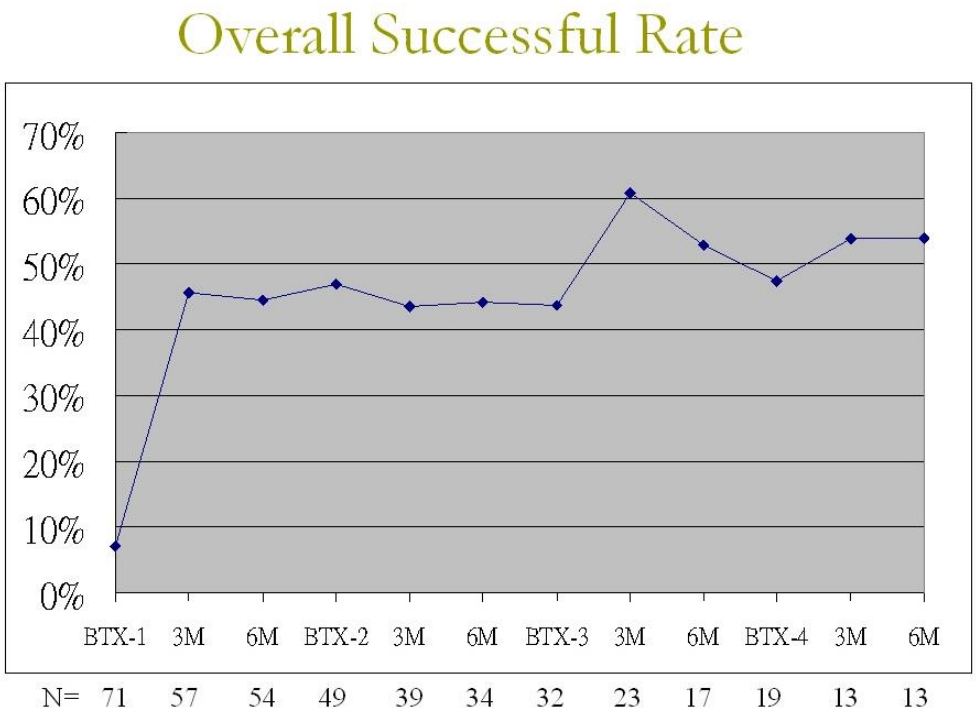
Table 1. Changes of baseline parameters before each time injection of BoNT-A.

Variable	BTX-1	BTX-2	BTX-3	BTX-4	p value
N	71	49	32	19	
Mean±SD					
ICSI	12.37±3.13	9.27±4.57	9.47±3.99	9.05±4.31	0.000*
ICPI	11.14±2.95	8.45±4.51	8.53±4.44	7.21±4.87	0.000*
OSS	23.51±5.84	17.71±8.74	18.00±8.21	16.21±9.08	0.000*
Pain VAS	5.41±2.32	3.94±2.44	3.91±2.37	3.11±2.28	0.000*
FBC	130.14±75.72	172.24±88.42	206.88±100.4	224.2±127.86	0.000*
Frequency	15.04±7.47	10.82±5.35	11.50±5.83	11.0±5.44	0.001*
Nocturia	4.48±3.89	3.10±1.81	3.31±2.29	3.68±3.30	0.082
Urodynamics					
FSF	111.13±50.97	131.83±52.31	134.76±65.88	143.1±69.19	0.057
FS	158.63±69.43	188.00±52.31	207.71±91.94	218.29±93.8	0.005*
US	203.54±89.81	238.93±72.80	241.70±79.69	238.60±88.85	0.156
CBC	257.18±110.52	306.2±119.46	344.62±139.1	327.4±175.48	0.011*
Pdet	20.14±10.10	18.54±9.73	19.04±12.36	19.87±11.60	0.887
Qmax	13.05±4.75	12.90±6.59	14.16±6.11	12.58±6.24	0.792

Volume	241.60±108.95	269.4±133.1	317.31±137.19	393.7±169.78	0.066
PVR	15.20±35.55	30.43±57.62	32.00±55.80	31.76±47.07	0.217
GRA	0.39±0.84	1.18±1.24	1.25±1.11	1.42±1.39	0.000*

*p<0.05

Figure 1. The overall success rate during the therapy course.



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Specify source of funding or grant	**None**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
Is this a Randomised Controlled Trial (RCT)?	**No**
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 and Ethics Committee of Tzu Chi university**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**