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REPEATED INTRAVESICAL ONABOTULINUMTOXIN-A INJECTIONS ARE EFFECTIVE IN THE TREATMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME REFRACTORY TO CONVENTIONAL TREATMENT

Hypothesis / aims of study

Botulinum toxin A is effective for the treatment of interstitial cystitis/ bladder pain syndrome (IC/BPS). However, long-term follow-up does not show successful outcomes after a single injection. We evaluate the efficacy and safety of repeated intravesical onabotulinumtoxinA (BoNT-A) injections for treatment of IC/BPS.

Study design, materials and methods

A total of 31 patients confirmed to have IC/BPS and refractory to conventional treatments were treated with **i**ntravesical injections of 100 U of BoNT-A plus hydrodistention every 6 months for up to 4 times. Primary end-point was 6 months after the fourth BoNT-A injection. Measured parameters included O'Leary-Sant symptom score (OSS) including symptom and problem indexes (ICSI/ICPI), visual analogue score (VAS) for pain, voiding diary variables, urodynamic parameters, maximal bladder capacity (MBC), glomerulation grade, and global response assessment (GRA). Multiple measurements and Wilcoxon rank-sum test were used for comparison between groups.

Results

A total of 31 patients (27 women and 4 men, mean age 48 years) completed the four BoNT-A injections and followed up for more than 6 months. The median duration of IC/BPS was 5 years (range, 3 to 23 years). GRA changed from 0.34±0.91 to 1.74±0.93 (p=0.000) at the end-point. The OSS total score (24.5±6.0 v 15.1±8.69, p=0.000), VAS (5.8±2.15 v 3.29±2.9, p=0.000), FBC (136±79.1 v 208± 10, p=0.000) and CBC (253±106 v 325±173, p=0.021) all showed significant improvement ay 6 months after four repeated injections. Although the glomerulation grade (1.77±1.06 v 1.19±1.05, p=0.026) showed significant improvement, MBC (705±217 v 721±207, p=0.504) did not improve significantly at the fourth repeated BoNT-A injections**.** The KCl test was positive in all patients at baseline and turned negative in 12 (40%) patients at baseline of the fourth BoNT-A treatment. In the continuing follow-up period, 7, 6 and 6 patients had persistent improvement at 6 to 12, 13 o 22, and 23 to 51 months, respectively, after the fourth BoNT-A injections. At 6 months after the fourth BoNT-A injection, 19 (61%) of 31 patients had a GRA ≥2 and 12 had a GRA <2. In the patients with a GRA≥2, OSS, ICSI, ICPI, VAS, FBC, frequency, CBC and glomerulation garde all showed significantly improved, However, no significant change of measured parameters was noted in patients with GRA <2. Compared the changes of all measured parameters from baseline to the end-point, patients with GRA ≥2 had significantly greater changes of OSS, ICPI, VAS, FBC, and CBC than those with a GRA <2 (Table 1). The therapeutic effects of OSS, VAS and glomerulation grade were significantly different after the second BoNT-A injection between patients with GRA ≥2 and GRA <2 (Fig.1). Among the 12 patients who did not satisfied with the repeated BoNT-A injection, five women were found to have Hunner's ulcer. Subsequent transurethral electrocauterization was performed and the bladder pain as well as irritative symptoms showed markedly improved.

Interpretation of results

The results of this study demonstrated that repeated intravesical injections of BoNT-A increase FBC, CBC and provided long-term pain relief in 61% of patients with IC/BPS who were refractory to conventional treatment. Patients with Hunner's ulcer are poor candidates for this treatment. Glomerulations after hydrodistention, but not MBC, also showed significant improvement after repeated BoNT-A injections. These therapeutic effects could involve not only inhibiting release of acetylcholine in the neuromuscular junctions of the detrusor, but also an anti-inflammatory response.

Concluding message

Four repeated intravesical BoNT-A injections were safe and effective for pain relieve and increased FBC and CBC in patients with IC/BPS. Improvement of bladder glomerulations and pain relief were more prominent than the reduction of frequency or nocturia after BoNT-A treatment.

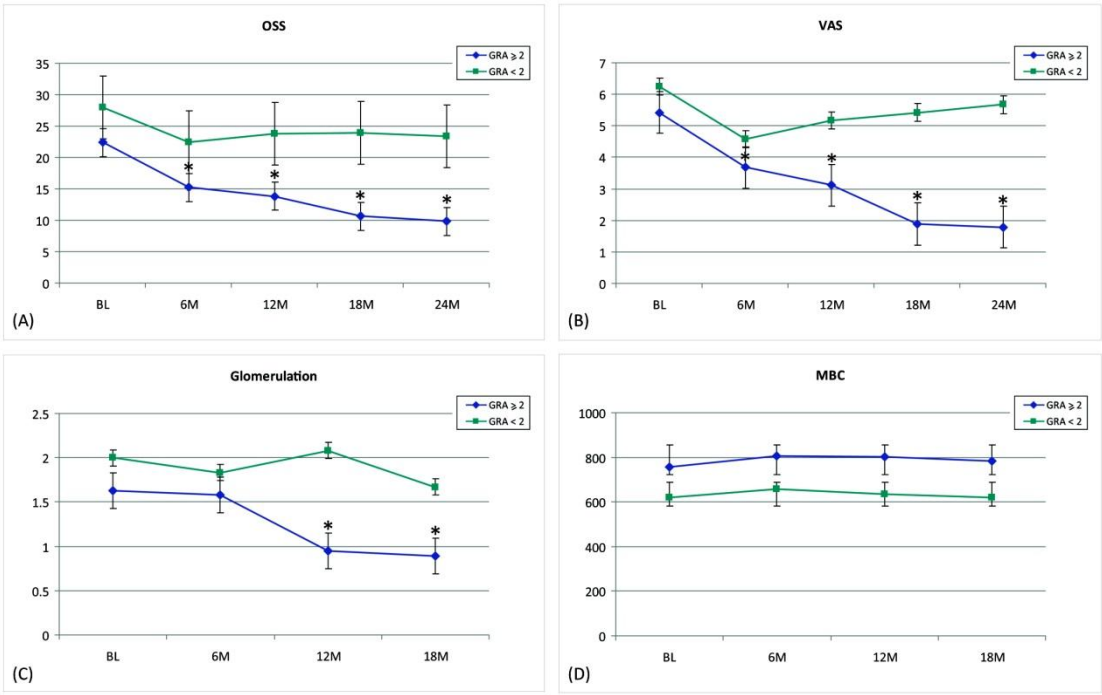
Table 1. The changes of measured parameters from baseline to end-point between patients with a GRA ≥2 and GRA <2 at the end-point.

	GRA ≥ 2 (n=19)	GRA <2 (n=12)	P values
ICSI	-5.58±3.55	-2.92±4.89	0.089
ICPI	-6.95±3.63	-1.58±4.06	0.001
OSS	-12.5±6.73	-4.50±8.53	0.007
VAS	-3.63±2.11	-0.58±2.64	0.001
FBC (ml)	61.6±121	-9.17±65.6	0.044
Frequency	-4.42±3.56	0.75±9.38	0.091
Nocturia	-0.95±1.62	1.42±3.73	0.057
Qmax (ml/s)	4.26±12.4	-0.17±8.06	0.317

Volume (ml)	48.9±168	-49.9±101	0.054
PVR (ml)	64.1±84.2	46.9±67.6	0.570
CBC (ml)	113±156	-3.0±80.8	0.012

CBC: cystometric bladder capacity, FBC: functional bladder capacity, GRA: global response assessment, ICSI: Interstitial Cystitis Symptom Indexes, ICPI: Interstitial Cystitis Problem Indexes, MBC: maximal bladder capacity, OSS: O'Leary-Sant Score, PVR: postvoid residual, Qmax: maximum flow rate, VAS: visual analog score of pain

Fig.1. The changes of: (A) O'Leary-Sant score (OSS), (B) visual analog sore of pain (VAS), (C) grade of glomerulations, and (D) maximal bladder capacity (MBC) in patients with a GRA ≥2 and GRA <2 at time points from baseline to the end-point. Data are expressed as mean ± standard errors. Asterisks indicate statistically significant difference between groups.



Disclosures

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