

DOWN REGULATION OF APOPTOTIC AND INFLAMMATORY PROTEINS ARE ASSOCIATED WITH IMPROVED CLINICAL CHARACTERISTICS OF PATIENTS WITH INTERSTITIAL CYSTITIS AFTER REPEATED INTRAVESICAL BOTULINUM TOXIN A INJECTIONS

Hypothesis / aims of study

Interstitial cystitis/ bladder pain syndrome (IC/BPS) is a debilitating, chronic disease involving apoptosis and chronic inflammation of bladder tissue. Previous studies have proved the efficacy of intravesical botulinum toxin type A (BoNT-A) injection on the treatment of IC/PBS. We investigated the changes of apoptotic activities and inflammatory proteins after repeated BoNT-A injections and their association with the clinical parameters.

Study design, materials and methods

A total of 23 women with IC/BPS who received single intravesical BoNT-A injection were enrolled. Among them 11 received three repeated injections every 6 months to improve their symptoms. Bladder biopsy was obtained before each BoNT-A injection and the clinical symptoms and urodynamic parameters were recorded. Immunohistochemistry (IHC) staining for TUNEL and mast cell activity, western blotting for tryptase, cytokines Bax, p-p38 and SNAP25 were assayed. The clinical parameters and IHC and western blotting data before and after BoNT-A treatments were analysed.

Results

Single BoNT-A injection decreased O'Leary-Sant Symptom Score (OSS), pain visual analog score (VAS) and daytime frequency (Table 1). In the histological analysis, mast cell activity stain and apoptotic cell count did not show significant reduction. However, the western blotting for Bax and p-p38 content revealed significant decrease after single BoNT-A injection. In the 11 patients receiving three repeated BoNT-A injections, more clinical parameters including OSS, pain VAS, functional bladder capacity (FBC), daytime frequency and glomerulation degree improved significantly after treatment (Table 2). The contents of tryptase, Bax and p-p38 and apoptotic activities in these bladder specimens all showed significant decrease (Fig.1). The improvement of clinical parameters was associated with the decrease of IHC and western blotting parameters. SNAP25 content also decreased after BoNT-A treatments, which confirmed the therapeutic effect of BoNT-A in these bladder tissues (Fig.1).

Interpretation of results

The results of this study demonstrated that the apoptotic signaling proteins Bax and p-p38, and mast cell activity tryptase expressions could be suppressed by repeated BoNT-A injections, suggesting that BoNT-A injection could have an anti-inflammatory effect on IC/BPS bladders and improved the clinical symptoms such as pain and frequency urgency. However, single BoNT-A injection could not relieve the symptoms and reverse the increased inflammation and apoptosis in part of IC/BPS patients. Repeated injections are necessary to achieve complete immunohistochemistry resolution.

Concluding message

Clinical symptom improvement in association with down regulation of apoptosis and inflammatory proteins could be achieved by repeated intravesical BoNT-A injection in IC/PBS patients.

Table 1. The clinical and IHC and western blotting parameters at baseline and 6 months after single BoNT-A injection in 23 IC/BPS patients

	Baseline	6 months	P value
Oleary-Sant Score	21.9±7.0	14.9±8.64	0.004
VAS pain score	5.30±2.46	3.70±2.62	0.037
Cystometric capacity (ml)	277.8±109.3	274.7±172.8	0.946
Pdet (cmH ₂ O)	20.35±9.93	20.21±8.77	0.951
Qmax (ml/s)	13.3±4.29	22.3±32.0	0.223
PVR (ml)	17.8±45.9	54.5±88.4	0.100
Functional bladder capacity (ml)	134.8±79.8	170.4±85.2	0.150
Frequency	13.0±4.56	9.48±4.87	0.014
Nocturia	3.74±1.76	2.91±1.98	0.142
Maximal bladder capacity (ml)	733±190	780±187	0.403
Glomerulation degree	1.65±0.88	1.65±0.93	1.000
Tryptase	1.0	0.94±0.20	0.143
P-p38	1.0	0.77±0.33	0.004
Bax	1.0	0.91±0.18	0.026
TUNEL	1.87±1.74	1.14±1.05	0.080

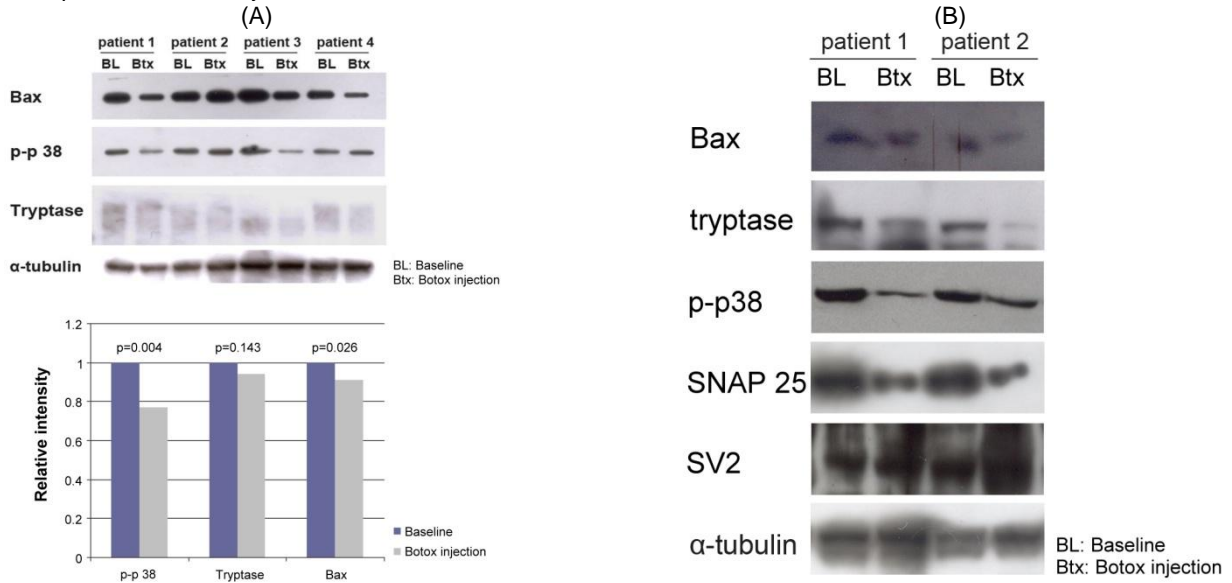
VAS: visual analog score, Pdet: detrusor pressure, Qmax: maximum flow rate, PVR: postvoid residual

Table 2. The clinical and IHC and western blotting parameters at baseline and 6 months after three repeated BoNT-A injections in 11 IC/BPS patients

	Baseline	6 months after 3 BoNT-A injections	P value
O'Leary-Sant Score	22.91±4.59	11.45±6.62	0.001
VAS pain score	5.91±1.51	1.91±1.38	0.000
Cystometric capacity (ml)	277.18±95.24	370.45±173.20	0.078
Pdet (cmH2O)	27.20±9.13	15.60±7.11	0.001
Qmax (ml/s)	13.18±4.56	12.73±6.75	0.843
PVR (ml)	13.27±29.49	55.45±87.33	0.186
Functional bladder capacity (ml)	122.73±64.05	259.09±131.94	0.010
Frequency	12.91±3.39	8.36±2.84	0.009
Nocturia	3.00±1.48	2.36±1.63	0.240
Maximal bladder capacity (ml)	713.64±216.90	785.45±208.15	0.718
Glomerulation degree	1.91±1.22	0.73±1.19	0.046
Tryptase	1.0	0.64±0.17	0.001
P-p38	1.0	0.66±0.16	0.001
Bax	1.0	0.84±0.22	0.050
TUNEL	2.30±1.83	0.86±1.00	0.026
SNAP25	1.0	0.53±0.18	0.001

VAS: visual analog score, Pdet: detrusor pressure, Qmax: maximum flow rate, PVR: postvoid residual

Fig. 1. The Western blotting of (A) the expressions of Bax, p-p38 and tryptase activity after single BoNT-A injection, and (B) after three repeated BoNT-A injections.



Disclosures

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