

EFFICACY AND SAFETY OF INTRA-TRIGONAL INJECTION OF ONABOTULINUM TOXIN A IN PATIENTS WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS. INTERIM ANALYSIS OF AN EXPLORATORY RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL

Hypothesis / aims of study

There are no curative treatments for Bladder Pain Syndrome/Interstitial cystitis (BPS/IC). Therefore, pain relief remains a key corner of current BPS/IC management. OnaBotulinum toxin A (OnaBotA) has been used as an analgesic therapy in BPS/IC patients refractory to conventional analgesic medication [1,2,3]. The present prospective, single-center, randomized, double-blind, placebo-controlled clinical trial aims to evaluate the efficacy and safety of intra-trigonal injection of 100 Units of OnaBotA in patients with BPS/IC refractory to common analgesics, using saline injections as control. Here we describe the pre-planned interim analysis after the study exit of the first sixteen patients.

Study design, materials and methods

The interim analysis included 16 women with refractory BPS/IC (8 patients in OnaBotA arm and 8 in saline arm) and a minimum pain score of 4 in a 0-10 visual analogue scale (VAS). All women gave informed consent. ESSIC classification was applied.

Patients were investigated with a VAS for pain, 3-day bladder diary, O'Leary-Sant score (OSS), and QoL from IPSS at 15 days before and 1, 2 and 3 months after treatment. Treatment Benefit Scale (TBS) was evaluated at 3 months. Side effects were registered, in particular post-void residual volumes (PVR) and urinary tract infections (UTI's).

All patients received 10 injections containing each one 1 ml of saline or saline with 10 U of OnaBotA (BotoxTM). The injections were performed in the bladder trigone only, under cystoscopic guidance and general anaesthesia.

The primary outcome of this study was the pain in a VAS at 3 months after treatment. Secondary outcomes included daily urinary frequency from a 3-day voiding chart, OSS, QoL from IPSS and TBS at the same time point.

Results are presented as average values plus standard deviation. T test was used to compare the two arms at each time point.

Results

Mean age in the OnaBotA arm was 47±8 years (range between 35-60 y) and 49±10 y in the placebo arm (range between 31-61 y). According to ESSIC classification each arm had 2 cases with Hunner's lesions. The OnabotA and the placebo arms had 5 and 7 patients with characteristic histological findings, respectively.

At baseline the two groups were also balanced for clinical variables. Pain score was 6.9±0.8 in OnaBotA and 6.5±0.9 in the placebo arm. Daily urinary frequency was 12.1±3.4 in OnaBotA and 11.1±2 in the placebo arm. O'Leary-Sant score was 22.8±4.4 in OnaBotA and 25.5±4.6 in the placebo arm. QoL was 5±0.9 in OnaBotA and 4.9±0.8 in placebo arm.

At the interim analysis all the primary and secondary endpoints were met. VAS for pain was significantly lower for OnaBotA arm (2.4±2.8 in OnaBotA versus 5±2.2 in Placebo arm, $p<0.05$). Reductions in daily urinary frequency, OSS, and QoL observed in the OnabotA arm were significantly more marked than in the placebo arm (see table). Treatment Benefit Scale at 3 months follow up was 1.8±0.9 in the OnabotA group versus 3±0.8 in the placebo group ($p<0.05$). Results at 1 and 2 months follow up are also presented in Table 1 and show significant improvement for all parameters 2 months after treatment. At 1 month follow up improvements in pain score and daily urinary frequency were only numerical superior in the Onabot arm, as differences to the placebo did not reach significance.

Three cases of UTI's occurred, 2 in placebo and 1 in the OnaBotA arm. No cases of voiding dysfunction were observed. Mean PVR at 1 month was 3,8±11 and 4±11 ml in the OnabotA and placebo groups, respectively.

Interpretation of results

The interim analysis of this exploratory RCT demonstrates that intra-trigonal injection of 100 U of OnaBotA is significantly better than placebo to reduce pain, frequency and OSS score and to improve QoL in patients with refractory BPS/IC.

Concluding message

Intra-trigonal injection of 100 U of OnaBotA seems an effective, safe treatment for patients with refractory BPS/IC.

Table 1. Results at 1, 2 and 3 months of follow up (*p<0.05).

	VAS (Pain)		Frequency		O'Leary Sant Score		QoL (IPSS)	
	OnaBotA	Placebo	OnaBotA	Placebo	OnaBotA	Placebo	OnaBotA	Placebo
Baseline	6.9±0.8	6.5±0.9	12.1±3.4	11.1±2	22.8±4.4	25.5±4.6	5±0.9	4.9±0.8
1 month	3.5±2.2	4.25±2.2	7.9±2.9	9.5±2.7	14.9±9.4*	21.4±4.2	2.3±1.9*	3.6±0.9
2 month	2.3±2.2*	4.1±2	6.9±1.8*	10±3.3	10.5±7.4*	21±5	1.5±1.8*	3.8±1.3
3 month	2.4±2.8*	5±2.2	7.4±1.5*	10.6±3.6	10.4±7.2*	21.6±6.6	1.5±2*	4±1.3

References

1. Eur Urol 2014; 65 (5): 981-90. doi: 10.1016/j.eururo.2013.10.033.
2. Eur Urol 2010; 58 (3): 360-5. doi: 10.1016/j.eururo.2010.02.031.
3. Neurourol Urodyn 2015. doi: 10.1002/nau.22760.

Disclosures

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