SHORT COMMUNICATION

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Different dose of botulinum toxin A injections for neurogenic detrusor overactivity

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Abstract

Objective: To evaluate the safety and efficacy of 200 U vs 300 U botulinum toxin A (BTX-A) injections in patients with neurogenic detrusor overactivity (NDO). **Methods:** we retrieved the data for the patients with spinal cord injury (SCI) who receive a single dose into the detrusor of BTX-A (300 U or 200 U). The clinical outcome included maximum detrusor pressure (P_{detmax}) during cystometry, voiding volume, urinary incontinence (UI) episodes per 24 hours, and patients with complete dryness. Related adverse events were recorded. **Results:** From July 2015 to June 2017, 28 cases received 300 U BTX-A injections (experiment group) while 19 cases received 200U BTX-A injections (control group). There was significant improvement in P_{detmax}, UI and I-QoL from baseline in the two groups. Patients in experiment group had more significant change than patients in the control group for P_{detmax} (-32.09 cmH2O vs. -28.02 cmH2O, P = 0.016), mean urinary incontinence episodes (-6.18/d vs. -5.01/d, P = 0.042), patients with complete dryness (11 vs. 2, P = 0.031), voiding volume (160.52 ml vs. 133.66 ml, P <0.001), and I-QoL (28.53 vs. 20.41, P <0.001) . **Conclusion:** Preliminary results indicate that 300 U BTX-A is more effective than 200 U BTX-A for SCI patients with NDO.

Keywords: Botulinum toxin A; 200U; 300U; Neurogenic detrusor overactivity; Spinal cord injury.

INTRODUCTION

Neurogenic detrusor overactivity (NDO) is defined as involuntary detrusor contractions during the filling phase which may be spontaneous or provoked in urodynamic test which may be caused by various diseases and events affecting the nervous systems

NDO can result in neurogenic lower urinary tract dysfunction. Undoubtedly, NDO may also limit their ability to undertake rehabilitation exercises [1].

Botulinum toxin type A (BTX-A) injection in the detrusor is the most effective minimally invasive treatment to reduce neurogenic detrusor overactivity which causes a long-lasting but reversible chemical denervation that lasts for about 9 months. Botulinum toxin A has been proven effective in a randomised placebo-controlled trial in NDO and repeated injections seem to be possible without loss of efficacy [2].

Until now, few studies presented the complete results about different dose BTX-A injections. The aim of the current report is to evaluate the clinical results of 200U and 300U BTX-A injections for NDO.

METHOD

From July 2015 to June 2017, inpatients with SCI and urodynamic DO were included. The inclusion criteria were: (1) Age >18 years; (2) Patients had experienced an inadequate response to oral anticholinergics. Patients were not eligible for inclusion if they were:(1) Acute urinary tract infections; (2) Patients or caregivers could not regularly performed clean intermittent catheterization (CIC). Our study complied with principles of the Declaration of Helsinki and was approved by the ethics committee at participating centers. All patients provided written informed consent. Three consecutive days bladder diaries, urodynamic test, and I-QoL were performed at baseline and 12 weeks post injections.

The injection of botulinum toxin was delivered via cystoscopic guidance. Patients were randomized to receive 300 units (experiment group) or 200 units (control group) of botulinum

toxin type A (Botox, Allergan Inc., Irvine, California) which was diluted in 30 mL of normal saline solution [3]. The clinical outcome included maximum detrusor pressure (P_{detmax}) during cystometry, voiding volume, urinary incontinence (UI) episodes between CICs per 24 hours, and number of complete dryness. Related adverse events were recorded.

Efficacy analyses were conducted using the intent-to-treat (ITT; all randomized patients) population and the primary time point was Week 12. Analysis of covariance (ANCOVA) was

used to compare changes from baseline in outcomes between experiment group and control groups. Safety analyses were performed on the safety population.

RESULTS

Patients were randomized to BTX-A 300 unit (experiment group, 28 cases), or BTX-A 200 U (control group, 19 cases), respectively (Table 1).

Patients in experiment group had more significant change those in the control group for P_{detmax} (-32.09 cmH_2O vs. -28.02 cmH_2O, P = 0.016), mean urinary incontinence episodes (-6.18/d vs. -5.01/d, P = 0.042), number of complete dryness (11 vs. 2, P = 0.031), mean voiding volume (160.52 ml vs. 133.66 ml, P <0.001), and I-QoL (28.53 vs. 20.41, P <0.001) (Table 2).

Table 1: Baseline demographic and disease characteristics

Characteristic	Experimental group (n = 28)	Control group (n = 19)
Age, yr, mean (SD)	32.12 (9.28)	31.22 (10.03)
Gender, men, n	20	16
Weight, kg, mean (SD)	60.11 (22.67)	60.59 (21.33)
Duration of spinal cord injury, months, mean (SD)	28.11 (10.18)	26.06(11.02)
Episodes of urinary incontinence,n/d, mean (SD)	9.22 (3.14)	8.93 (3.31)
Level of SCI injury, C6-C8/ T1-T12, n	3/25	1/18
AIS grade, A/B/C, n	20/7/1	16/1/1
Prior anticholinergic drugs use, n	28	19
Prior CIC use, n	28	19

AIS= the American social injury association; SD = standard deviation; SCI = spinal cord injury; CIC= clean intermittent catheterization.

Table 2: Mean baseline and change from baseline in clinical outcomes

Outcome	Experimental group (n = 28)	Control group (n = 19)	P Value
P_{detmax}, cmH_2O, mean (SD)			
Baseline	60.11 ± 15.34	61.83 ± 16.22	0.524
Week 12	-32.09 ±22.27	-28.02 ±15.18	0.016
UI, n/d, mean (SD)			
Baseline	9.22 ± 3.14	8.93 ± 3.31	0.864
Week 12	-6.18 ± 2.61	-5.01 ± 1.96	0.042
Complete dryness, n			
Baseline	0	0	NS
Week 12	11	2	0.031
Voiding volume, ml,mean (SD)			
Baseline	180.43 ± 62.18	186.74 ± 59.04	0.473
Week 12	160.52 ±78.05	133.66 ±52.94	< 0.001
I-QoL, mean (SD)			
Baseline	32.44±9.29	33.73 ± 9.13	0.813
Week 12	28.53±14.33	20.41±11.18	< 0.001

P_{detmax}= maximum detrusor pressure; UI= urinary incontinence

No related adverse events were recorded.

DISCUSSION

In patients with high detrusor pressure during the filling phase, treatment is aimed primarily at conversion of an active, aggressive high-pressure bladder into a passive low-pressure reservoir [4]. Significant improvements were observed in both experiment group and control group. Specifically, the P_{detmax} reduced more significantly of 300U rather than 200U to protect the renal function.

Improve the patient's quality of life (QoL) was also the primary aims for patients with NDO [5]. In this study QoL were significantly increased from baseline in both groups. However, compared with 200 unit BTX-A, the improvement of I-QoL in 300 unit BTX-A was relatively greater (28.53 vs.20.41, $P<0.001$). The reason may be related to the following changes :(1) Significant reduction of daily urinary incontinence episodes in experiment group; (2) greater increase in voiding volume in the experiment group; and (3) most importantly, 11 patients in experiment group appeared complete dryness postoperatively, and I-QoL from these patients was very high.

No one reported related adverse events. Similar results have also been reported by other study [6].

CONCLUSION

Preliminary results indicate that 300 U BTX-A is more effective than 200 U BTX-A for SCI patients with NDO. The lack of this study was small sample size, and further studies are necessary.

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Conflict of interest: None.

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