The treatment of Botulinum toxin A injections and baclofen for patient with detrusor overactivity secondary to spinal cord injury

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Abstract
Objective: To evaluate the clinical outcome of Botulinum toxin A (BTX-A) with oral baclofen for patients with detrusor overactivity secondary to spinal cord injury (SCI).

Methods: A total of 9 SCI patients (mean age, 32 years; male 7, female 2) with urodynamic detrusor overactivity were included into the study between June 2017 and June 2019. All the patients received BTX-A intradetrusor injections and baclofen. Patients were evaluated at baseline, and 4 weeks after injection. The efficacy and safety outcomes included voiding diary, urodynamic data. Adverse events were also recorded.

Results: Compared to the baseline data, the patients’ incontinence quality of life (I-QOL) score, mean maximum detrusor pressure (MDP) and mean maximum cystometric capacity (MCC) improved significantly at 4-week follow-up. No adverse and toxic effect was observed.

Conclusions: The treatment of BTX-A with baclofen is effective and safe for patients with detrusor overactivity secondary to SCI. However, it is necessary to observe its long term outcome.

Keywords: botulinum toxin a; detrusor overactivity; spinal cord injury

Introduction
Detrusor overactivity (DO) is characterized by spontaneous or provoked involuntary detrusor contractions during storage phase in urodynamic investigation [1]. Neurogenic detrusor overactivity (NDO) is DO caused by various neurogenic diseases such as brain tumours, dementia, multiple sclerosis (MS), Parkinson’s disease (PD), stroke and spinal cord injury (SCI). NDO can result in vesicoureteric reflux, increase the chance of urinary tract infection and renal damage, and severely injury the patient’s quality of life [2]. The purpose of this study was to investigate effects of BTX-A injections combined with oral baclofen in treatment of patients with detrusor overactivity after SCI.

Methods
A total of 9 patients with SCI (mean age, 32 years; male 7, female 2) were included into the study From January 2014 to December 2019. All patients had a typical history of SCI caused by trauma. The dose of oral baclofen of all the patients was 30mg/day in 3 divided doses before BTX-A injection. All the patients underwent urodynamic examination and voiding diary was recorded. 300 U of BTX-A was dissolved in 30 ml of saline, and the solution of BTX-A was injected into 30 different points in detrusor avoiding the trigone using a flexible cystoscopic needle. The efficacy of BTX-A injections combined with oral baclofen was shown in Figure 1 and Figure 2.

Results
Compared to the baseline data, the patients’ I-QOL score showed that the quality of life of patient increased significantly at 4-week (Figure 2). At the same time, the mean maximum cystometric capacity (MCC) increased from 124.11 ml to 237.67 (Figure 1), mean maximum detrusor pressure (MDP) decreased from 69.78 to 44.44 cmH2O (Figure 2). No adverse and toxic effect was observed.
Fig 1: Improvement in MCC between preoperation and postoperation

Fig 2: Improvement in MDP between preoperation and postoperation

Discussion
The key in the treatment of detrusor overactivity is to reduce bladder pressure, incontinence, and improve I-QOL so as to protect the upper urinary tract function. BTX-A firstly acts on the pre-synaptic terminal of peripheral motoneuron, secondly inhibits release of calcium-mediated acetylcholine at the pre-synaptic neuromuscular junction by decomposing synaptic protein synaptosomal-associated protein-molecular weight 25 KDa (SNAP-25), and finally cause muscle relax by chemical denervation. The clinical effects of oral baclofen include decreased resistance to passive range of motion, decrease in hyperreflexia, and reduction in painful spasms. Our preliminary results showed that BTX-A combined with oral baclofen seems to be well tolerated in patients whom received treatment. They had a rapid onset at 1-2 weeks and reached maximum effects usually in 6-8 weeks. According to the follow-up results, except for slight hematuria, there was no obvious discomfort and postoperative complications, which may be related to the close
combination of botulinum toxin A and neuromuscular endplate to prevent the toxin from entering the circulatory system.

**Conclusions**

Our experience suggests that BTX-A injection into detrusor combined with oral baclofen to treat detrusor overactivity in patients with SCI may be an effective, safe, feasible and micro invasive treatment choice. However, it is necessary to observe its long term outcome.

**Acknowledgments**

This study was supported by research foundation of Guangdong Provincial Work Injury Rehabilitation Hospital, China (grant number 2018C012-B).

**Conflict of Interest Statement**

The authors declare no conflict of interest.

**References**