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ORIGINAL ARTICLE

Therapeutic outcome and patient adherence to repeated onabotulinumtoxinA detrusor injections in chronic spinal cord-injured patients and neurogenic detrusor overactivity

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botulinum toxin A;
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Background/Purpose: To investigate the continuous therapeutic effects and urinary incontinence severity after repeated detrusor injections of 200-U of onabotulinumtoxinA (BoNT-A) in chronic spinal cord-injured (SCI) patients.
Methods: Between 2006 and 2010, patients with chronic SCI and refractory neurogenic detrusor overactivity (DO) were treated with repeated sets of 200-U BoNT-A injected into 20 sites every 6 months. All patients underwent urological examinations and video-urodynamic studies at baseline and after each BoNT-A treatment. The outcomes were measured using Urogenital Distress Inventory 6-item short form (UDI-6) for urinary incontinence. The severity of urinary incontinence and urodynamic parameters were compared after each BoNT-A injection.
Results: A total of 59 SCI patients with a mean age of 42.1 ± 13.1 years were enrolled. The UDI-6 incontinence scores persistently improved for up to three injections. The rate of dryness and mild incontinence reported by patients persistently improved from 25.4% at baseline to 74% at 3 months after the fourth injection, but decreased slightly after the fourth injection. The overall satisfaction rate after single or repeated injections was 59.3% (35 patients), and the failure rate was 33.9% (20 patients), and discontinuation rate owing to adverse events (2 recurrent UTI, 2 autonomic dysreflexia) was 6.8% (4 patients). Among the 20 patients who reported failure to treatment, 10 patients (16.9%) reported no significant improvement after one or repeated injections, eight converted to augmentation enterocystoplasty.

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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Conclusion: Repeated 200-U BoNT-A injections every 6 months for neurogenic DO in chronic SCI patients provided a satisfactory initial outcome. However, only 20% patients continued the repeated treatment.

Introduction

Spinal cord injury (SCI) is a significant cause of morbidity and mortality in developing countries, with a global annual incidence of 1:25,000.[1] Neurogenic voiding dysfunction and urinary symptoms in patients with SCI lead to several complications. If not well managed, high intravesical pressure will damage the upper urinary tract, causing renal scarring and chronic renal insufficiency, which impair the quality of life.[2] The first-line treatment for SCI induced neurogenic detrusor overactivity (DO) is antimuscarinic agents with or without clean intermittent catheterization (CIC).[3,4] However, most of the patients have an incomplete response to antimuscarinic agents, which can also cause undesirable systemic side effects.[5]

OnabotulinumtoxinA (BoNT-A) detrusor injections were introduced in 2000 as a minimally invasive treatment option for neurogenic DO.[6] In addition to the benefit of decreased detrusor pressure to prevent renal damage, it significantly improved quality of life.[7] In 2011, a global Phase 3 clinical trial concluded both 200-U and 300-U injections provided the same therapeutic effect.[8] However, most previously published studies used 300-U BoNT-A detrusor injections; only a few studies focused on 200-U BoNT-A injections for the treatment of neurogenic DO. As most patients with neurogenic DO require repeated treatments, the efficacy and safety of multiple BoNT-A injections need to be addressed. This study investigated the therapeutic effects of repeated 200-U BoNT-A injections in the detrusor muscle for the treatment of urinary incontinence and refractory neurogenic DO among SCI patients. We also investigated the adherence of SCI patients to repeated BoNT-A injections throughout the study course.

Methods

Patients with SCI and neurogenic DO, requiring CIC or not, and who were refractory to antimuscarinic treatment were consecutively enrolled in this prospective study. Video-urodynamic studies (VUDS) were routinely performed prior to enrollment to prove the presence of DO with or without detrusor sphincter dyssynergia, and exclude the patients with detrusor underactivity, anatomical obstruction, or intrinsic sphincter deficiency. Patients were also excluded if they had an active urinary tract infection at enrollment, urinary tract cancer, history of lower urinary tract surgery, or chronic systemic diseases such as congestive heart failure and chronic renal failure.

VUDS was performed according to the recommendations of the International Continence Society.[9] The urodynamic parameters of cystometric bladder capacity (CBC), maximum flow rate (Qmax), post-voiding residual (PVR) volume, voided volume, involuntary detrusor contraction (IDC) and voiding detrusor pressure at Qmax (Pdet.Qmax) were recorded in detail. In addition, the lower urinary tract symptoms were evaluated using the Urogenital Distress Inventory short form (UDI-6) questionnaire.

The patients were designed to receive initial four repeated injections each of 200-U of BoNT-A (Allergan, Irvine, CA, USA) in the detrusor muscle at baseline and every 6 months thereafter. The BoNT-A injections were performed under light intravenous general anesthesia in the operating room. The 200-U BoNT-A was diluted with 20 mL of normal saline and the diluted solution was injected into 20 sites in the bladder wall, excluding the bladder trigone. The patients were evaluated every 3 months for the therapeutic effects, quality of life in urinary incontinence, and VUDS for evaluation of the bladder condition.

All patients were scheduled for four sets of BoNT-A injections (Phase I). However, patients were also allowed to withdraw from the trial if they were dissatisfied with the treatment outcome, having intolerable adverse events, or were effective to treatment but did not want to continue the injection. After completion of four sets of BoNT-A injection and follow-up, patients were allowed to receive two additional BoNT-A injections every 6 months (Phase II) if they wished to continue this mode of treatment for their urinary incontinence. The causes of discontinuation of BoNT-A injection were analyzed, and patients were considered to have effective treatment based on their subjective reports.

This study was approved by the Ethics Committee of Tzu Chi General Hospital, Hualien, Taiwan (TCGH 098-53 and 098-088); written, informed consent to participate was obtained at enrollment. All patients had been informed and educated for CIC after treatment. Patients had to agree to perform CIC prior to when they were enrolled in the study.

The primary efficacy parameter was the severity of urinary incontinence (caused by all etiologies) as perceived by the patient's subjective scoring of urinary leakage at each follow-up visit. The incontinence severity score was adapted from three incontinence items from the UDI-6. The severity of urinary incontinence was graded as dry if the sum of UDI-6 incontinence items was 0, mild in the sum of 1—3, moderate in the sum of 4—6, and severe in the sum of 7—9. Secondary efficacy parameters were the changes in VUDS parameters at 3 months and 6 months after each set of BoNT-A injections. Any adverse events were also recorded throughout the study. Urinary tract infection was defined as a febrile episode with a white blood cell count of more than 10 cells per high-power field on urinalysis. Asymptomatic pyuria was not considered an adverse event.

Results

A total of 59 patients with SCI and neurogenic DO were enrolled in this study, including 21 women and 38 men.