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Original article

Onabotulinumtoxin type A improves lower urinary tract symptoms and quality of life in patients with human T cell lymphotropic virus type 1 associated overactive bladder

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ABSTRACT

Aim: To evaluate the efficacy of the onabotulinum toxin type A in the treatment of HTLV-1 associated overactive bladder and its impact on quality of life (QoL).

Methods: Case series with 10 patients with overactive bladder refractory to conservative treatment with anticholinergic or physical therapy. They received 200Ui of onabotulinum-toxin type A intravesically and were evaluated by overactive bladder symptoms score (OABSS) and King's Health Questionnaire.

Results: The mean (SD) of the age was 52 + 14.5 years and 60% were female. All of them had confirmed detrusor overactivity on urodynamic study. Seven patients had HAM/TSP. The median and range of the OABSS was 13 (12–15) before therapy and decreased to 1.0 (0–12) on day 30 and to 03 (0–14) on day 90 ($p < 0.0001$). There was a significant improvement in 8 of the 9 domains of the King's Health Questionnaire after the intervention. Hematuria, urinary retention and urinary infection were the complications observed in 3 out of 10 patients. The mean time to request retreatment was 465 days.

Conclusion: Onabotulinum toxin type A intravesically reduced the OABSS with last long effect and improved the quality of life of HTLV-1 infected patients with severe overactive bladder.

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Introduction

The human T cell lymphotropic virus type 1 is the causal agent of the HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP). About 10 million people are infected by HTLV-1 worldwide.[1] HAM/TSP is characterized by back pain, hyperreflexia, spastic paraparesis, and Babinski sign.[2] Manifestations of the genitourinary system such as erectile dysfunction, increased urinary frequency and urgency, with or without incontinence, and nocturia are documented in virtually all patients with HAM/TSP.[3–5] Moreover, these manifestations may be detected in a large percentage of HTLV-1 subjects who do not fulfill criteria for HAM/TSP.[5] The urinary complaints are responsible for serious impairment of quality of life, development of depression, and increased risk for upper urinary tract infection and kidney dysfunction due to increased intravesical pressure and residual urine volume.[6–8] The main urodynamic findings in patients with urinary dysfunction associated with HTLV-1 are overactivity of the detrusor, sphincter-detrusor dyssynergia, and impaired bladder contractility.[8,9] As only few studies have addressed the treatment of such events in this population, it remains undefined if the therapeutic interventions used in individuals not infected with HTLV-1 have the same response in those infected by the virus. The onabotulinumtoxin type A has been used with success to improve urinary symptoms in patients with overactive bladder symptoms due to multiple sclerosis or spinal cord injury.[10,11] We had previously shown in a limited number of patients with urologic dysfunctions the short-term results of the use of onabotulinumtoxin.[12] Here we extend this observation to a large number of patients, besides evaluating the long-term therapeutic response to onabotulinumtoxin type A in HTLV-1 infected patients with overactive bladder refractory to conservative treatment with anticholinergic drugs or physical therapy.

The aim of this study was to determine the effect of onabotulinumtoxin type A in controlling symptoms of lower urinary tract in patients infected with HTLV-1 refractory to conservative treatment with anticholinergic and pelvic floor physical therapy associated with parasacral or intracavitary neuromodulation (vaginal or anal).

Methods

Patients and case definitions

Participants of the study were selected from a cohort study of 419 HTLV-1 infected subjects, of whom, 142 presented urinary symptoms. Eighty-six patients were on conservative treatment for HTLV-1 associated overactive bladder, 34 were not receiving regular treatment and 22 of these were considered refractory to drug therapy. Overactive bladder was defined according to International Continence Society (ICS) criteria[13] and refractory overactive bladder was defined as failure to control urgency and incontinence using two different anticholinergic drugs in maximal tolerated dosage.[14–16] All patients underwent an urodynamic study done before treatment.

The diagnosis of HAM/TSP and probable HAM/TSP was performed according to De Castro Costa criteria.[17] Patients with probable HAM/TSP had urologic dysfunctions as the main symptoms. The amount of onabotulinumtoxin available was enough for only 10 patients and the first 10 cases who agreed to use the onabotulinumtoxin type A were enrolled in the study.

Administration of onabotulinumtoxin type A

Patients were anesthetized and positioned in lithotomy. All patients were on fluoroquinolone antibiotic prophylaxis. They received spinal or general anesthesia and 20 mL of lidocaine gel into the urethra. Onabotulinumtoxin type A (Botox®, Allergan, Inc., Irvine, CA) was prepared according to the fabricant recommendation: A standard dose of 200 UI was reconstituted in 30 mL of NaCl 0.9% solution. Then, the medication was injected in the detrusor muscle by cystoscopy in 30 different points of the supra trigonal region. One milliliter of the solution was administered in each site of application.[18]

The choice of 200 UI dose was based in a previous study by Cruz et al. who showed that dose to have the same efficacy of 300 UI in patients with urinary incontinence due to detrusor overactivity.

Clinical evaluation

The efficacy of the onabotulinumtoxin type A in controlling overactive bladder symptoms in HTLV-1 patients were assessed by a 3-day voiding diary and by the overactive bladder symptom score (OABSS). These parameters were assessed pre- and post-treatment. Moreover, patients were evaluated after 30, 90 and 365 days after the therapeutic intervention. The impact on quality of life was measured using the King's Health Questionnaire.[19] We considered a high post void volume as over 50% of the estimated bladder capacity (400 mL), as previously established by Asimakopoulos et al.[20]

Statistics analysis

The demographics and clinical data are described as mean ± standard deviation (SD) or median (range). The Wilcoxon paired test was applied to compare pre- and post-intervention changes in frequency of voiding symptoms, OABSS and King's Health Questionnaire. p-Values < 0.05 were considered statistically significant.

Results

Table 1 summarizes demographic and clinical features of patients undergoing treatment with onabotulinumtoxin type A. All of them had already used at least two anticholinergic drugs (oxybutynin and propantheline bromide), given orally in full tolerated dosage. Of the 10 participants of the study, three had received in addition to oral, intravesical oxybutynin, but remained with urge incontinence. Two cases also had physical therapy with sacral, vaginal or trans-anal electrical stimulation with no improvement. The majority of the patients had illness duration for a long period. Detrusor overactivity was

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