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BOTULINUM TOXIN A (BOTOX®) IN NEUROGENIC URINARY INCONTINENCE: RESULTS FROM A MULTI-CENTRE RANDOMISED, CONTROLLED TRIAL

Hypothesis / aims of study

Recent evidence suggests that botulinum toxin type A (BOTOX®) may provide effective relief from neurogenic urinary incontinence in patients who have failed on oral anticholinergic therapy (1,2). This first placebo-controlled study aimed to show the safety and efficacy of two different doses of BOTOX® for the management of urinary incontinence caused by neurogenic detrusor overactivity.

Study design, materials and methods

This double-blind, multi-centre, randomised, placebo-controlled study was conducted in 59 patients (53 spinal cord injury; 6 multiple sclerosis) with urinary incontinence caused by neurogenic detrusor overactivity requiring clean intermittent self-catheterisation, who had failed on oral anticholinergic therapy. Following a 2-week screening period, each patient was randomised to receive a single masked treatment of BOTOX® (200U or 300U) or placebo at Day 0. Cystoscopic guidance was used to deliver the treatment as thirty injections, each of 1 ml, evenly over the detrusor muscle, avoiding the trigone. Patients were assessed during follow-up visits at weeks 2, 6, 12, 18 and 24. Changes in frequency of urinary incontinence episodes were monitored via patient bladder diary over the 24-week study period. Key urodynamic assessments (maximum cystometric capacity (MCC), reflex detrusor volume (RDV)) and maximum detrusor pressure during bladder contraction (MDP) were used to provide objective measures of treatment effect on bladder function at weeks 2, 6 and 24. Impact of treatment on quality of life parameters was assessed using the Incontinence Quality of Life questionnaire (I-QoL). The study was conducted in accordance with Independent Ethics Committee Regulations and in compliance with Good Clinical Practice and the Declaration of Helsinki, at 8 centres across Belgium, France and Switzerland.

Results

Significant reductions compared to baseline ($p \leq 0.05$) in number of incontinence episodes were observed within both BOTOX® groups, but not within the placebo group. Mean reductions ranged from 32-54% and 42-58% in the 200U and 300U BOTOX® groups, respectively. Twenty-nine subjects experienced at least one week with no incontinence episodes; 83% of these subjects were in the BOTOX® treatment groups. Effects were apparent by the first assessment (week 2) and were maintained throughout the study period. Improvements in bladder function were also observed using the urodynamic assessments within both BOTOX® groups. Significant increases ($p \leq 0.020$) in mean MCC values and significant decreases ($p \leq 0.023$) in MDP values from baseline were apparent at all post-treatment timepoints. No such changes were observed with placebo treatment. Twenty-three subjects experienced no RDV for at least 1 follow-up visit; 91% of these subjects were in one of the BOTOX®-treated groups. For subjects who did have a post-treatment RDV, significant increases ($p \leq 0.021$) from baseline were apparent at week 6 (300U BOTOX®) and week 24 (200U BOTOX®). Robust improvements ($p \leq 0.002$) in mean change in total I-QoL score from baseline were recorded at all timepoints in BOTOX®-treated subjects throughout the 24 week study period. Incidence of adverse events was not significantly different between treatment groups, and no event was considered related to study drug. No cases of autonomic dysreflexia or systemic events were seen.

Interpretation of results

These results show rapid and sustained reduction in episodes of urinary incontinence following treatment with 200U and 300U BOTOX® in patients with neurogenic detrusor overactivity. Improvements in bladder function were evidenced by the urodynamic evaluations, which show an increased ability of the bladder to hold and retain urine following

BOTOX® treatment and a reduced risk of vesicoureteric reflux, potentially preventing upper urinary tract deterioration and possible kidney damage. Improvements in signs and symptoms were appreciable by subjects as reflected in the higher I-QoL scores observed throughout the 24-week study period. No clear difference in clinical effect was apparent between the two BOTOX® doses.

Concluding message

This first controlled study demonstrates that treatment with a single dose of botulinum toxin type A (BOTOX®) combines rapid and sustained efficacy with a low incidence of side effects and represents a valuable option for managing urinary incontinence caused by neurogenic detrusor overactivity. The impact of dose on duration of action requires further evaluation.

References

1. Schurch B, Stöhrer M, Kramer G, Schmid DM, Gaul G, Hauri D. Botulinum-A toxin for treating detrusor hyperreflexia in spinal cord injured patients: a new alternative to anticholinergic drugs? Preliminary results. J Urol 2000;164(3):692-697.
2. Reitz A, von Tobel J, Stöhrer M, et al. European experience of 200 cases treated with botulinum-A toxin injections into the detrusor muscle for neurogenic incontinence. Eur Urol (Suppl 2) 2003:140

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