

SUBGROUP ANALYSIS TO DETERMINE IMPACT OF PATIENT DEMOGRAPHICS ON URODYNAMIC RESPONSE TO FOCAL ADMINISTRATION OF BOTULINUM TOXIN A

Hypothesis / aims of study

Botulinum toxin A (BTX-A) has previously been shown to be effective in significantly reducing symptoms of urinary incontinence and improving urodynamic parameters in such patients¹. Little is known, however, of how patient demographics and/or baseline disease severity affect treatment-related changes in urodynamics. This study investigated the effects of patient demographics on urodynamic function in response to two different doses of BTX-A used in the treatment of neurogenic urinary incontinence in an attempt to identify specific characteristics that would aid in the selection of patients for treatment.

Study design, materials and methods

A 26-week double-blind, randomised, placebo-controlled study performed at eight centres across Belgium, France and Switzerland. Participants had a history of urinary incontinence due to neurogenic detrusor overactivity, had failed on previous oral anticholinergic therapy, and required clean intermittent self-catheterisation. After an initial 2-week screening period, 59 patients (53 spinal cord injury; 6 multiple sclerosis) were randomised to receive a single dose of BTX-A 200U or 300U, or placebo (saline). Doses were administered to the detrusor muscle as 30 x 1 ml injections, using cystoscopic guidance. Bladder function was monitored for 24 weeks post-treatment using measurements of maximum detrusor pressure during bladder contraction (MDP), reflex detrusor volume (RDV), and maximum cystometric capacity (MCC). Subgroup analyses were performed for voiding pattern (catheterised only or mixed), gender, age (<30 years or 30-65 years old) and for severity of detrusor overactivity (mild, moderate or severe). The study was conducted in accordance with Independent Ethics Committee Regulations and in compliance with Good Clinical Practice and the Declaration of Helsinki.

Results

BTX-A produced substantial improvements in all urodynamic parameters, showing increased ability of the bladder to hold and retain urine, which was sustained throughout 24 weeks. 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 of the 59 subjects included in the study experienced no RDV for at least one follow-up visit; 91% of these subjects were in one of the BTX-A-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) and week 24 (200U).

Gender: There was a trend towards greater improvements in all three parameters in female than in male subjects, with the exception of MCC at the 200U dose.

Voiding: For MCC and MDP results, no difference was found between results from mixed voiding and catheterised only groups. For subjects who had a post-treatment RDV, greater improvement was found in mixed voiding patients.

Age: Age did not appear to affect the response to treatment, although improvements from baseline were significant ($p < 0.05$) at more time points in the older population. This may, however, reflect the larger number of patients in this age group.

Detrusor overactivity: Changes in all three parameters appeared to reflect the severity of detrusor overactivity, with improvement from baseline increasing with severity of overactivity. However, unlike in the less severe patients, improvements in urodynamics in the severe overactivity population did not reach significance at any timepoint. While the mean change in values increased with increasing severity of overactivity, the mean values at each post-

treatment timepoint were similar between groups. Results for each of the parameters did not appear to be influenced by dose.

Interpretation of results

Improvements in urodynamic parameters appeared to be largely unaffected by patient demographics. Populations within each subgroup analysis appeared to respond equally well to 200U and 300U doses, although the study was not designed to look at differences between doses. Whilst increases in dose may not afford any greater change in specific measurements, they may prolong the duration of response. The severity of overactivity did seem to influence response to treatment, with greater changes being observed in patients with more severe detrusor overactivity. However, the similarity in mean urodynamic values between mild, moderate and severe overactivity groups at each timepoint suggests that there may be a ceiling of treatment effect beyond which urodynamics cannot be improved upon in this population, even with an increase of dose.

Concluding message

Botulinum toxin A was well tolerated and produced substantial improvements in urodynamic parameters in patients with neurogenic bladder, substantially improving their ability to hold and retain urine.

Patient demographics do not appear to greatly influence in response to BTX-A treatment, although greater responses to treatment were observed in patients with more severe detrusor overactivity. Further large-scale studies are required to show more clearly the impact of BTX-A dose on urodynamic response and duration of effect in these sub-groups.

1. Botulinum toxin type A is a safe and effective treatment for neurogenic urinary incontinence: Results from a single-treatment, randomised, placebo-controlled 6-month study. *J Urol*, in press.

FUNDING: Allergan