

## **EFFECTS OF BOTULINUM TOXIN B ON REFRACTORY DETRUSOR OVERACTIVITY: A RANDOMISED, DOUBLE - BLIND, PLACEBO CONTROLLED, CROSS OVER TRIAL**

### Hypothesis / aims of study

Botulinum toxin (BTX) is one of the most potent naturally occurring neurotoxins known to man. There are seven distinct but structurally similar types of Botulinum toxins: A, B, C, D, E, F and G. Of these, type A and B have been used widely with a clinically beneficial effect in many neuromuscular disorders. Botulinum toxin type B (BTX B) has been little studied in lower urinary tract symptoms. The unique immunogenicity of the various serotypes of the toxin, along with the fact that both toxins interact with different target proteins means that BTX B has therapeutic potential in patients unresponsive to BTX A particularly those who have become resistant after repeated injections, consequent upon the antibody response. Open, observational studies of intra-detrusor injections of Botulinum toxin in cases of detrusor overactivity have reported beneficial effects. We present the first randomised, double-blind, placebo controlled cross-over trial for Botulinum toxin B.

### Study design, materials and methods

The trial was a randomized double-blind, placebo controlled crossover design of 13 weeks. There was a one-week run-in to collect baseline data, and two six-week randomly allocated, crossed treatment arms.

20 patients, aged 18-80 years, with refractory detrusor overactivity demonstrated by urodynamics, participated. They were injected with either placebo (20mls normal saline) or botulinum toxin B (5000 IU diluted up to 20mls) intra-deturosr in a day case setting. After six weeks, the treatments were crossed over. The primary outcome was the difference in change in the average voided volumes. Frequency, incontinence episodes and differences in the quality of life (QOL) were the secondary outcome measures. The King's Health Questionnaire (KHQ) measured QOL. Analysis was by intention-to-treat.

### Results

Average voided volume was non-normal on a Q-Q plot, so a non-parametric test, the Wilcoxon Signed Ranks Test was used to test the difference in change between treatment phases. There were clinically significant differences in the change in average voided volume, urinary frequency and episodes of incontinence between active treatment and placebo (AV Void Vol: 95% CI diff 16, 122; Z = -2.5; p=0.012 / Weekly Freq: 95% CI -21, -1; Z = -2.1, p=0.033 / Weekly incont: 95% CI -26, -7; Z=-3.3; p=0.001). There were similarly significant differences in the change in quality of life affecting five domains of the KHQ

### Interpretation of results

This study provides evidence of efficacy of Botulinum Toxin B in the treatment of the overactive bladder. The data suggest that this formulation and dose has a rapid onset of action (24 to 48 hours) but short duration, about six weeks. The experiment illustrates the utility of a cross-over design. This has not been favoured for studies of urinary incontinence because of speculative beliefs about the influence of carry-over effects confounding the treatment response. Unlike an oral medication, with a short half-life, BTX-B showed measurable effects up to six weeks and there is evidence of a carry-over into the placebo arm.

This center bought the test drug independently on the open market. The placebo and active components were prepared by the hospital pharmacy. The study was effected independently of the manufacturer

### Concluding message

The study provides evidence of the efficacy of BTX-B as a treatment of the overactive bladder.