

THE EFFECT OF REPEATED INJECTIONS OF BOTULINUM TOXIN TYPE A ON THE EFFICACY OF THE TREATMENT AND THE URINARY BLADDER

Hypothesis / aims of study

Recently, a randomized controlled study confirmed the efficacy and safety of endoscopic injections of botulinum toxin type A into the detrusor muscle in patients suffering from neurogenic detrusor overactivity and incontinence [1]. However, little is known about the effect of repeated injections of botulinum toxin type A on the efficacy of the treatment and the urinary bladder itself.

We studied patients with severe neurogenic detrusor overactivity and incontinence before and after repeated injections of botulinum toxin type A, asking for in 1.) the treatment efficacy measured as number of incontinence episodes per day as well as 2.) changes in urodynamic parameters compliance, reflex volume, maximum detrusor pressure during voiding and maximum cystometric bladder capacity.

Study design, materials and methods

17 patients were included, 16 patients had spinal cord injury and 1 patient multiple sclerosis. All patients had severe neurogenic detrusor overactivity and incontinence. 13 patients performed intermittent self-catheterization, 4 emptied their bladder by voluntary voiding. 300 units of botulinum toxin type A were injected in the detrusor muscle at 30 sites (10 units per ml per site, sparing the trigone). Clinical and a urodynamic follow-ups were done at examination 1 (before first injection), at examination 2 (after first injection) and examination 3 (after last repeated injection).

Mean number of injections was 5.4 ranging from 3 to 9 procedures. The urodynamic parameter compliance, reflex volume (filling volume at the beginning of first bladder contraction), maximum detrusor pressure during voiding and maximum cystometric bladder capacity were compared between examinations 1, 2 and 3 as well as between examination 2 and 3 by non parametric Friedman's test ($\alpha < 0.05$). Pair wise comparisons were made using Wilcoxon's signed rank test. For this test, alpha was adjusted for multiple comparisons ($\alpha < 0.025$). Second examination was performed 78.4 +/- 48.9 days after first injection, third examination after 133.8 +/- 62.9 days both performed at a time with full effect of treatment.

Results

Mean number of incontinence episodes per day decreased from 2.6 per day at baseline to 0 after the first injection, and it remains 0 after the last injection. 4 patients had 3 repeated injections, 4 patients had 4, 1 patient had 5, 2 patients had 6, 3 patients had 7, 2 patients had 8 and 1 person had 9 repeated injections.

After the first injection the maximum cystometric bladder capacity plus or minus standard deviation significant increased from 348.8 +/- 115.8 ml before treatment to 499.1 +/- 3.6 ml after first injection ($p < 0.0002$). Repeated injections did not induce more increase than the first injection (maximum cystometric bladder capacity after last injection 461.8 +/- 63.7ml, $p < 0.06$).

There was an significant decrease after treatment in maximum detrusor voiding pressure from 75.5 +/- 27.2 cm H₂O to 28.8 +/- 12.8 cm H₂O after the first injection ($p < 0.0001$). There was no significant difference between the maximum detrusor voiding pressure at examination 2 and examination 3 (27.4 +/- 9.4 cm H₂O), ($p < 1$).

Reflex volume increased from examination 1 (205.9 +/- 91.6 ml) to examination 2 (351.2 +/- 11.0 ml) significantly ($p < 0.0005$). There was no significant difference ($p < 0.9$) between examination 2 and examination 3 (after last injection 381.4 +/- 109.4 ml)

No difference in compliance was found between examination 1 (34.0 +/- 16.5 ml/cm H₂O), examination 2 (53.8 +/- 42.4 ml/cm H₂O; $p < 0.03$) and examination 3 (48.9 +/- 20.9 ml/cm H₂O; $p < 0.04$).

Interpretation of results

Repeated injections are as efficient as the first injection. Repeated injections of botulinum toxin type A do not have any negative effect on bladder compliance, reflex volume, maximum detrusor pressure during voiding and maximum cystometric bladder capacity. There was neither evidence on drug tolerance nor exacerbation of regional symptoms, which could have postulated for enhancement of pathological innervation [2].

Concluding message

According to our results botulinum toxin type A injections into the detrusor is a safe and valuable therapeutic option in patients with neurogenic detrusor overactivity and incontinence. After repeated injections the effect of the therapy on urodynamic parameter remains constant. There is no evidence for side effects of repeated injections on the urinary bladder.

Figure 1

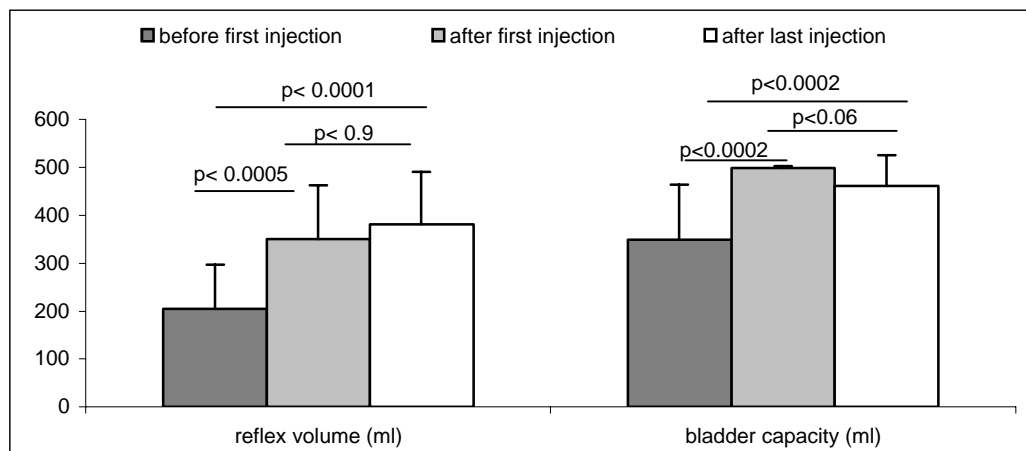
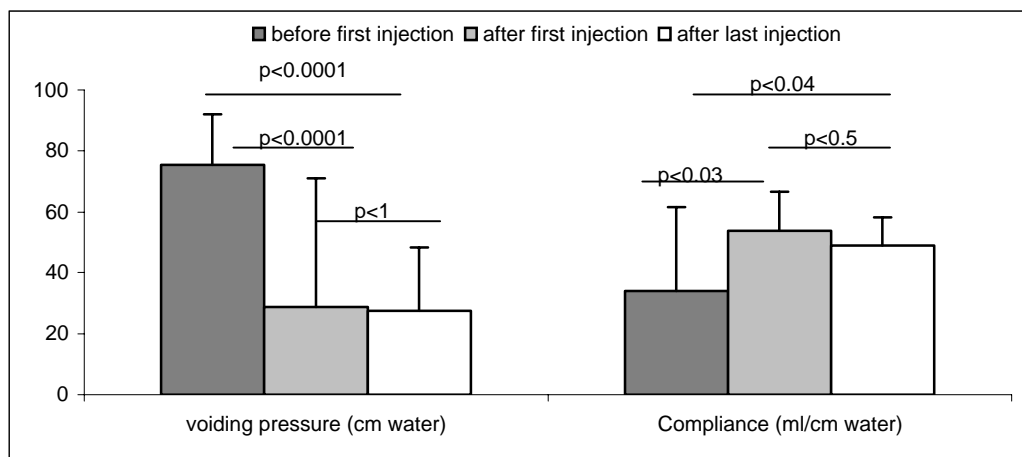


Figure 2



References

- 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 2005 (in press)
- 2 Harper M, Fowler CJ, Dasupta P, Botulinum toxin and its applications in the lower urinary tract. BJU INTERNATIONAL 2004 93: 702-706

