

INTRAVESICAL ONABOTULINUMTOXIN-A INJECTIONS DECREASE BOTH NERVE GROWTH FACTOR AND BRAIN DERIVED NEUROTROPHIC FACTOR LEVELS IN BLADDER TISSUE AND URINE IN PATIENTS WITH IDIOPATHIC AND NEUROGENIC DETRUSOR OVERACTIVITY

Hypothesis / aims of study

To investigate the impact of intravesical injections of BTX-A on neurotrophin activity in patients with idiopathic and neurogenic detrusor overactivity. Bladder tissue and urine NGF and BDNF levels were assayed and clinical and urodynamic data also collated.

Study design, materials and methods

A total of 20 patients (11 Multiple Sclerosis(MS), 9 with Idiopathic Detrusor Overactivity(IDO)) had clinical evaluation with ICIQ-OAB, ICIQ-LUTSqol, and 3-day bladder diary at baseline (Visit0), 2-weeks post BTX-A (Visit1), and at return of symptoms (Visit2). Patients received 100Units (IDO) and 200Units (MS) respectively. Urodynamic assessment was also made to confirm detrusor overactivity both before BTX-A and after return of symptoms (from 6-12months post injection). Urine samples and flexible cystoscopic bladder biopsies were collected at these time intervals. BTX-A was injected under local anaesthesia in the outpatients department. Local NHS Ethical committee approval was obtained prior to initiating the study. Neurotrophin levels were measured in urine and tissue homogenate by enzyme-linked immunosorbent assay (Abcam).

Results

For all patients combined, across the three time points, visit0, visit1, and visit2, ICIQ-OAB scores improved at visit1 and returned to baseline by visit2, from 39.6, 13.3, and 41.3 respectively and similarly with ICIQ-LUTSqol from 193.1, 98.2 and 191.5. Similarly bladder Diary reported daily frequency episodes changed from 10.8, 6.3, 8.9, and daily urge leakage episodes changed from 6.2, 0.8, to 3 respectively over visits 1,2 and 3. At these time points urinary BDNF/Creat and NGF/Creat levels also correlated with the observed clinical changes from 0.28, 0.19 and 0.29 and 0.2, 0.15, to 0.17 respectively. At the same time points decreases were also seen in BDNF and NGF bladder tissue content from 16.3, 9.14 and 11.07, and 0.41, 0.26 and 0.57 pg/g respectively. The neurotrophin levels in both tissue and urine followed the trend of clinical symptom and bladder diary parameters with an improvement 2-weeks after BTX-A from baseline and then return to near baseline levels once clinical efficacy had disappeared.

Interpretation of results

This study is the first of its kind to correlate the activity of neurotrophin markers in both tissue and urine simultaneously in patients with demonstrated detrusor overactivity before BTX-A injection, 2-weeks after, and on return of clinical symptoms.

Concluding message

Treatment of detrusor overactivity with BTX-A injections, reduces neurotrophin activity in both tissue and urine in concordance with clinical efficacy. This is seen to reverse once clinical efficacy is worn off.

References

1. Giannantoni A, Di Stasi SM, Nardicchi V, et al. Botulinum-A toxin injections into the detrusor muscle decrease nerve growth factor bladder tissue levels in patients with neurogenic detrusor overactivity. J Urol. 2006 Jun; 175:2341-4

Disclosures

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