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INTRAVESICAL BOTULINUM TOXIN-A INJECTIONS DECREASES URINARY ATP CONCENTRATIONS IN PATIENTS WITH OVERACTIVE BLADDER (OAB)

Hypothesis / aims of study

Intravesical botulinum toxin-A (BoNT-A) injections have emerged as a good treatment option for patients with OAB refractory to antimuscarinic therapy. BoNT-A may affect both sensory and motor pathways of the urinary reflex by inhibiting the release of signaling molecules from bladder nerves and non-neuronal cells, like the urothelium. It has been shown that BoNT-A decreases the release of ATP from cultured urothelial cells from animal models . Previous data from our group demonstrated that urinary ATP may be a dynamic biomarker of detrusor overactivity in women with OAB. The present study was designed to evaluate modifications in the urinary ATP content in OAB patients after injection of BoNT-A to establish its predictive value of therapeutic outcome in this condition.

Study design, materials and methods

We prospectively evaluated 20 patients (14 women and 6 men) with OAB refractory to antimuscarinics before and 4-8 weeks after injection of 100 U of onabotulinic toxin-A into the bladder wall distributed by 20 different spots. All patients signed an informed consent form and completed a Portuguese version of the OABq (overactive bladder questionnaire). Patients were asked to void at normal desire into a sterile cup. Voided volume was recorded and mid-stream urine samples were tested for infection and for creatinine amounts. Samples used for ATP measurements (by the luciferin-luciferase assay) and lactate dehydrogenase (LDH) activity determinations were immediately snap-frozen and criopreserved at -80ºC until being processed.

Results

Injection with BoNT-A caused an overall improvement of patients' symptom scores as evaluated by increments in bothersome and QOL domain scores of the OABq questionnaire. One female patient was considered a non-responder. The average urinary ATP concentration decreased from 4.62±2.46 nM to 3.04±2.26 nM (p=0.096) after injecting BoNT-A into the bladder wall. This decrease reach statistical significance (p=0.044) if one only considers the responders to treatment; in this case, urinary ATP diminished from 4.73±2.48 nM to 2.82±2.64 nM (n=19). The voided volumes were consistently augmented (p=0.01) in OAB patients submitted to BoNT-A treatment (275.8±143.3 ml) compared to the situation before toxin injection (180.0±95.1 ml). However, urinary ATP diminishes after BoNT-A independently of the voided volume. Although urinary ATP before BoNT-A injection did not correlate with the bothersome domain score of the OABq questionnaire (r=0.216, p=0.361), we found a significant inverse correlation between urinary ATP concentration before the toxin and the degree of improvement in the QOL domain (r= -0.571, p=0.008).

Interpretation of results

Reduction of urinary ATP concentration parallels the significant clinical improvements of OAB patients submitted BoNT-A treatment. This finding strengthens our initial assumption that urinary ATP may be a sensitive biomarker of OAB severity. Moreover, our data suggest that a higher initial urinary ATP concentration is associated with limited benefits in the quality of life score after BoNT-A treatment.

Concluding message

In conclusion, our findings suggest that besides the merit of urinary ATP as a highly sensitive biomarker of detrusor overactivity in OAB patients, urinary ATP may also predict BoNT-A treatment outcome in these patients.

References

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