

## INTRAVESICAL OXYBUTYNIN: A LOCAL ANESTHETIC EFFECT ON THE ICE WATER TEST AND ELECTRICAL PERCEPTION TRESHOLDS

### Hypothesis / aims of study

The ice water test (IWT) was first described for spinal cord injured patients and based on spinal reflex contraction, normally inhibited by supraspinal centers. More recent literature showed that these test also differentiated lesions from sacral motor nerves and suprasacral lesions with intact sacral motor nerves. The C-fiber-mediated reflex responsible for the bladder cooling reflex and the determination of the electrical perception thresholds (EPTs) in the lower urinary tract have both been proposed to detect and differentiate forms of neurologic bladder dysfunction. Because neurogenic deviations of the C afferent nerves could provoke a decreased bladder control, the importance of mechanisms of these nerves is still an important topic to investigate in patients, and remains unfortunately unclear. The aim of the study was to find out the local effect of oxybutynin on the determination of the repeated IWT and electrical perception thresholds (EPTs).

### Study design, materials and methods

A total of 17 patients between 16 and 78 years old were included in this study. Mean age was 43 ± 19 years. They were 12 men and 5 women. All patients had a known neurogenic bladder dysfunction. Exclusion criteria were drug treatment interfering with bladder function and patients with a urinary infection. All patients attended the urodynamic clinic as part of their diagnostic work-up, and were considered fully cooperative. Inclusion criteria were detrusor overactivity during the bladder filling and a positive response on repeated IWT. For urodynamic investigation an 8 Fr 3 lumen catheter with 2 pressure lines was inserted transurethrally. The bladder was emptied. Abdominal pressure was measured using a single lumen balloon catheter introduced in the rectum and protected by a condom. All pressure lines were connected to a 6-channel urodynamic unit. Simultaneously, the vesical, urethral and rectal pressures were measured. All patients were evaluated using a standardized protocol, including cystometry, determination of the EPTs, and the repeated IWT(1). After these initial tests, a urethral catheter was used for the intravesical instillation of 30mg oxybutynin (1mg/ml) while the patients were positioned in the supine position on a urological table. The drug was left in the bladder for 15 minutes and then washed out. EPTs and IWT were again assessed as described with the patients in the same position as during initial investigations. After these tests a single dose of 3mg fosfomycin was given orally to prevent lower urinary tract infection. Computerised statistical analysis was done with nonparametric tests (Wilcoxon test). Values of P<0.05 were considered statistically significant.

### Results

The IWT was positive in all participants. Mean detrusor pressure increase was 105±/ 65 cm water before instillation of oxybutynin. After the drug was washed out, the bladder cooling reflex could not be initiated, even after 3 instillations, in 16/17 (mean pressure of 0 cm water). This was considered a negative IWT. In the remaining patient, the bladder cooling reflex could be provoked after the second and third instillation of ice water after the oxybutynin was washed out. Detrusor pressure increase before instillation was 53 cm water, after oxybutynin 82 cm water. The bladder EPT before instillation was 29.7±/ 11.3 mA, which increased to 39.1±/ 15.7 mA after the oxybutynin was washed. The wilcoxon matched pairs tested showed a significant difference (p=0.001). No difference was found on the control EPT determined on the left fore arm (p=0.208)

Table 1: Results of repeated IWT in neurologic patients with DOA before and after intravesical oxybutynin

Repeated IWT	Before Oxybutynin n=17		(15 minutes) After Oxybutynin n=17	
	IWT positive	IWT negative	IWT positive	IWT negative
First instillation	10	7	0	17
Second instillation	16	1	1	16
Third instillation	17	0	1	16

### Interpretation of results

In patients with a neurogenic bladder, intravesical oxybutynin inhibits the C-fiber mediated bladder cooling reflex and decreases the electrical sensitivity in the bladder. This suggests that (1) oxybutynin exerts its effects, at least partly, by inhibiting bladder C-fiber afferents and (2) the evaluation of the bladder electrical perception threshold may be used a biomarker for these C-fiber afferents.

### Concluding message

The C-fiber mediated bladder cooling reflex can be blocked by intravesical oxybutynin. Bladder EPT's might be used as biomarker for C-fiber related sensitivity.

### References

1. Urology (2007) 70; 772-776.

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<b>Is this a clinical trial?</b>	<b>Yes</b>
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<b>What were the subjects in the study?</b>	<b>HUMAN</b>
<b>Was this study approved by an ethics committee?</b>	<b>Yes</b>
<b>Specify Name of Ethics Committee</b>	<b>Local Ethics Committee</b>
<b>Was the Declaration of Helsinki followed?</b>	<b>Yes</b>
<b>Was informed consent obtained from the patients?</b>	<b>Yes</b>