

BILATERAL PELVIC NERVE CRUSH IN THE RAT AS A MODEL OF DETRUSOR UNDERACTIVITY: REDUCTION OF URETHRAL SPHINCTER ACTIVITY AND ISOVOLUMETRIC CONTRACTION AMPLITUDE

Hypothesis / aims of study

The International Continence Society defines detrusor underactivity as a contraction of reduced strength and/or duration resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying within a normal time span. [1] There is no established rat model for euglycemic non-obstructive detrusor underactivity. We present such a model for the purpose of testing therapies aimed at improving bladder emptying.

Study design, materials and methods

44 female SD rats were divided into two experimental groups: bilateral pelvic nerve crush (PNC) and control. Bilateral PNC was performed in 23 rats under isoflurane anesthesia. A straight Jacobson micro mosquito clamp was used to crush each pelvic nerve for 30 seconds. The crush was performed proximal to each pelvic nerve's entry into the major pelvic ganglion. Prior to crushing, the identity of the pelvic nerve was verified by electrical stimulation with a bipolar electrode to confirm visual bladder contraction. 21 control rats underwent a sham operation where pelvic nerves were exposed but not crushed. At 1, 2, and 4 weeks following PNC or sham surgery, the rats underwent continuous cystometry and external urethral sphincter (EUS) EMG testing under urethane anesthesia (1.2g/kg) using a PE90 transvesical catheter and a saline infusion rate of 0.04 ml/min [2]. Periurethral EUS EMG fine wire electrodes were inserted percutaneously. Following continuous cystometry and single cystometric evaluations, isovolumetric cystometry was performed to measure bladder contractile strength by tying off the urethra. Data were collected using PowerLab from AD Instruments. Statistical comparisons between groups were performed using two-way ANOVA with GraphPad from Prism.

Results

Following bilateral PNC, intercontraction interval (ICI) increased at 1 week and remained doubled at 4 weeks during continuous CMG. This was paralleled by similar increases in bladder compliance. A striking reduction (50%) in EUS EMG activity during filling was also seen with PNC. Isovolumetric CMG in the PNC groups revealed a 40% reduction in peak bladder contraction pressures over baseline and a 30% reduction in isovolumetric bladder contraction areas under the curves.

Interpretation of results

Increased ICI, bladder compliance, and decreased EUS activity are consistent with decreased afferent sensitivity after bilateral PNC. Decreased bladder contraction strength is consistent with compromised efferent function after bilateral PNC.

Concluding message

In this continued model development, we further support bilateral pelvic nerve crush in the rat as a promising, long-lasting model of detrusor underactivity. Both bladder and outlet dysfunction are seen after bilateral pelvic nerve crush. By establishing a chronic rat model for detrusor underactivity in otherwise normal animals, we can test potential therapies for treating detrusor underactivity and voiding dysfunction, thereby addressing both afferent and efferent dysfunction. Future experiments will involve testing the afferent effect with intravesical 0.25% acetic acid and the efferent effect with 4 aminopyridine and strychnine.

References

1. Abrams P, Cardozo L, Fall M et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn* 2002; 21:167-178.
2. Cannon TW, Damaser MS. Effects of anesthesia on cystometry and leak point pressure of the female rat. *Life Sci.* 2001; 69:1193-1202.

Disclosures

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