

BLADDER AND URETHRAL FUNCTION IN AN UNDERACTIVE BLADDER MODEL: ANALYSIS USING SIMULTANEOUS VESICAL AND URETHRAL PRESSURE MONITORING AS WELL AS CONTINUOUS CYSTOMETRY IN AWAKE LUMBAR CANAL STENOSIS RATS

Hypothesis / aims of study

As far as underactive bladder/detrusor underactivity (UAB) models are concerned, partial decentralization models would probably be more useful than complete decentralization models for elucidation of the pathophysiology and evaluation of the therapeutic implications of a specific drug. In that respect a rat lumbar canal stenosis (LCS) model seems to be useful as one of the UAB model1). In preliminary experiments, voided volume of LCS rats revealed some variation when cystometry (CMG) was continued for few hours because underactivity might cause inconsistent micturition reflex in each of the micturitions (Fig. 1). In clinical settings alpha adrenoceptor antagonist (AB) or cholinesterase inhibitor (ChE-I) has been empirically used in UAB patients2). Therefore, we examined the lower urinary tract function of the rat LCS model with in vivo cystometry up to five micturitions before and after taking alpha adrenoceptor antagonist or cholinesterase inhibitor. In addition, we measured intravesical pressure (Pves) and intraurethral perfusion pressure (Pura) simultaneously in awake normal and LCS rats in order to elucidate whether urethral relaxation was concomitant with bladder contraction during voiding in LCS rats (Fig. 2).

Study design, materials and methods

Wistar rats (180 to 190 g) were employed in the present study. One small hole drilled at fifth lumbar vertebral arch (Sham group), and a rectangular piece of silicone rubber (0.5×3.5×5.0 mm) was then placed into the L5 to L6 epidural space (LCS group). After surgery, rats underwent bladder expression at least twice a day in order to avoid bladder overdistension. Experiment 1: Awake CMG was performed 2 weeks after surgery, with vehicle, tamsulosin (TAM, 0.1 mg/kg) or distigmine (DIS, 1 mg/kg) being orally administered. We carefully observed CMG traces up to five micturitions, and the following cystometric parameters were investigated: Infused volume (Vinf), total voided volume (TVV), postvoid residual urine volume after five micturitions (PVR), and maximum Pves (Pves.max). We compared these parameters between pre- and post-drug administration.

Experiment 2: We measured Pves and Pura simultaneously in awake rats. After phasic bladder contraction occurred, the following parameters were investigated: baseline Pves (Pves.base), Pves.max, baseline Pura (Pura.base), and minimum Pura (Pura.min). Then, delta Pves (Pves.max minus Pves.base) and delta Pura (Pura.min minus Pura.base) were calculated. In addition, we measured duration of bladder contraction (Cont.ves) and urethral contraction (Cont.ur) on the traces.

Results

As shown in Fig. 3, DIS significantly decreased Vinf and PVR without any significant changes in TVV or Pves.max. TAM did not reveal any favourable effects on CMG parameters. As shown in Fig. 4, urethral relaxation occurred in LCS rats. However, delta Pves and delta Pura, were significantly smaller, and cont. ves and cont. ura were significantly shorter in LCS rats than in LCS rats.

Interpretation of results

When we performed continuous CMG up to five micturitions, ChE-I had positive effects on UAB in LCS rats. However, in terms of mechanisms of action of ChE-I, this drug might not augment detrusor contraction during voiding, but decrease bladder capacity. So, ChE-I might mainly act on the afferent limb of the micturition reflex directly and/or indirectly. At least in LCS rats, AB did not work well. Micturition in LCS rats was composed of bladder contraction and urethral relaxation, which was virtually a lesser degree in LCS rats than in normal rats. Therefore, LCS rats void not as a consequence of overflow incontinence, but as a consequence of reduced micturition reflex.

Concluding message

Micturitions in LCS rats is driven by reduced micturition reflex, and ChE-I is supposed to act on afferent limb of the reflex arch.

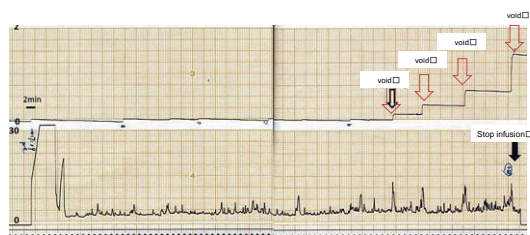


Figure1. CMG trace in a LCS rat. Voided volume at each of the micturitions reveals apparent variation. □

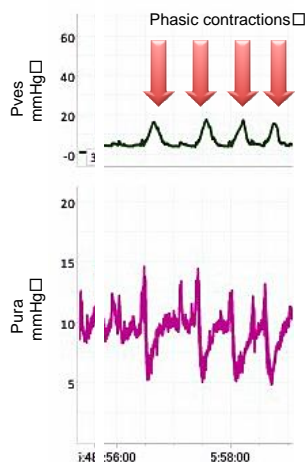


Figure 2. Simultaneous recordings of Pves and Pura in LCS rats

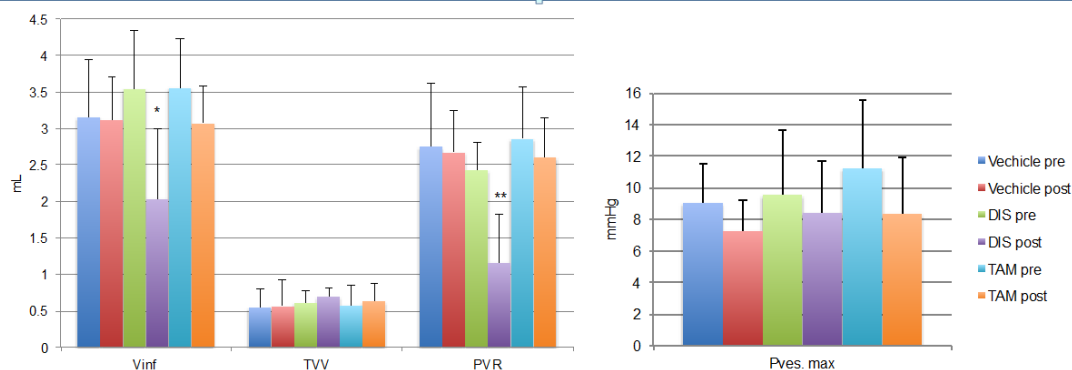


Figure 3. CMG parameters in LCS rats. After administration of DIS, Vinf ($p=0.0154$) and PVR ($P=0.0021$) significantly decrease (t-test). Values are expressed as mean \pm SD.

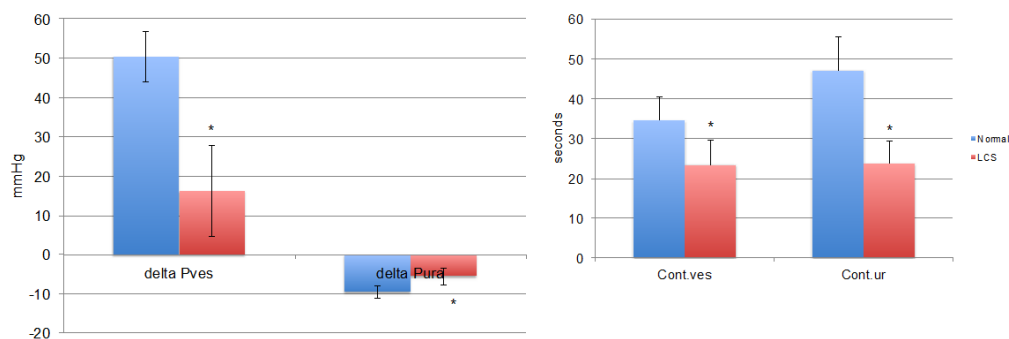


Figure 4. Results of the Simultaneous recordings of Pves and Pura in normal and LCS rats. Values are expressed as mean \pm SD. * $p<0.0001$: significant differences between the groups (t-test).

References

1. NUD 2012;31:1190-6
2. IJU 2004;11:88-96

Disclosures

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