

DIFFERENT CYSTOMETRIC RESPONSES BETWEEN MALE AND FEMALE MICE TO THE LOWER URINARY TRACT IRRITATION BY ACETIC ACID

Hypothesis / aims of study

Numerous studies examining the lower urinary tract (LUT) functions have been conducted in female rodents. Thus, there are few reports detailing the differences between the sexes in the LUT functions, except for the activity of urethral sphincters which have marked anatomical differences between males and females [1]. Clinically, on the other hand, prevalence of some diseases is significantly different between males and females. In urological field, for example, epidemiological studies revealed that an incidence of interstitial cystitis in the female is five times higher than that in the male [2]. What causes such significant difference between the sexes? One possible explanation can be that the female LUT is more sensitive and vulnerable to an irritation or an inflammation, resulting in the evident manifestations. To examine this hypothesis, we conducted the present study using an intravesical infusion of diluted acetic acid to both male and female mice.

Study design, materials and methods

Animal preparations: Experiments were performed on 12-14 week-old 12 mice (male and female, $n=6$ for each) under decerebrate, unanesthetized conditions. All surgical procedures were conducted under sevoflurane anesthesia (2-3% in oxygen 0.2 ml/min flow). A precollicular decerebration was performed using a scalpel and a blunt spatula after skull being removed with a fine rongeur. A transvesical bladder catheter connected to a pressure transducer was used to record bladder pressure during continuous infusion cystometrograms (30 μ l/min) with physiological saline (SAL) or diluted acetic acid (A/A; pH 3). Experiments were performed 2 h after decerebration.

Evaluations and statistics: Parameters evaluated in the study were: maximal voiding pressure (MVP, cm H₂O) which was a peak intravesical pressure during voiding, and inter-micturition interval (IMI, sec) which was defined as a time between peaks of two consecutive voiding contractions. All values are expressed as mean \pm S.E.M. Repeated measures ANOVA was used when applicable. $P<0.05$ was considered significant.

Results

Baseline values of IMI and MVP measured during saline infusion (i.e., before A/A infusion) were: 288 \pm 55 sec and 23 \pm 1 cm H₂O in females and 243 \pm 28 sec and 25 \pm 1 cm H₂O in males. No differences were detected in these parameters between the sexes. In the female mice, A/A (pH 3) intravesical infusion significantly reduced the IMI and the MVP ($P<0.0001$ and $P=0.03$, respectively), whereas in the male it did not change either parameters ($P=0.98$ and $P=0.66$, respectively) (Figure 1).

Interpretation of results

A decrease of IMI implies a reduction of functional bladder capacity, which may be caused by an increase of afferent excitability, residual volume or both. A suppression of MVP can be induced by a decrease of detrusor contractility, urethral resistance, or both. These experiments suggested a possibility that an activity of LUT in females was markedly sensitive to the irritation by diluted A/A (pH 3), whereas that in males was resistant to the noxious stimulation.

Concluding message

The present study revealed that the female LUT was more sensitive and vulnerable to the irritation by diluted acetic acid (pH 3), demonstrating that there was a significant difference between the sexes in reflex bladder responded to the noxious stimulation. What genetic factors make the difference between the sexes in the LUT sensitivity? Further studies using molecular biological approaches are warranted to determine the associated genes and proteins.

References

[1] ICS 2006 Abstract No. 210, 2006.

[2] J. Urol. 173:98-102, 2005.

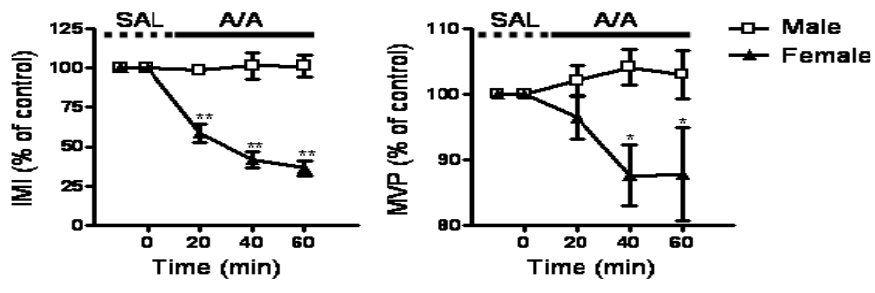


Figure 1

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ANIMAL SUBJECTS: This study followed the guidelines for care and use of laboratory animals and was approved by The Institutional Animal Care and Use Committee, University of Yamanashi