509

Yoshiyama M[1], Kobayashi H[1], Araki I[1], Zakoji H[1], Takeda M[1]
1. *Department of Urology, University of Yamanashi Interdisciplinary Graduate School of Medicine and Engineering*

EFFECT OF INTRAVESICAL INFUSION OF CAPSAZEPINE, A TRPV1 BLOCKER, ON ACTIVITY OF THE LOWER URINARY TRACT IRRITATED BY ACETIC ACID IN UNANESTHETIZED DECEREBRATE MICE

Hypothesis / aims of study

Previous study revealed sex difference in lower urinary tract (LUT) activity responding to intravesical acetic acid infusion in mice, demonstrating that the female bladder was more sensitive to the noxious stimulation than the male bladder [1]. The candidate molecules responsible for the sex difference include transient receptor potential channel V1 (TRPV1), acid-sensing ion channels (ASICs), estrogen receptors, progesterone receptors, nerve growth factor, interleukin-1, 5-hydroxytryptamine, and bradykinin in bladder afferent mechanism [1]. The present study was conducted to determine whether TRPV1 in the bladder was involved in afferent signal transduction generated by intravesical acid irritation. TRPV1 is known to participate in mechanosensory signaling from the bladder under physiological conditions [2].

Study design, materials and methods

Twenty-four C57BL/6 mice (n=12 for each sex; 12-13 week-old) were used. The animals were anesthetized with sevoflurane during surgery including precollicular decerebration. A low midline abdominal incision was made, and a PE-50 tube was inserted into the bladder dome to record intravesical pressure. Experiments were started 2 h after decerebration and conducted under unanesthetized conditions. After an equilibration period of 2 h, intravesical pressure recordings were started by continuously infusing (30 μl/min) saline at room temperature. Cystometric (CMG) parameters measured were: pressure threshold for inducing voiding contraction (PT), maximal voiding pressure (MVP), bladder compliance (BCP), bladder contraction duration (BCD), and inter-contraction interval (ICI). Capsazepine (CZP) solution (100 μM) with diluted acetic acid (A/A, pH 3.0) and its vehicle solution (saline containing 0.2 % ethanol and A/A) were prepared and effects of these solutions intravesically applied after baseline saline infusion were evaluated and compared. All values are expressed as mean ± S.E.M. Statistical analysis was made using Mann-Whitney *U* test and two-way repeated measures ANOVA with actual values. $P < 0.05$ was considered significant.

Results

Baseline values of CMG parameters during saline (SAL) infusion in female and male mice were measured as presented in Table 1. Fig. 1 shows CMG activity during infusion of SAL and subsequent A/A containing CZP or its vehicle in female and male mice. There were significant differences between the female and male in response to A/A containing the vehicle in PT, MVP, BCD and ICI, but not in BCP (Fig. 2). No difference was shown between CZP- and the vehicle- containing A/A infusions in changes of the evaluated parameters in both sexes (Figs. 1 and 2).

Table 1

	PT (mmHg)	MVP (mmHg)	BCP (μl/mmHg)	BCD (s)	ICI (s)
Female (n=12)	7.1 ± 0.5	26.4 ± 0.9	40.3 ± 3.9	29.5 ± 1.2	306 ± 21
Male (n=12)	5.2 ± 0.3**	23.3 ± 1.3	34.9 ± 4.4	36.6 ± 2.7*	186 ± 2**

Comparisons between female and male mice in CMG parameters: *$P < 0.05$, **$P < 0.01$ (Mann-Whitney *U* test).

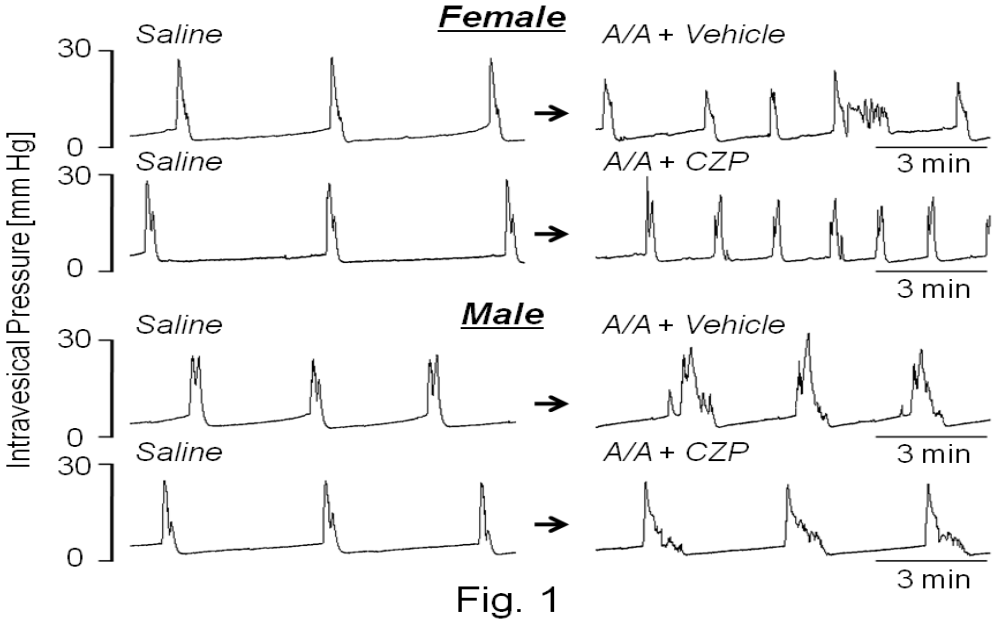

Fig. 1

Interpretation of results

The A/A infusion altered the LUT activity in different fashions between the female and male mice, demonstrating that the female bladder is more sensitive and vulnerable to the irritation, according to degrees of decreased ICI and suppressed MVP. CZP did not affect the CMG parameter changes by the intravesical A/A in both female and male mice.

Concluding message

The results of the experiments using A/A with intravesical infusion of CZP or its vehicle suggested that TRPV1 was less likely to be important in acid-induced afferent signal transduction in the bladder and in the sex difference in activity of the irritated LUT.

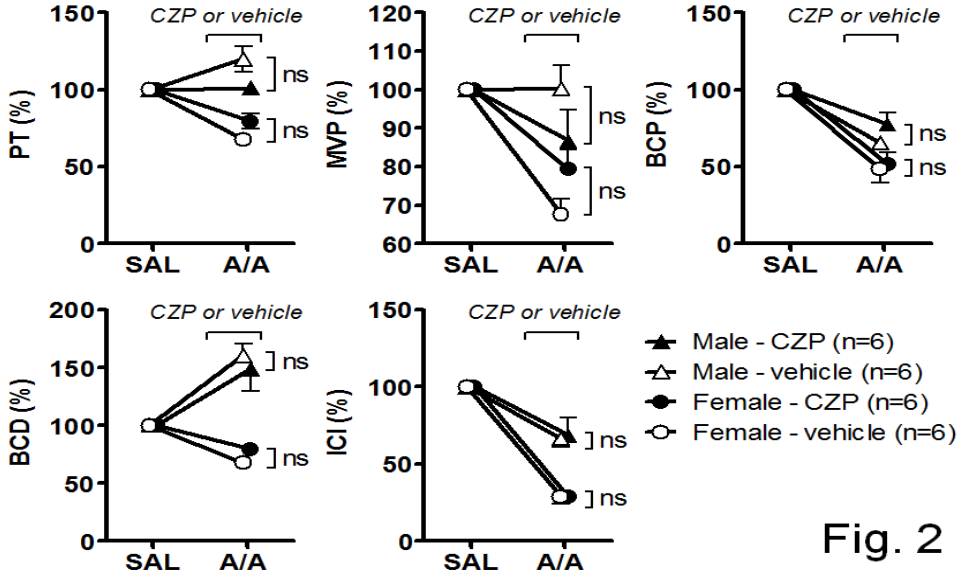

Fig. 2

References

1. Am J Physiol Regul Integr Comp Physiol (2008) 295:R954-R960
2. Nat Neurosci (2002) 5:856-860

Specify source of funding or grant	**Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan (No. 19591839)**
Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**University of Yamanashi Institutional Animal Care and Use Committee**