409

Kwon J[1], Suzuki T[1], Takaoka E[1], Shimizu N[1], Takai S[1], Cho D[2], Yoshimura N[1]
1. *Department of Urology, University of Pittsburgh School of Medicine, Pittsburgh, USA,* ***2.*** *Department of Urology, Cha University School of Medicine, Gumi, South Korea*

FUNCTIONAL ANALYSIS OF URETHRAL CONTINENCE REFLEXES USING SIMULTANEOUS BLADDER AND URETHRAL PRESSURE RECORDINGS IN A RAT MODEL OF SUI INDUCED BY MULTIPLE SIMULATED BIRTH TRAUMAS.

Hypothesis / aims of study
One of the major aetiology of stress urinary incontinence (SUI) in women is vaginal childbirth. Rats with simulated birth trauma induced by vaginal distention (VD) has been used as a model of child birth-related SUI; however, the SUI condition in this model is usually short lasting (7~10days) [1]. Also, multiparity with 3 or more live births reportedly increases the risk of SUI [2]. In addition, the measurement of leak point pressure (LPP), which is the bladder pressure at urine leakage, has often been used to access the urethral function; however, the actual changes in urethral pressures during LPP evaluation are not well characterized. Therefore, we used a novel method capable of measuring LPP and urethral pressure simultaneously under the bladder neck open condition, and investigated the functional changes in the urethral continence function in a rat model of multiple simulated birth traumas.

Study design, materials and methods
Thirty-two female SD rats were used. All rats underwent spinal cord transection at the T8-9 level to block the spino-bulbo-spinal voiding reflex under isoflurane anesthesia. First, after a PE60 catheter was inserted into the bladder through the dome, LPP without a urethral catheter was measured under urethane anesthesia. Thereafter, a microtransducer-tipped catheter was inserted into the mid urethra at 10-14 mm from the urethral meatus. Then, LPPc (leak point pressure with a urethral catheter), UBP (urethral baseline pressure), dUP (differential values of urethral pressure during intravesical pressure elevation), VPuc (vesical pressure when urethral contraction begins), dUC (differential values of urethral pressure during a reflex urethral contraction), and MUP (maximal urethral pressure at leakage) were measured under urethane anesthesia. LPP and LPPc were defined as the intravesical pressure at which the fluid leakage occurred by increasing intravesical pressure gradually using a water reservoir connected to the bladder. UBP was measured as the urethral pressure at 0 cmH_2O intravesical pressure for more than 2 minutes. dUP was defined as the highest urethral pressure differential value just prior to the fluid leakage. VPuc was measured as the bladder pressure when reflex urethral contractions began to increase. dUC was measured as a mean value of pressure changes during individual reflex urethral contraction. MUP was calculated as the maximal urethral pressure at fluid leakage (Fig. 1).
Experiment 1. 20 untreated rats were used to validate the methodology to confirm that simultaneous recordings of bladder and urethral pressures with urethral catheter insertion does not affect LPP values, which were obtained without urethral catheter insertion.
Experiment 2. Other 12 rats were divided into 2 groups; (1) sham-operated rats without VD (n=6) and (2) SUI rats with 3-times VDs (n=6), which were conducted every 2 weeks. VD was induced with a balloon catheter inflated in the vagina for 4 hours under isoflurane anesthesia. Simultaneous recordings of bladder and urethral pressures were performed at 2 weeks after the last VD to compare LPPc and other parameters between 2 groups.

Results
Experiment 1. There was no significant difference between LPP and LPPc (Fig. 2) when these two parameters were consecutively measured in the same animal (n=10). LPPc always exceeded MUP and the mean difference of LPPc and MUP (LPPc-MUP) was 5.5 ± 1.4 cmH2O (n=20) (Table.1).
Experiment 2. The multiple VD group showed lower LPPc by 31.4%, UBP by 34.3%, dUP by 41.2%, VPuc by 21.6%, dUC by 39.7%, and MUP by 34.3% than the sham group. However, the mean value of LPPc-MUP was not significantly different between two groups (4.25 and 4.0 cmH2O) (Fig.3). In addition, VPuc showed a significant correlation with UBP and LPPc (Table.2), and dUC had a significant correlation with dUP and LPPc (Table.3).

Interpretation of results
These results indicate that simultaneous recordings of bladder and urethral pressures using an intravesical catheter and a urethral microtransducer-tipped catheter are useful for detailed characterization of the urethral continence function in a SUI animal model and that the urethral catheter insertion does not affect the measurement of UPP during passive intravesical pressure elevation. We observed a gradual rise of urethral pressure when intravesical pressure was below the UBP level (Fig. 1); however, when intravesical pressure exceeded UBP, rhythmic urethral contractions (shown in inset E of Fig. 1), which are possibly mediated by striated muscle sphincter contractions, started (point D of Fig. 1) and lasted until fluid leakage occurred (point A of Fig. 1). In the multiple birth trauma model with 3-times VDs, this rhythmic urethral contractions started earlier (at lower VPuc), but the amplitude of sphincter contractions (dUC) was smaller in association with significant reductions in other parameters (LPPc, UBP and MUP) compared to sham rats (Fig. 3), indicating the impaired urethral continence reflex activity in multiple VD rats. Also, it seems that a higher pressure (4-5.5cmH_2O) in the bladder (LPPc) than in the urethra (MUP) is needed to induce fluid leakage in both sham and SUI rats.

Concluding message
Rats with multiple VDs, which showed the relatively long-lasting SUI condition (> 2 weeks after VDs), would be a reliable model to study the pathophysiology of multiple child birth-related injuries inducing SUI. Our new method of simultaneous recordings of bladder and urethral pressures would also be useful to fully evaluate the functional change in urethral continence function in SUI models.

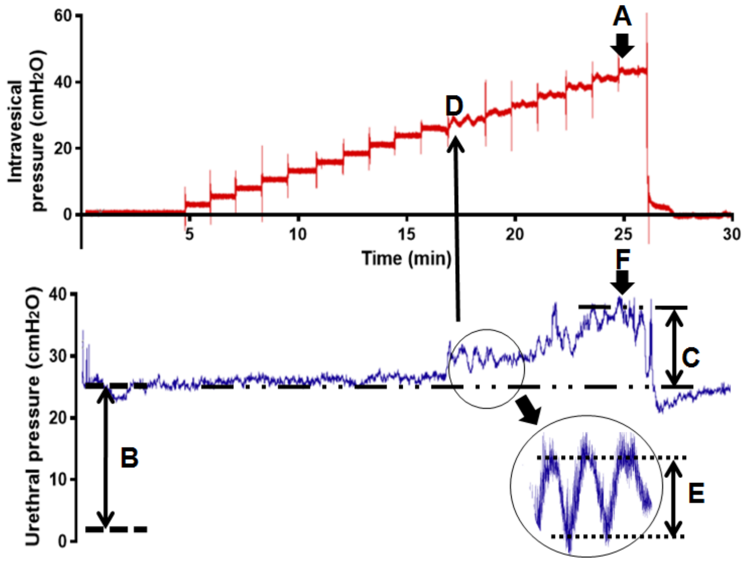

Fig. 1. Representative recordings of LPPc (A; leak point pressure with urethral catheter), UBP (B; urethral baseline pressure), dUP (C; differential values of urethral pressure during intravesical pressure elevation), VPuc (D; vesical pressure when urethral contraction begins), dUC (E; differential values of urethral pressure during a reflex urethral contraction), and MUP (F; maximal urethral pressure at leakage)

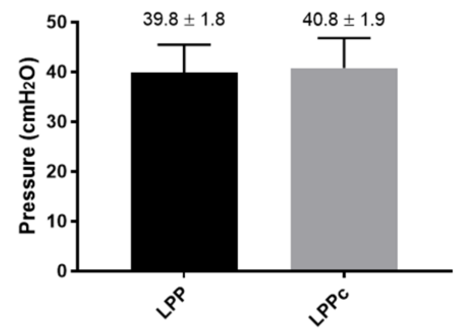

Fig. 2. Comparison between LPP and LPPc (same rat comparison, N=10). p = 0.351 by Wilcoxon's rank test.

Table. 1. Mean values of all parameters in normal rats.

	N	Mean ± SEM
LPPc (cmH2O)	20	41.3 ± 1.2
UBP (cmH2O)	20	21.4 ± 1.1
dUP (cmH2O)	20	20.6 ± 0.7
VPuc (cmH2O)	19	20.7 ± 0.9
dUC (cmH2O)	18	7.6 ± 0.5
MUP (cmH2O)	20	35.7 ± 1.6
LPPc-MUP (cmH2O)	20	5.5 ± 1.4

1 missing value for VPuc, 2 for dUC

Table. 2. Spearman's correlation coefficient between VPuc, UBP, and LPPc

	VPuc	UBP	LPPc
VPuc	1.000	0.586*	0.775**
UBP	0.586*	1.000	0.787**
LPPc	0.775*	0.787**	1.000

* P < 0.05, ** p < 0.01

Table. 3. Spearman's correlation coefficient between dUC, dUP, and LPPc

	dUC	dUP	LPPc
dUC	1.000	0.769**	0.743**
dUP	0.769**	1.000	0.899**
LPPc	0.743**	0.899**	1.000

* P < 0.05, ** p < 0.01

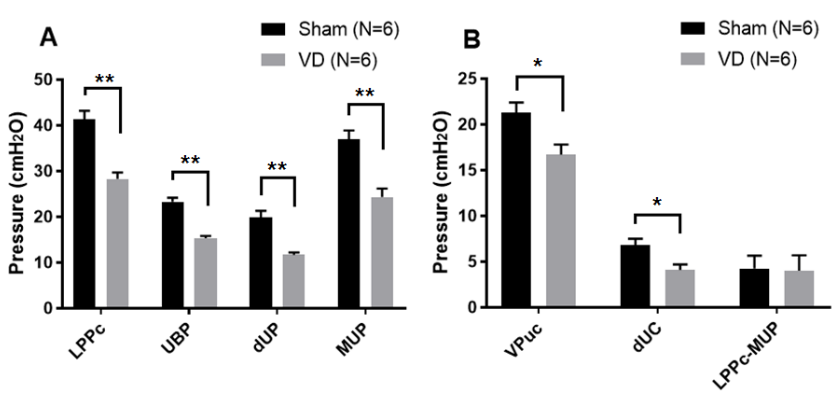

Fig. 3. Comparison of parameters between VD and control group. LPPc, UBP, dUP, and MUP (A), VPuc, dUC, and LPPc-MUP (B). * p < 0.05, ** p < 0.01 by Mann-Whitney's U test.

References
1. J Urol. 2014 Feb;191(2):529-38.
2. Climacteric. 2013 Dec;16(6):653-62.

Disclosures
Funding: NIH R01 DK107450 **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** The University of Pittsburgh Institutional Animal Care and Use committee