

EFFECTS OF MULTIPLE SIMULATED BIRTH TRAUMA INJURIES IN COMBINATION WITH OVARIECTOMY ON URETHRAL CONTINENCE REFLEXES IN RATS

Hypothesis / aims of study

Stress urinary incontinence (SUI) is defined as involuntary leakage of urine under abdominal stress conditions such as sneezing. Childbirth and estrogen deficiency are shown to be major risk factors for SUI. It is well known that single stimulated birth trauma injury induced by vaginal distension (VD) elicits SUI condition in rats, which is usually restored within 10 days (1); however, less is known about the effect of multiple VDs with or without estrogen deficiency on the urethral continence function. In this study, we therefore examined the effect of multiple VDs in combination with ovariectomy (OVX) on urethral function in two types of continence reflexes using rats.

Study design, materials and methods

Adult female Sprague-Dawley rats were divided into 6 groups; (1) control (sham), (2) one-time VD without OVX [Non-OVX+VD(1)], (3) three-times VDs without OVX [Non-OVX+VD(3)], (4) OVX only without VD [OVX+Non-VD], (5) one-time VD with OVX [OVX+VD(1)] and (6) three-times VDs with OVX [OVX+VD(3)]. VD was performed with a balloon catheter inflated in the vagina for 4 hours under anaesthesia. In one-time VD group, VD was performed 2 weeks before the *in vivo* evaluation. In multiple VD group, VD was repeated every 2 weeks and the final VD was performed 2 weeks before the evaluation. Bilateral OVX was performed under isoflurane anaesthesia. Six weeks after OVX with or without VD, LPP during passive intravesical pressure elevation (intravesical pressure clamp method) or sneeze induced urethral closure reflex (s-UCR) measured by a microtransducer-tipped catheter inserted into the mid-urethra was evaluated and compared among groups (2).

Results

In LPP evaluation, the Non-OVX+VD(1) group did not show any change in LPP, but, the Non-OVX+VD(3) and OVX+Non-VD groups showed significant decreases in LPP (27.4 and 18.5% reduction, respectively) compared to control (Fig. 1). The combination group [OVX+VD(3)] showed the largest decrease in LPP (47.7% reduction from control) with significant difference compared to the Non-OVX+VD(3) group (Fig.1).

In s-UCR evaluation, the Non-OVX+VD(1) group showed a tendency to decrease the amplitudes of urethral responses during sneezing (A-URS) without statistical significance compared to control (Fig. 2B). However, the Non-OVX+VD(3) group showed significant decreases in both urethral basal pressure (UBP) and A-URS compared to control (Fig. 2A and 2B); and also showed incontinence episodes during sneezing in 5 out of 6 rats (Fig.2B). The OVX+Non-VD group showed a significant decrease in A-URS with incontinent episodes during sneezing in 3 of 6 rats. The combination group [OVX+VD(3)] showed the largest decrease in A-URS (88.3% reduction from control) with significant difference compared to the OVX+Non-VD(1) or Non-OVX+VD(3) group ($p < 0.001$ or $p < 0.05$, respectively) (Fig. 2B). The OVX+VD(3) group showed SUI in 100% of animals (6 of 6 rats) during sneezing with the lowest s-LPP value (33.6cmH₂O) among groups that exhibited SUI during sneezing.

Interpretation of results

These results indicate that multiple birth trauma injuries or estrogen deficiency induces long-term damage of continence reflexes induced during passive intravesical pressure elevation or sneezing, resulting in SUI, and that the combination of VD and OVX further enhances the deficiency in the urethral closure reflexes.

Concluding message

The present study demonstrated that both multiple birth trauma and estrogen deficiency play significant roles in inducing SUI and that the combination of these two risk factors could accelerate the disease process of SUI in women.

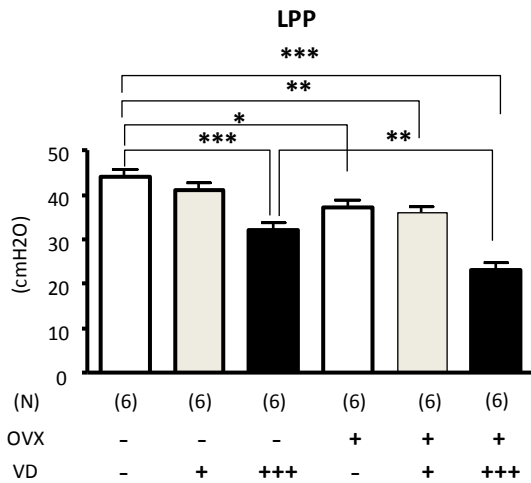


Fig. 1. Effects of single or multiple vaginal distension (VD) with or without ovariectomy (OVX) on LPP during passive intravesical pressure elevation. The (+) or (-) sign indicates the presence or absence of OVX and VD. The (+++) sign indicates the multiple VDs. The number of rats in each group is shown in parentheses. *p<0.05, **p<0.01, p***<0.001 (Tukey's Multiple Comparison Test)

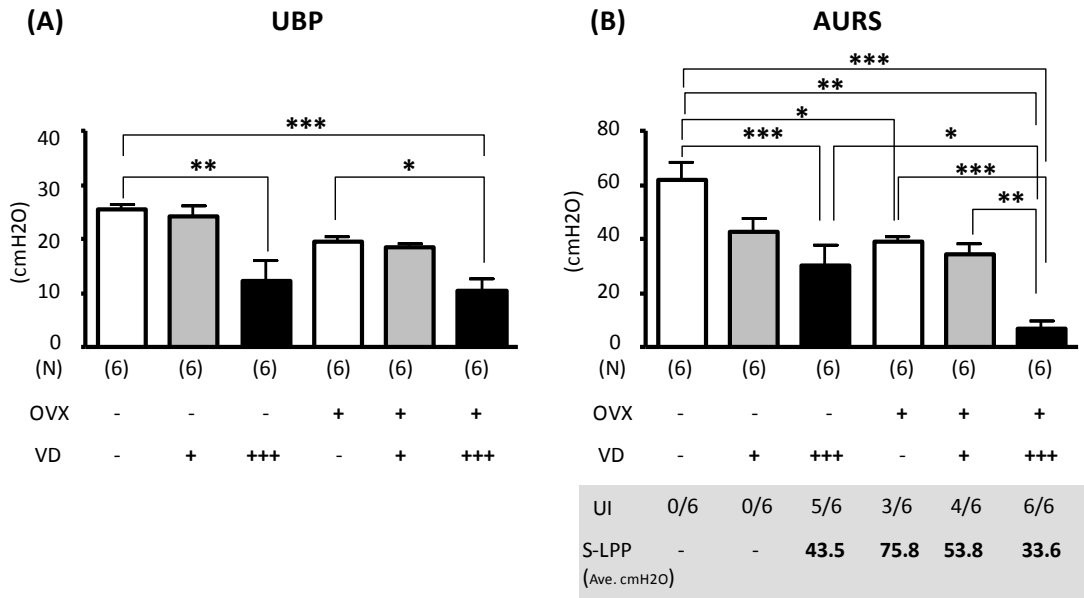


Fig. 2. Effects of single or multiple vaginal distension (VD) with or without ovariectomy (OVX) on urethral baseline pressure (UBP) (A) and amplitudes of urethral responses during sneezing (A-URS) (B). The (+) or (-) sign indicates the presence or absence of OVX and VD. The (+++) sign indicates the multiple VDs. The number of rats in each group is shown in parentheses. The prevalence of urinary incontinence (UI) during sneezing and sneeze-LPP (sLPP) are shown underneath the graph B. *p<0.05, **p<0.01, p***<0.001 (Tukey's Multiple Comparison Test)

References

1. Am J Physiol Renal Physiol (2009) 296; 277–83.
2. Am J Physiol Regul Integr Comp Physiol (2003) 285; 356-65.

Disclosures

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