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DEVELOPMENT OF A NOVEL RAT MODEL OF STRESS URINARY INCONTINENCE

Hypothesis / aims of study

The vaginal distension (VD) model is widely used to study mechanisms of injury and tissue recovery of stress urinary incontinence (SUI)[1]. Since urethral sphincter injury induced by VD usually recovers in a short period (within approximately 4 weeks), the VD model is not suitable to assess the long-term effect of various therapeutic treatments on SUI. In order to develop a novel physiological and sustained SUI model, we created a rat model of urethral sphincter injury by combination treatment of VD with bilateral ovariectomy (OVX), and examined sphincteric contractility and histology in the urethra of the model.

Study design, materials and methods

In 200-gm Sprague-Dawley (SD) rats under anesthesia, a 10Fr Foley catheter was inserted into vagina and dilated for 3 hours to develop a urethral injury VD model. After the catheter was removed, bilateral ovary was resected through a median incision of lower abdomen (VD/OVX group, n = 12). Rats received VD alone (VD group, n = 12), rats received OVX alone (OVX group, n = 12) were also created, and non-injured rats served as controls (Control group, n =12). At 2, 4, and 6 weeks after injury, leak point pressure (LPP) was measured under urethane anesthesia in 4 rats from each group. Then urethra tissues were harvested, fixed, sectioned and stained with hematoxylin-eosin, Masson-Trichrome, and immunostained for α-smooth muscle actin and sarcomeric actin to evaluate histological changes among the groups.

Results

At 2 weeks after injury, LPP in the VD/OVX group (14.2 ± 3.7 mmHg) and VD group (10.0 ± 1.99 mmHg) were significantly ($p < 0.05$) lower than in the Control group (27.2 ± 3.4 mmHg). The levels in the VD group were recovered subsequently by Week 4, whereas the levels in the VD/OVX group were sustained at least until Week 6. Reduced levels of LPP were also observed at Week 4 and 6 in the OVX group; however, the levels in the OVX group were significantly ($p < 0.05$) higher than those in the VD/OVX group (29.5 $\pm$ 2.2 vs 13.0 $\pm$ 2.0 mmHg at Week 6). Histological analysis revealed that shedding and thinning of longitudinal smooth muscle layers in the urethra were observed more prominently at Week 6 in the VD/OVX group, as compared to the other groups.

Interpretation of results

In the VD/OVX model, reduced levels of LPP and the atrophic change of urethral sphincter muscle were induced and sustained at least for 6 weeks.

Concluding message

The combination treatment of VD with OVX induced a sustained impairment of sphincteric contractility with the atrophic change of urethral sphincter in SD rats. The VD/OVX model appears to allow long-term observational assessment for various therapeutic treatments on SUI.

References

1. Cannon TW, Wojcik EM, Ferguson CL, Saraga S, Thomas C, Damaser MS. Effects of vaginal distension on urethral anatomy and function. BJU Int. 2002; 90: 403-7.

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