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ESTROGEN-INDUCED FUNCTIONAL HYPERTROPHY IN FEMALE RABBIT BLADDER

Hypothesis / aims of study

Estrogen is a modulator of cellular growth and differentiation. Even though its main targets in females are uterus and mammary glands, this hormone is essential for maintenance of bone, brain, cardiovascular system as well as the urogenital tract. Postmenopausal women are subjected to bladder dysfunctions, such as incontinence and bladder overactivtiy. It is believed that alterations in female sex hormones play a role in mediating these dysfunctions, which include bladder smooth muscle weakness.[1,2] In animal studies, ovariectomy can result in smooth muscle atrophy whereas estrogen supplementation results in smooth muscle hypertrophy. We hypothesize that functional proteins of smooth muscles including myosin light chain kinase (MLCK), Calponin and Tropomyosin may be altered by ovariectomy and estrogen supplements.

Study design, materials and methods

24 female New Zealand White rabbits were divided into 6 groups of 4 each. Group 1 served as control, group 2 rabbits were ovariectomized (Ovx 14 days only group), group 3 to 6 were given 17-β Estradiol (42 mg/tablet, 14 days release) subcutaneous implant, with medication days of 1, 3, 7 and 14 days, respectively. Bladders were excised, weighed and bladder strips were taken. Contractile responses to all the following stimulations: field stimulation, 2, 8, 32 Hz; ATP, Carbachol and KCl. were done and compared to controls. Proteins were extracted from all groups of animals and used for Western blotting.

Results

Bladder weights were significantly increased in the 3, 7, and 14 days estradiol treatment groups. Contractile function responses to field stimulations, ATP, Carbachol, and KCl were found to be decreased in the ovariectomized group (group 2). However, they were significantly increased compared to the ovariectomized group by the estradiol treatment (Fig 1, 2).Routine histology (H&E and Trichrome stains) demonstrated a significant atrophy of the ovariectomized bladders and significant hypertrophy of the 7 and 14 days estradiol groups. In Western blotting, we have found significant increases in the expression of total myosin and myosin light chain kinase (MLCK, an enzyme of myosin activation) in the 14-day estradiol treatment group, while their expressions was downregulated in the ovariectomized groups when compared to the controls. Further, thin filament associated proteins Calponin and Tropomyosin were also found elevated in the 14-day Estradiol treatment group.

Fig 1.

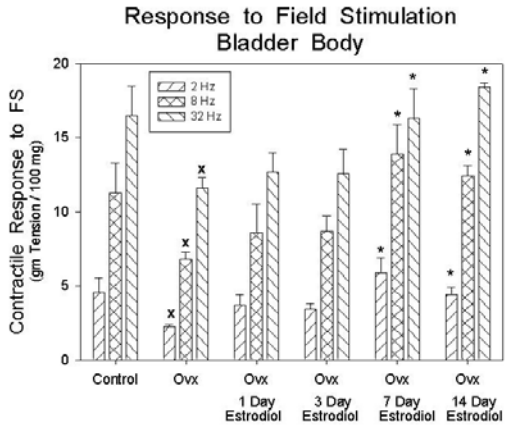
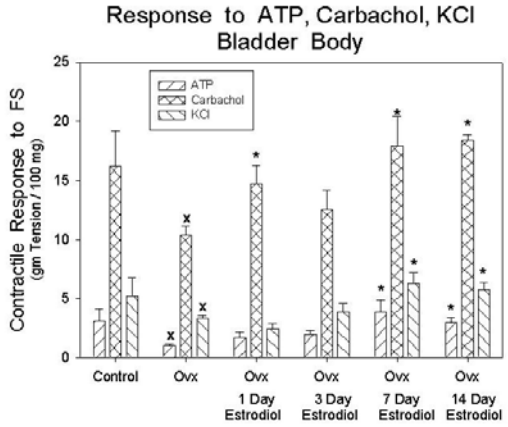


Fig 2.



Interpretation of results

Ovariectomy resulted in decreased contractile function, whereas Estradiol-associated modulation showed enhanced contractile function than controls. It is our opinion that Estradiol resulted in "Functional hypertrophy" of the bladder in female rabbits. The increased expression of contractile proteins provides support for the observed functional hypertrophy.

Conclusion

The present study provided evidence of utilization of estrogen supplement in postmenopausal women with dysfunctional bladder. Further investigation of molecular mechanism of estrogen-induced hypertrophy would be interesting.

Reference

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