

EFFECT OF OVARECTOMY ON CONTRACTILE PROPERTIES OF VAGINAL SMOOTH MUSCLE IN RATS

Hypothesis / aims of study

A functional diversity of the vaginal smooth muscle has been investigated mainly with regard to sexual arousal using isolated muscle strips from a distal part of the vagina (1). However, according to evidence of altered properties of vaginal smooth muscle cells in patients with pelvic organ prolapse (POP)(2,3), there is a possibility that the vaginal smooth muscle also contributes as a pathophysiologic factor to the emergence of POP. It is also reported that POP is often seen in postmenopausal women. However, little is known about the functional properties, especially about cholinergic and adrenergic contractile mechanisms, of the proximal part of the vagina. Therefore, the aim of this study is to investigate fundamental properties of the proximal vagina strips and detect their changes in vaginal muscle strips from rats with ovariectomy (OVX).

Study design, materials and methods

Female Sprague-Dawley rats were used in this study. Bilateral OVX were performed 6 week prior to the experiments. 1x5 mm vaginal strips were harvested from the rats with OVX or age-matched control rats. These strips were mounted in organ baths filled with 37 °C aerated Krebs solution. Tension generated by non-cumulative applications of carbachol (CCh) or phenylephrine, electrical field stimulations (EFS) at frequencies of 0.5, 1, 2, 4, 8, 16, 32 and 64 Hz, and EFS (64Hz) in the presence of prazosin or atropine was measured. Maximum force generated by 120mM KCL application was also measured and used as a control contraction.

Results

1) Single application of 120mM KCL

Maximum force elicited by 120mM KCL solution was not influenced by OVX when the data were corrected by strip weight.

2) Non-cumulative applications of phenylephrine or carbachol (Fig.1, Fig.2)

The maximum contraction force (Emax) elicited by phenylephrine or CCh were reduced in the strips from OVX rats compared with controls (phenylephrine: control n=9, OVX n=12, p<0.05, CCh: control n=12, OVX n=12, p<0.01). However, EC50s of these drugs were decreased in the strips from OVX rats (p<0.01 and p<0.001 respectively). Phenylephrine and CCh-induced contractions were completely abolished by prazosin and atropine, respectively.

3) EFS-induced contraction (Fig.3)

In accordance with the changes in phenylephrine or carbachol responses, EFS-induced contractions in the strips from OVX rats (n=20) were induced at lower frequencies (2-8 HZ) compared to control rat strips (n=24). However, force generated at high frequencies (32-64Hz) was smaller in the strips from OVX rats, although these differences were not statistically significant.

4) Inhibition of a 64Hz EFS-induced contraction by prazosin or atropine.

5x10⁻⁶ M prazosin partially reduced the 64Hz EFS-induced contraction and the degree of decrements was smaller in the strips from OVX rats compared to control rats. On the other hand, 5x10⁻⁶ M atropine completely blocked the EFS-induced contraction in both OVX and control rats.

Interpretation of results

Smooth muscles of proximal vagina strips showed not only adrenergic, but also cholinergic nerve-mediated contractions. Furthermore, inhibition of the EFS-induced contraction by the blocker of each pathway indicates the dominance of cholinergic innervation of the vaginal smooth muscle. Estrogen deficiency induced by ovariectomy decreased the maximal contraction elicited by adrenergic or cholinergic agonists while it increased sensitivity of the smooth muscle to these agonists. Similar tendency was seen in the contractions induced by EFS, in which stimulation frequency was gradually increased. Furthermore, estrogen deficiency decreased the contribution of adrenergic nerve activation to EFS-induced contraction. We speculate that possible reasons for these altered properties following estrogen deficiency could be denervation supersensitivity of receptors and/or alterations in signal transduction mechanisms inducing smooth muscle contractions.

Concluding message

These results suggest that in the proximal vaginal smooth muscle, both adrenergic and cholinergic pathways have significant roles in inducing vaginal smooth muscle contractions and that estrogen deficiency elicits the hypersensitive status of adrenergic and cholinergic receptors and decreases the maximum response to contractile stimulations. It is speculated that these alterations in functional properties of the proximal vaginal muscle might be related to a loss of the vaginal wall tone, which could contribute to the emergence of POP often seen in postmenopausal women.

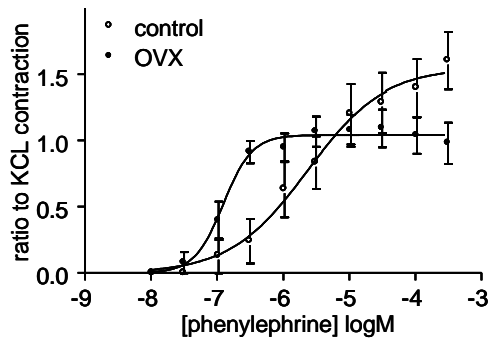


Fig.1 phenylephrine induced contractions

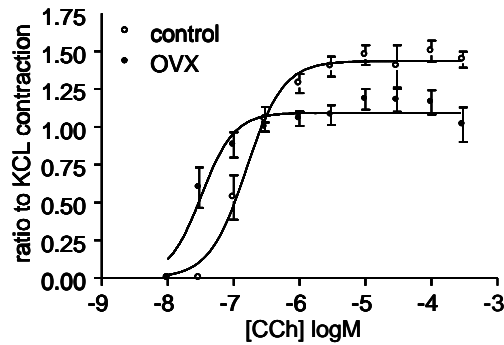


Fig.2 carbachol induced contractions

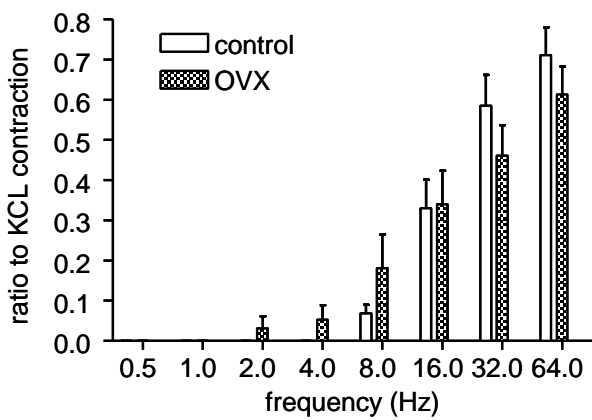


Fig.3 EFS induced contractions

References

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Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	Yes
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