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EFFECTS OF OVARIECTOMY AND ESTROGEN REPLACEMENT ON BLADDER BLOOD FLOW AND BLADDER FUNCTION IN FEMALE RATS

Hypothesis / aims of study

Menopause and subsequent estrogen deficiency have been implicated in the etiology of overactive bladder (OAB) in elderly females. Recently, attention has focused on ischemia of the bladder as a common pathophysiological mechanism for lower urinary tract symptoms (LUTS), including OAB [1]. In the present study, we investigated the effects of ovariectomy (OVX) and estrogen replacement on bladder blood flow (BBF) as well as on bladder function in female rats.

Study design, materials and methods

Virgin Sprague-Dawley rats (24-week old) randomly received a sham operation (SHAM), ovariectomy (OVX), and ovariectomy plus estrogen replacement (OVX+E). In the OVX+E group, the rats were immediately treated with 1mg/Kg weekly injection with **β**-estradiol for 4weeks.

Four weeks after OVX, rats from the three groups anesthetized with urethane, and the anterior bladder was exposed for the measurement of BBF. A laser speckle blood flow imager (OMEGAWAVE, INC. Tokyo, Japan) was used to measure BBF. We determined BBF in the empty bladder because the measurement of BBF during bladder filling did not provide reliable data in preliminarty experiment. Cystometric study was also performed in awaked rats 4 weeks after surgery. Three days before cystometry, rats from the 3 groups were anesthetized and underwent catheter implantation in the bladder for continuous cystometry. The cystometric parameters investigated were micturition interval (MI), bladder capacity (Bcap), micturition volume (MV), post-void residual volume (PVR), maximum pressure (MP), baseline pressure (BP), and threshold pressure (TP).

Results

A significant decrease in BBF was observed in OVX rats. When the bladder was empty, BBF in the OVX group was significantly lower than in the SHAM group. This decrease in BBF was significantly suppressed by estradiol treatment (Fig.1).

Cystometric evaluation showed that OVX induced bladder hyperactivity (Fig.2, Table 1). In the OVX group, MI, Bcap, and MV were significantly less than in the SHAM group (Table1). In the OVX+E group, the MI, Bcap, and MV were significantly larger than in the OVX group, and not significantly different from that in the SHAM group (Table1). There was no significant difference in BP, TP, MP, and PVR among the three groups (Table1).

Fig.1 – Bladder blood flow measurements in 9 SHAM, 9 OVX, and 10 OVX+E rats. Double asterisks indicate p < 0.01 SHAM and OVX+E groups versus OVX group.

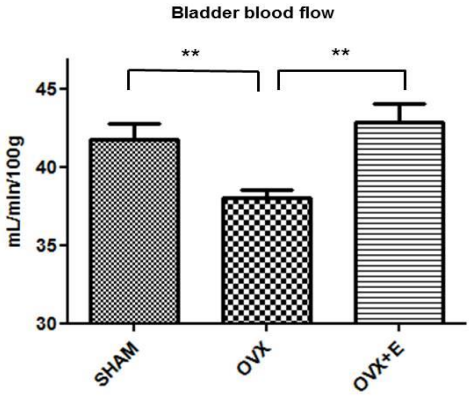


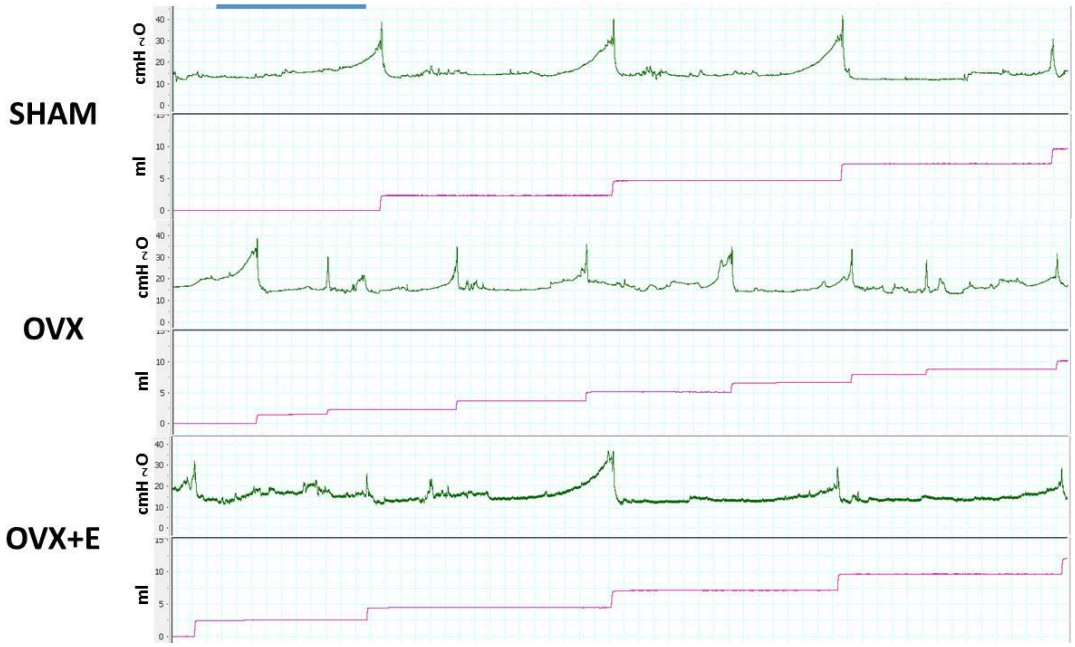
Table1 – Cystometric parameters from 11 SHAM, 11 OVX, and 7 OVX+E rats.

	SHAM	OVX	OVX+E
Micturition intervals, min	12.64 ± 0.6364	10.06 ± 0.5270 **	12.29 ± 0.5172 ††
Bladder capacity, ml	2.106 ± 0.1061	1.676 ± 0.08783 **	2.049 ± 0.08619 ††
Micturition volume, ml	2.064 ± 0.1016	1.636 ± 0.08091 **	1.994 ± 0.1023 †
Postvoid residual volume, ml	0.04177 ± 0.01735	0.03959 ± 0.01864	0.05430 ± 0.01938
Baseline pressure, cmH2O	13.43 ± 0.3871	14.23 ± 0.3384	13.65 ± 0.8035
Threshold pressure, cmH2O	30.06 ± 0.9493	30.28 ± 0.7899	29.78 ± 1.005
Maximum pressure, cmH2O	41.60 ± 1.497	39.81 ± 1.051	42.94 ± 4.348

SEM = standard error of the mean. Data shown as mean ± SEM

** p < 0.01 versus sham † p < 0.05 versus OVX †† p < 0.01 versus OVX

Fig.2 – Typical cystometrogram recordings in SHAM, OVX, and OVX+E groups . Scale bar represents 10min.



Interpretation of results

The present study showed that OVX reduced BBF (ischemia of the bladder) and induced bladder hyperactivity that was characterized by decreases in MI and Bcap. Estrogen replacement was shown to restore BBF and bladder function to normal. Since bladder ischemia is known to cause functional and structural alterations of the bladder, decreased BBF and consequent ischemia may play a potential role in the development of bladder hyperactivity in rats with estrogen deficiency.

Concluding message

This study implicates that bladder ischemia caused by estrogen deficiency may be a contributing factor to the development of OAB in elderly women.

References

1. Nomiya M et al. The effect of atherosclerosis-induced chronic bladder ischemia on bladder function in the rat. Neurourol Urodyn.2012 Jan;31(1):195200

Disclosures

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