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DECREASED EXPRESSION RATIO OF ESTROGEN RECEPTOR-B AGAINST ESTROGEN RECEPTOR-A IN THE BLADDER OF RATS WITH PARTIAL BLADDER OBSTRUCTION

Hypothesis / aims of study

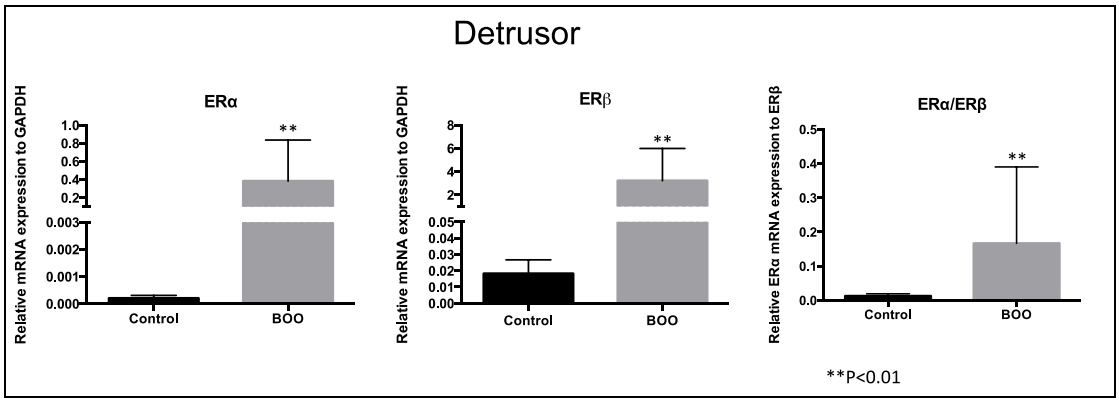
The effect of estrogen is mediated via its intracellular receptors; the estrogen receptor (ER)-α and the ERβ. It has recently been reported that ERβ have a crucial role in anti-inflammatory effects in the brain, uterus, heart and skin, leading to anti-tissue remodelling [1]. It is also known that the decrease of ERβ is a main cause of inflammation in the central nerve system (CNS). Therefore, ERβ becomes a therapeutic target in patients with degenerative CNS diseases such as multiple sclerosis and Parkinson's disease [2]. Furthermore, the ERα/ERβ ratio is shifted to the ERα side in pathological conditions such as uterine adenomyosis. Even though ERβ is the predominant receptor in the bladder, it is not known whether changes in the expression of ERα and/or ERβ are involved in the development of bladder dysfunction. Therefore, we investigated the changes in ERα, ERβ and other related molecules in rat bladders with partial bladder outlet obstruction (BOO).

Study design, materials and methods

Female 8 weeks old SD rats were divided into BOO (n=5) and control groups (n=5). In the BOO group, the proximal urethra was exposed via a lower abdominal incision under isoflurane anaesthesia. The urethra was intubated with a PE-50 catheter, and a 4-0 silk ligature was placed loosely around the proximal urethra, producing a partial urethral obstruction, and the catheter was then removed. The control group underwent a sham operation without urethral ligation. Three weeks after surgery, awake cystometry was performed, and urodynamic parameters were evaluated, including non-voiding contraction (NVC), pressure threshold (PT), maximum voiding pressure (MVP) and post-void residual volume (RV). After cystometry, the bladder was excised, and separated into mucosa and detrusor muscle layers under a microscope. The mRNA expression levels of ERα, ERβ, tumor necrosis factor-α (TNFα), NF-κb, collagen I and connexin-43 (Cx43) were investigated by RT-PCR.

Results

PT, RV, MVP and the number of NVCs were significantly increased in BOO rats compared with control rats (P<0.05). In detrusor muscle, the mRNA expression of ERα, ERβ, TNFα, NF-Kb, collagen I and Cx43 were significantly increased in BOO rats compared with control rats (P<0.01). Furthermore, The ERα/ERβ ratio in detrusor muscle was increased in BOO rats vs. control rats (P<0.01) (Figure). On the other hand, in the mucosa, there was no significant difference in ERβ mRNA expression between BOO and control rats.



Interpretation of results

These results suggest that BOO induces bladder overactivity as shown by NVCs during urine storage, which is possibly induced by upregulation of Cx43 via activation of NF-kb signalling pathways in detrusor muscle, and that the decrease of ERβ ratio against ERα could be involved in activation of NF-κb and TNFα, which leads to tissue remodeling evidenced by increased collagen I. Therefore, activation of ERβ and/or inhibition of ERα could be effective for reducing bladder overactivity and remodeling after BOO.

Concluding message

Imbalance of ERα and ERβ expression (i.e., increased ERα/ERβ ratio) in detrusor muscle could contribute to bladder overactivity and remodeling after BOO. Therefore, activation of ERβ and/or suppression of ERα could be effective for treating BOO-associated bladder dysfunction. Especially, the ERβ might be an effective target for the treatment of patients with BOO because ERβ activation reportedly has therapeutic effects on tissue inflammation and remodeling [1].

References

1. Am J Physiol Regul Integr Comp Physiol. 2010;298:1597-606.
2. Proc Natl Acad Sci USA. 2013;110:3543-8.

Disclosures

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