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EXPRESSION OF SEX STEROID RECEPTORS IN PATHOGENESIS OF PELVIC ORGAN PROLAPSE

Hypothesis / aims of study

The pathophysiology of pelvic organ prolapse (POP) is multifactorial. Putative factors include aging, parity, obesity, menopause, or prior pelvic surgery (1). Recent investigations have focused on the heredity or association of expression of specific genes with POP. Among them, genes coding estrogen receptor (ER), collagen matrix protein, or elastic fibers of the pelvic floor tissues have been investigated (1-3). Estrogen-related receptor□□□ (ERR□), one of steroidal nuclear super families, shares a significant homology to ER□ at the DNA-binding domain and has overlapping function with ER biology, such as cell proliferation by selective estrogen receptors modulators. However, the status of ERR□□in POP patients remains unclear. The aim of study is to evaluate the expression of ERR□□in addition to including other steroidal nuclear receptors in POP.

Study design, materials and methods

Full thickness samples of redundant anterior vaginal walls were excised from consecutive 29 postmenopausal women undergoing trans-vaginal mesh surgery. Control tissues (n=3) were obtained from patients without POP undergoing radical cystectomy or vaginal hysterectomy. Total RNA was isolated, cDNA was synthesized, and quantitative real-time polymerase chain reaction (PCR) was conducted to assess the mRNA expression of androgen receptor (AR), ER□, ER□, and ERR□. The amount of expression was adjusted by GAPDH mRNA. The significance of the difference of mRNA expression between prolapse and control tissues was tested using Mann–Whitney U Test.

Results

There was no significant difference between age of controls and POPs, 65.3±8.1 (56-71), 70.8±7.8 (58–86), respectively. Relative mRNA expression of AR, ER□, ER□, and ERR□ in POP patients was 0.06±0.11, 1.09±3.46, 0.65±1.92, and 0.00029±0.001, respectively. The corresponding values in control subjects were 0.04±0.03, 0.14±0.15, 0.04±0.02, and 0.18±0.28, respectively (Figure 1). Significant suppression of ERR□ mRNA expression was found in vaginal tissues of POP patients (p=0.0039).

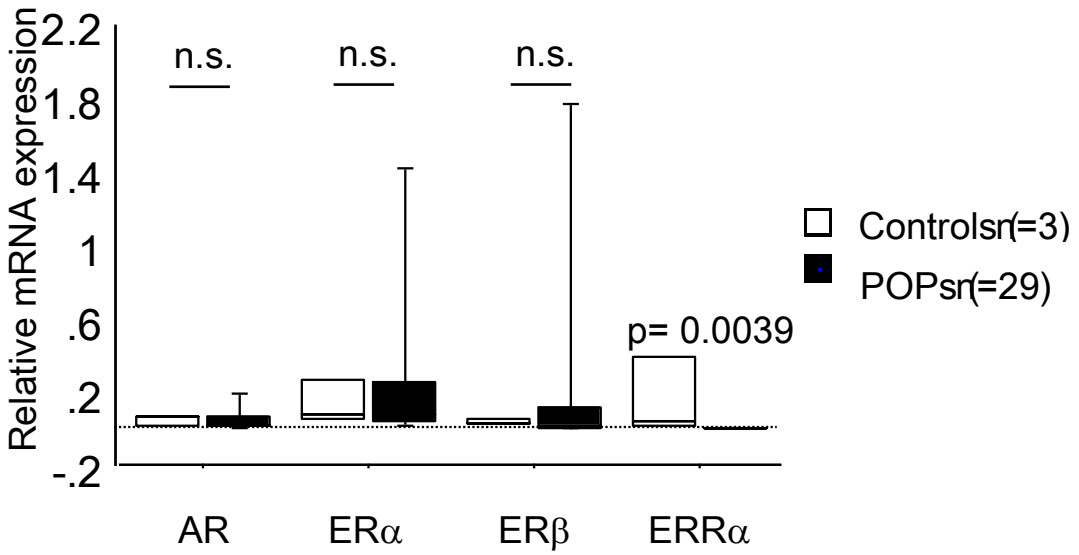
Interpretation of results

The expression of ERR□ has been detected in several tissues requiring high metabolic activities such as heart, brown adipose tissue, and skeletal muscle. For example, ERR□ has an important role in the heart for energy cycle and functional adaptation to cardiac pressure overload. Suppressed ERR□ gene expression in vaginal wall, a part of pelvic floor tissues, may be implicated to the loss of adaptation to persistent pressure to the pelvic floor. Stimulation of ERR□ gene expression or supplementation of ERR□ gene products can be a target of pharmacological therapy of POP.

Concluding message

Expression of ERR□ mRNA is suppressed in vaginal wall of POP patients.

Figure1



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Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Our institutional review board.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**