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Takacs P[1], Zhang Y[2], Yavagal S[1], Candiotti K[2], Medina C[1]
1. *University of Miami, Miller School of Medicine, Dept. of OB/GYN,* ***2.*** *University of Miami, Miller School of Medicine, Dept. of Anesthesiology*

ESTROGEN INHIBITS VAGINAL SMOOTH MUSCLE CELL ELASTIN PRODUCTION: POTENTIAL ROLE IN THE PATHOPHYSIOLOGY OF STRESS URINARY INCONTINENCE

Hypothesis/ aims of the study:
Estrogen appears to increase the risk of urinary incontinence among continent women and worsen the characteristics of incontinence among symptomatic women after 1 year of use [1]. However the pathophysiological mechanism for estrogens' ability to worsen urinary incontinence is not completely understood. Our aim was to measure the effects of estrogen on vaginal smooth muscle cell (SMC) proliferation, elastin and transforming growth factor (TGF)-β1 production. We hypothesized that estrogen may inhibit elastin production *in vitro* and may contribute to the development of urinary incontinence.

Study design, materials and methods: Primary SMC cultures were performed from vaginal wall biopsies, grown to confluence and characterized by immunocytochemistry with primary antibodies against caldesmon, desmin and smooth muscle actin to verify the smooth muscle phenotype. SMC were incubated with estradiol (0.1 μM, 1 μM, 10 μM), in 96-well plates and cell proliferation was assessed by 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazoliumbromide (MTT) assay at 48 hrs. Supernatants were collected and elastin production was measured by the Fastin Elastin Assay kit and TGF-β1 levels were assessed by ELISA.

Results: SMC proliferation was significantly increased by estradiol [relative cell number, mean±SE, estradiol 0.1 μM 116±19% of control (*P*=NS), 1 μM 127±13% of control (*P*<0.05), 10 μM 153±26% of control, (*P*<0.05)]. Elastin production was significantly decreased by estrogen [mean±SE, estradiol 0.1 μM 78±2% of control (*P*<0.05), 1 μM 76±4% of control (*P*<0.05), 10 μM 67±3% of control, (*P*<0.05)] Figure 1]. In addition, TGF-β1 production was significantly decreased [mean±SE, estradiol 0.1 μM 96±4% of control (*P*=NS), 1 μM 84±6% of control (*P*<0.05), 10 μM 70±6% of control, (*P*<0.05)].

Interpretation of the results: Estrogens' ability to inhibit elastin production *in vitro*, potentially through the inhibition of TGF-β1 (potent stimulant of elastin production) [2], may results in abnormal composition of extracellular matrix. Inhibition of elastin production by estrogen may contribute to the development of stress urinary incontinence. However, estrogen increases SMC proliferation and for this reason may be beneficial for post surgical healing.

Conclusion: Estrogen increases vaginal SMC proliferation, inhibits elastin and TGF-β1 production. Estrogen's ability to inhibit TGF-β1 production may be responsible for the inhibition of elastin production.

References
1. Hendrix SL et al. (2005) Effects of estrogen with and without progestin on urinary incontinence.
2. McGowan SE, McNamer R (1990) Transforming growth factor-beta increases elastin

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Was this study approved by an ethics committee?	**Yes**
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Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**