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THE LOSS OF ESTROGEN PROMOTES APOPTOSIS OF PERIPHERY URETHRAL STRIATED MUSCLE CELLS IN RATS WITH STRESS URINARY INCONTINENCE

Hypothesis / aims of study
We established an animal model to study the apoptosis of periphery urethral striated muscle cells in stress urinary incontinence (SUI) caused by birth trauma and loss of estrogen.

Study design, materials and methods
Forty female Sprague-Dawley rats were used to establish the animal model of SUI induced by simulated birth trauma and the loss of estrogen. Group I (10 rats) received no treatment and served as controls; Group II (10 rats) underwent colpectasis; Group III (10 rats) underwent ovariectomy, and Group IV (10 rats) had both colpectasis and ovariectomy. After 3 months, the abdominal leak point pressure (ALPP) was recorded, and the peripheral urethral striated muscle tissues were stained with TUNEL to evaluate apoptosis.

Results
The mean ALPP of Groups II (52.71±2.62cmH2O), III (52.87±2.69cmH2O) and IV (25.10±2.18cmH2O) was significantly lower than that of Group I (77.04±3.53cmH2O) ($p<0.01$). However, there was no obvious difference in ALPP between Group II and Group III ($p=0.898$). Groups III (48.3±4.37%) and IV (51.8±2.82%) had substantially higher apoptosis rates than the control group I (34.7±3.59%) ($p<0.01$). However, there was no significant difference between Group III and Group IV ($p=0.072$). The apoptosis rate in Group III was significantly higher than Group II (37.7±3.00%) ($p<0.01$). By contrast, there was no significant difference between Group II and the control group I ($p=0.069$).

Interpretation of results
Our results showed that colpectasis or ovariectomy reduced ALPP compared to control animals, suggesting that these two factors could be separately evaluated in our animal model. Furthermore, animals that underwent both colpectasis and ovariectomy had the lowest ALPP, indicating that these two factors work additively in causing SUI.
In this study, we did not notice any difference in ALPP between the colpectasis and ovariectomy groups. This could be attributed to the fluctuation of ALPP over time in our model. It has been reported that the ALPP value decreased significantly in the colpectasis group shortly after operation. However, the ALPP did not change in the ovariectomy group. With time, the damage caused by delivery can be repaired to some extent, and as a consequence, the ALPP recovers. Ovariectomy treatment reduces estrogen levels continuously, which could lead to a more dramatic decrease in ALPP. Therefore, SUI is more severe shortly after delivery. On the other hand, low estrogen levels lead to more severe SUI at later stages. In this study, we analyzed the animals 3 months post-operation. It is possible that animals in Group II were recovering (ALPP increasing), while the ALPP in Group III was further decreasing.
We found that estrogen levels inversely correlated with apoptosis rates in the peripheral urethral muscle tissue. The loss of estrogen resulted in a high apoptosis rate (Group III vs. Group I, $p<0.01$). However, consistent with previous reports, birth trauma had no effect on apoptosis (Group II vs. Group I, $p=0.069$). Therefore, we concluded that SUI induced by decresing estrogen levels is due to apoptosis in peripheral urethral muscle tissue.

Concluding message
The loss of estrogen promotes apoptosis of periphery urethral muscle cells, while simulated birth trauma has little effect on apoptosis of these cells.

Disclosures
Funding: no **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** Ethics committee of laboratory animals, Fudan University