

EFFECT OF ESTROGEN THERAPY ON THE POSTMENOPAUSAL INFLAMMATORY BLADDER STATE

Hypothesis / aims of study

This original work was designed to explore the relationship between the postmenopausal bladder state, vaginal estrogen therapy, and urinary tract infections (UTIs). Urinary tract infections are common and can result in significant healthcare morbidity, especially in the aging population. Postmenopausal women are at increased risk for recurrent UTIs, which may be related to the relative estrogen deficiency leading to inflammation and increased susceptibility to infection in the genitourinary tract [1,2]. Topical vaginal estrogen therapy has been shown to decrease the risk of recurrent UTIs in postmenopausal patients, but the mechanism of action is still unclear [3]. The objective of our work is to characterize the postmenopausal inflammatory profile to assess whether this contributes to increased susceptibility to UTIs and whether vaginal estrogen therapy modulates this risk.

Study design, materials and methods

We prospectively enrolled post-menopausal patients (>65 years) into one of three cohorts: 1) postmenopausal *without* a history of UTIs who are currently using vaginal estrogen therapy; 2) postmenopausal women *with* a history of UTIs who are currently using vaginal estrogen therapy; and 3) postmenopausal women *with* a history of recurrent UTIs who are *not* receiving vaginal estrogen therapy but are willing to start. We followed patients over a 6-month course and collected urine and serum samples from each patient at study enrollment, 3 months, and 6 months. Comprehensive cytopathologic analysis was performed using Pap and Hema-staining, urine inflammatory scoring was performed, and urothelial cell shedding was closely monitored.

Results

We have recruited a total of 41 patients into the pre-defined cohorts: 1) no UTI on vaginal estrogen (n=20); 2) patients with UTIs on vaginal estrogen (n=15); 3) patients with recurrent UTIs not on estrogen but willing to start (n=6). At this time, 23 (56%) have returned for one follow-up visit, and 13 (32%) have completed the full 6 months of follow-up. On cytologic analysis, urine from post-menopausal patients without a history of recurrent UTIs shows scant urothelial cell shedding, while patients with history of recurrent UTIs demonstrate increased inflammatory cells, debris, and exfoliated urothelial cells (Figure). Urine inflammation scores are significantly higher in post-menopausal women with recurrent UTIs compared to women without UTIs (1.25 and 1.67 vs 0.12, $p < 0.05$) (Figure).

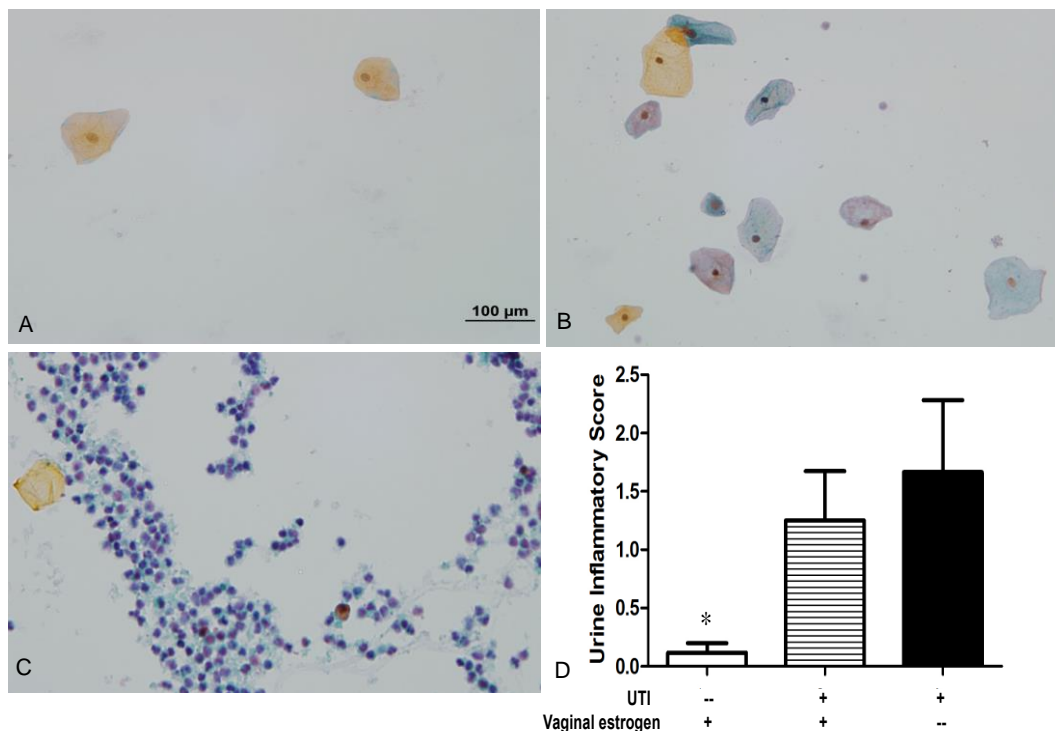


Figure. Vaginal estrogen treatment decreases infiltration of neutrophils in the urine from postmenopausal women with UTI. Pap stained urine cytology from a postmenopausal woman without UTIs on vaginal estrogen (A), postmenopausal woman with recurrent UTIs on vaginal estrogen (B), and postmenopausal woman with recurrent UTIs not on vaginal estrogen (C). Inflammation score indicates neutrophil infiltration in postmenopausal women who are on vaginal estrogen therapy (D). * $p < 0.05$.

Interpretation of results

Postmenopausal women with recurrent UTIs demonstrate increased urine inflammation scores and urothelial cell shedding. Vaginal estrogen therapy appears to modulate this effect with reduced urine inflammation and decreased cell shedding in women

with recurrent UTIs already on an established vaginal estrogen regimen. Further studies using urine and serum inflammatory markers will be performed to further analyze the effect of vaginal estrogen therapy on the post-menopausal inflammatory profile.

Concluding message

This novel work should help further delineate the role of the postmenopausal inflammatory state in UTIs and the role vaginal estrogen plays in reversing these effects and reducing UTI risk.

References

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3. Perrotta C, Aznar M, Mejia R, Albert X, Ng CW. Estrogens for preventing recurrent urinary tract infection in postmenopausal women. 2008. *Cochrane Database Syst Rev* 2008, Issue 2. Art. No.: CD005131. DOI: 10.1002/14651858.CD005131.pub2.

Disclosures

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