Effects of Menopause on Innate Immune Defense Mechanisms in Urinary Cells

Ariel Y. Chen, BA, Lina M. Loza, MD, Fernando Pereira Beserra, PhD, Humberto D. Escobedo, PhD, Annika Smith, BA, Kathleen A. Connell, MD, Michael Schurr, PhD, Joshua Johnson, PhD and Marsha K. Guess, MD, MS.

Introduction:

Urinary tract infections (UTIs) are the most common bacterial infection worldwide with recurrent infections (rUTI) reported following more than 25% of initial infections. Postmenopausal women have increased susceptibility to rUTI and hypoestrogenism is thought to play a crucial role. To date, the underlying mechanisms influencing this predisposition for rUTI are relatively unknown. We hypothesize that postmenopausal women have downregulated expression of antimicrobial peptides (AMPs) at baseline which predisposes them to developing UTIs.

Methods:

Self-identified cisgender women ≥ 18 years old were recruited from the University of Colorado Urogynecology clinics at the Anschutz Medical and Lone Tree campuses. Patients with an active infection, bladder pathology, a genitourinary malignancy, or fecal incontinence as well as those receiving antibiotics, hormone therapy, or supplements to prevent UTI <1 month prior to presentation were excluded. Urine samples from mid-stream clean catch were obtained from all participants and stratified based on menopausal status. Urinary cells were isolated from urine samples, mRNA was extracted, and AMP expression was quantified via reverse-transcriptase quantitative polymerase chain reaction (RT- qPCR). The transcription of genes encoding the AMPs secretory leukocyte peptidase inhibitor (SLPI) and psoriasin (S100A7) were quantified. The transcription levels for the pro-inflammatory cytokine interleukin-1 beta (IL-1β) was also assessed. All genes were normalized to the housekeeping gene *GAPDH* encoding glyceraldehyde 3-phosphate dehydrogenase. Unpaired two-tailed student's *t*-tests were used to compare gene expression mean fold change between pre- and post-menopausal patients. A p-value <0.05 was deemed significant.

Results:

Urinary cells from 39 postmenopausal and 19 premenopausal participants were obtained, RT-qPCR was performed, and outliers were excluded. Compared to premenopausal women, postmenopausal patients had significantly lower expression of S100A7 (0.7388 vs 6.791, p<0.0001). Cells from postmenopausal women were also shown to have a reduction in SLPI gene expression compared to cells from premenopausal women but lacked significance (0.8674 vs 1.380, p=0.0828). The gene expression for IL-1β was significantly increased in postmenopausal patients compared to premenopausal women (4.383 vs 0.2373, p=0.0015).

Conclusion:

Our study showed that postmenopausal participants had significantly lower expression of the gene encoding the AMP, S100A7, and increased expression of the gene encoding the proinflammatory

cytokine, IL-1β, compared to premenopausal participants. AMPs serve as an important first response in innate immunity. A loss of innate immune defense and a predisposition to inflammation may play an important role in increased rUTI incidence in postmenopausal women.