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THE FEMALE URINARY MICROBIOTA RELATES TO INCONTINENCE MEDICATION EFFICACY

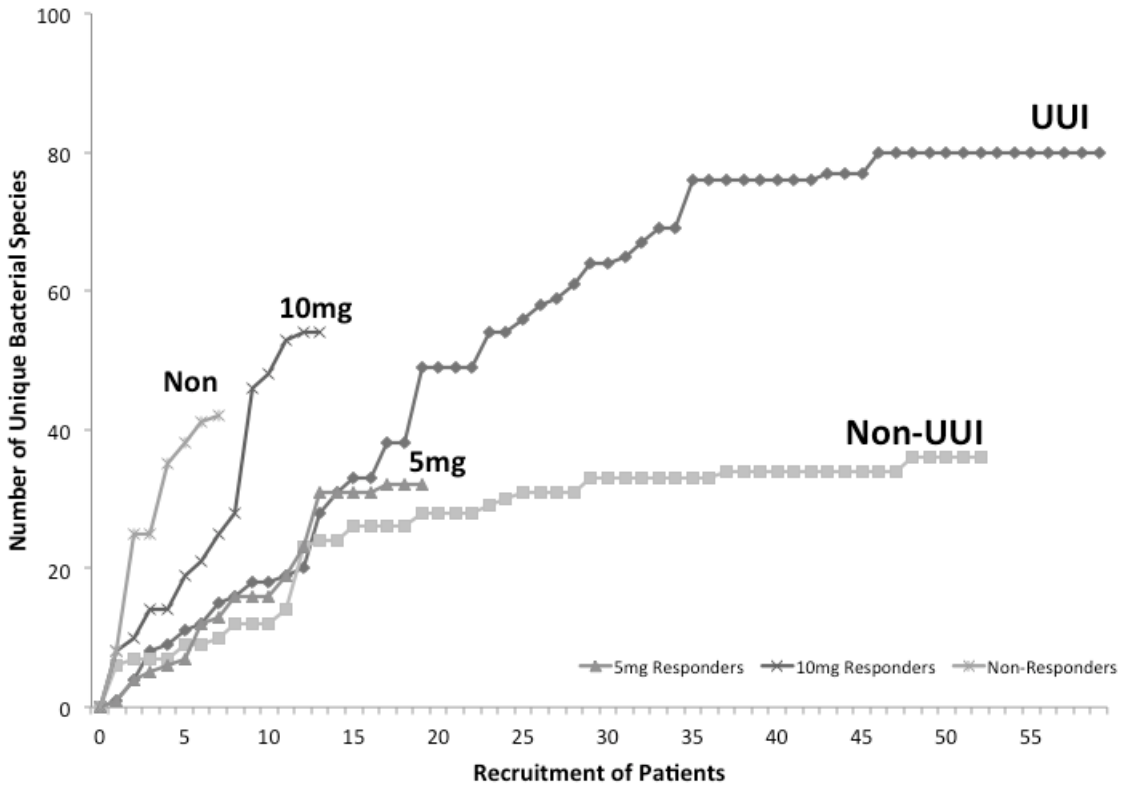
Hypothesis / aims of study
To determine whether urinary microbiome/microbiota characteristics are related to a clinically relevant treatment response to oral urinary urgency incontinence medication, using two complementary methods of bacterial assessment.

Study design, materials and methods
In a tertiary care health care system, two groups of adult women were recruited: those initiating oral medication treatment for UUI and a group of unaffected women for baseline comparison. All participants provided baseline clinical data and a catheterized urine; women with UUI were followed for up to 12 weeks, with additional data and urine samples collected at 4 and 12 weeks. Women with UUI were treated with Solifenacin 5mg, with potential for dose escalation to 10mg for inadequate UUI symptoms control at 4 weeks. Clinically relevant UUI symptom control was defined as a score of 4 or 5 on the validated Patients Perception of Bladder Condition (PPBC) questionnaire. At 12 weeks, the primary outcome, treatment response, was determined using the PPBC. Each urine specimen was sequenced using the V4 region of the 16S rRNA gene and cultured using an expanded quantitative urine culture (EQUC). The sequenced data was classified to the genus-level using the mothur software package. The growth of bacteria in EQUC was classified to the species-level using MALDI-TOF mass spectrometry.

Results
At baseline, participants included 74 UUI-affected women and 60 controls. The cohorts were similar with respect to race/ethnicity, diabetes, and smoking. Participants with UUI were more likely to suffer from hypertension [35% versus 18%, p=0.02] and coronary artery disease [12% versus 2%, p=0.02]. The UUI population also was older [61.5 years (SD:11.5) versus 49 (SD:14.7), p<0.001], heavier [BMI 32.7 (SD:8.4) versus 28 (SD:5.5), p<0.001], and less likely to be using estrogen [88% versus 43%, p-value<0.001]. As expected, UUI symptoms were significantly worse in UUI- than non-UUI participants. The baseline urinary microbiome/microbiota characteristics of women with and without UUI differed. Women with UUI had a greater number of bacteria and a more diverse bacterial community (Figure 1). Of the 50 participants who provided primary outcome, 25 were considered responders. The clinical response to solifenacin in participants with UUI was related to the baseline urinary bacterial community, with responders being more likely to have fewer bacteria and a less diverse community at baseline than non-responders. In addition, the diverse community of non-responders often included bacterial genera, such as *Actinomyces* and *Corynebacterium,* which were not typically found in responders. Bacterial assessments of participant urine using sequencing and expanded cultures were complementary, although both techniques were not available for all participants.

Interpretation of results
The response to oral UUI medication (solifenacin) may relate to individual urinary microbiota characteristics that are detectable prior to treatment. Two complementary tools, DNA sequencing and expanded urine culture, provide information about specific resident organisms that appear related to UUI incontinence status and UUI treatment response in this population of adult women. Our findings, especially the importance of organism diversity, offer promising possibilities for new ideas for prevention and treatment of UUI in women.

Figure 1. Diversity of urinary microbiota is distinct between cohorts and response groups at baseline.



Concluding message

Adult womens' individual urinary microbiome/microbiota differ based on presence of UUI; in addition, the urinary microbiota relates to UUI treatment response in women treated with oral UUI medication. Expanded urine culture and DNA sequencing are complementary tools for urinary microbiome/microbiota evaluation.

Disclosures

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