

## IMPACT OF ANTIBIOTIC ALLERGY AND RESISTANCE ON ORAL FIRST-LINE ANTIBIOTIC TREATMENT CHOICE FOR RECURRENT URINARY TRACT INFECTIONS IN OLDER WOMEN

### Hypothesis / aims of study

To review the rate of antibiotic allergy and resistance in older women with recurrent urinary tract infections (RUTIs) as determinants for a suitable oral antibiotic treatment choice.

### Study design, materials and methods

Following IRB approval, a prospectively maintained database of women 65 years old and older with documented RUTIs ( $\geq 3$  UTI/year) and trigonitis on cystoscopy was reviewed for demographic data (age, race, BMI, diabetes, immunosuppression), known drug allergies, blood urea nitrogen (BUN), creatinine, estimated GFR, and antibiotic susceptibility. Data was acquired through an electronic medical record (EPIC) by a reviewer (YW) not involved in patient care, with all values taken from the most recent available test results. Women with no antibiotic susceptibility profiles available for review were excluded. Three commonly used antibiotics for the management of RUTIs were further analyzed: trimethoprim-sulfamethoxazole (TMP-SMX) and other sulfonamides, fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin), and nitrofurantoin.

### Results

From 2006 to 2014, 86 of 168 women with RUTIs met study criteria. Mean age was  $77.9 \pm 7.8$  with 94% (81/86) being Caucasian and 10% (9/86) with controlled adult-onset diabetes mellitus. Mean BMI was  $24.4 \pm 6.1$ . Mean BUN and creatinine were  $17.3 \pm 8.3$  and  $0.84 \pm 0.29$ , respectively. eGFR  $>60$  mL/min was noted in 65% and eGFR  $>30$  mL/min in 94%. Mean number of known allergies to all medications was  $3.5 \pm 3.9$  and to only antibiotics was  $1.6 \pm 1.8$ . The mean number of antibiotic resistances was  $4.3 \pm 3.5$ . Percentage of women either allergic and/or who had resistance to TMP-SMX, fluoroquinolones, or nitrofurantoin was 77% (66/86), 56% (48/86), and 35% (30/86), respectively. (Table 1) Twenty-nine percent (25/86) of women who were allergic and/or resistant to TMP-SMX and fluoroquinolones were neither allergic nor resistant to nitrofurantoin. Twenty percent (17/86) were allergic and/or resistant to all three antibiotics. Women who were either allergic or resistant to TMP-SMX had a significantly higher number of other antibiotic resistances compared to women that were sensitive to TMP-SMX ( $4.9 \pm 3.6$  versus  $2.1 \pm 2.3$ ;  $p < 0.0001$ ). Similarly, women with either fluoroquinolone allergy or resistance had significantly more antibiotic resistances than those that were fluoroquinolone sensitive ( $5.8 \pm 3.5$  versus  $2.3 \pm 2.5$ ;  $p < 0.0001$ ). However, there was no significant difference in number of antibiotic resistances in women with nitrofurantoin allergy or resistance compared to those who were nitrofurantoin sensitive ( $4.5 \pm 3.0$  versus  $4.2 \pm 3.8$ ;  $p = 0.70$ ).

**Table 1.** Summary of antibiotic allergy and/or resistance findings, N=86

	Allergy Only	Resistant Only	Both Allergy and Resistant	Antibiotic Sensitivity
TMP-SMX*	28	25	13	20
Fluoroquinolone**	12	29	7	38
Nitrofurantoin	14	12	4	56

\*Trimethoprim-sulfamethoxazole

\*\*Includes ciprofloxacin, levofloxacin, and moxifloxacin

### Interpretation of results

In choosing the optimal antimicrobial therapy for women with RUTI, drug allergies, antimicrobial susceptibility, and adverse side effects must be considered. Antimicrobial-resistant RUTIs have increased in both frequency and spectrum in the hospital and community. Bacterial selective pressure due to pervasive antimicrobial use, transmission of drug resistance between pathogens, and other microbial characteristics all have contributed to the increased resistance. [1] Factors that may influence antimicrobial resistance on an individual basis are advanced age, travel history, chronic medical conditions, recent hospitalizations, and recent antibiotic courses. In the most recent Beers Criteria for potentially inappropriate medication use in older adults, Nitrofurantoin was mentioned as a concern in the treatment of RUTIs in older women because of the "potential for pulmonary toxicity, hepatotoxicity, and peripheral neuropathy, especially with long-term use." [2] Therefore, the current recommendation is to use safer alternatives when possible and avoid use in individuals with creatinine clearance  $<30$  mL/min. It is not recommended for long-term bacterial suppression.

We found 29% of women with RUTIs had only nitrofurantoin available as an oral antibiotic option due to allergy and/or antibiotic resistance to TMP-SMX and fluoroquinolones. The vast majority of women in our study (94%) had eGFR  $>30$  mL/min. Also, women were equally likely to be sensitive to nitrofurantoin regardless of the number of other antibiotic allergies/resistances or if they were sensitive to TMP-SMX/fluoroquinolones. Therefore, nitrofurantoin remains an important antibiotic alternative in the management of RUTIs in older women along with careful monitoring for rare, but potentially serious adverse events.

#### Concluding message

This study reaffirms that due to allergy and/or antibiotic resistance several first-line antibiotics are not available for many Caucasian women with RUTIs. In a significant number of women, nitrofurantoin is the only viable alternative in the management of these more complex patients.

#### References

1. Shepherd, A. K., Pottinger, P. S.: Management of urinary tract infections in the era of increasing antimicrobial resistance. Med Clin North Am, 97: 737, 2013
2. By the American Geriatrics Society Beers Criteria Update Expert, P.: American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc, 2015

#### Disclosures

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