Impact of Initial Inappropriate Antibiotic Therapy on Outcome for Uncomplicated Urinary Tract Infection Due to Fluoroquinolone Non-susceptible Enterobacteriaceae

Sailaja Puttagunta, MD, Steven Aronin, MD, Vikas Gupta, PharmD, BCPS®, John Murray, MPH, and Michael Dunne, MD

Iterum Therapeutics, Old Saybrook, CT 06475; 2Becton, Dickinson and Company, Franklin Lakes, NJ.

ABSTRACT

Background: Urinary tract infection (UTI) is the most common outpatient bacterial infection. Rising resistance rates among gram-negative bacteria have made common oral antibiotics ineffective for uncomplicated UTI (cUTI), highlighting the risk of adverse outcome related to initial inappropriate antibiotic therapy (IIAT). There’s limited published data quantifying the impact of IIAT in patients with UTI treated in the outpatient setting due to cUTI and non-susceptible Enterobacteriaceae.

Methods: The BD Insights Research Database was used to evaluate antimicrobial fill history for patients from 15 US institutions with a positive urinary culture for an uropathogen. Patients who initially filled a prescription for a fluoroquinolone were further categorized into those with a urine culture positive for a fluoroquinolone-susceptible (QS) versus fluoroquinolone-non-susceptible (QNS) pathogen. Outcome was assessed using two surrogate endpoint hospital admission and re-prescription within 28-days of initial fluoroquinolone fill. Results: A total of 2,184 ambulatory urine culture episodes with a fluoroquinolone fill identified in 1,999 patients. Hospitalization data was available for 2,025 of these patients. 1,576 (72%) had >100,000 CFU/mL and 808 (38%) had <100,000 CFU/mL. QNS pathogens were isolated in 28%-day fill rate hospital admission rate 1,712 (27.2) vs 272 (15.9) p<0.001; 371 (34.0) vs 47 (27.1) p=0.023. Overall* 100.0 271/1,707 (15.9) 177/472 (37.5) 136/1,595 (8.5) 71/440 (16.1)

RESULTS

Table 1: Effect of Fluoroquinolones on 28 Day Outcomes in Uncomplicated UTI

Table 2: 28-Day Quinolone Outcomes by Susceptibility for Enterobacteriaceae, by Individual Pathogens

CONCLUSIONS

- Quinolone non-susceptibility is seen in over 20% of isolates from the urinary tract in the US.
- Driven primarily by E. coli and P. mirabilis.
- Over the subsequent 28 days, patients with a quinolone resistant pathogen who received a quinolone for cUTI were significantly more likely:
  - To require another antibiotic prescription and/or hospitalization
  - To be hospitalized and receive antibiotics.

Further research is needed to understand if these findings can be extrapolated to uUTI patients treated without urine cultures.

These findings highlight the need for novel oral antimicrobial options with activity against QNS pathogens.

Methods:

- Randomized prospective study
- US adult ambulatory patients with cUTI
- All patients with a positive ambulatory urine culture for an uropathogen
- Retrospective database analysis

Escherichia coli

Klebsiella spp.

E. coli 71.2 152/1,141 (13.3) 157/415 (37.8) 65/1,068 (6.1) 55/384 (14.3)

K. pneumoniae 15.6 72/317 (22.7) 8/24 (33.3) 41/298 (13.8) 4/23 (17.4)

P. mirabilis 5.4 14/96 (14.6) 0/1 (0.0) 12/96 (12.5) 1/1 (100)

E. aerogenes 0.5 0/1 (0.0) 0/1 (0.0) 0/1 (0.0) 0/1 (0.0)

K. oxytoca 7/2 (28) 0/1 (0.0) 3/2 (15) 0/1 (0.0)

S. marcescens 1/1 (100) 0/1 (0.0) 1/1 (100) 0/1 (0.0)

M. morganii 5/12 (42) 0/1 (0.0) 1/12 (8) 1/1 (100)

Table 2: Impact of Quinolones for uncomplicated UTI on Outcomes

Parameter

Suscetteable Non-Susceptible

Antibiotic re-prescription rate*, n (%) 277 (15.9) 177 (37.5)
P value <0.001

Hospitalization*, n (%) 136/1,195 (8.5) 74/440 (16.1)
P value <0.001

With IV/PO antibiotics 108/1,195 (6.8) 59/440 (13.4)
P value <0.001

With IV/PO antibiotics appropriate for QNS pathogens 95/1,195 (6.0) 55/440 (12.5)
P value <0.001

*Based on susceptibility testing performed at the local institution.

- All patients with a positive ambulatory urine culture for an uropathogen.
- Retrospective database analysis

- Bacteria were isolated from urine cultures
- The IDSA uUTI guidelines
- Quinolone non-susceptibility is seen in over 20% of isolates from the urinary tract in the US.

- Quinolone non-susceptibility is seen in over 20% of isolates from the urinary tract in the US.
- Driven primarily by E. coli and P. mirabilis.
- Over the subsequent 28 days, patients with a quinolone resistant pathogen who received a quinolone for cUTI were significantly more likely:
  - To require another antibiotic prescription and/or hospitalization
  - To be hospitalized and receive antibiotics.

Further research is needed to understand if these findings can be extrapolated to uUTI patients treated without urine cultures.

These findings highlight the need for novel oral antimicrobial options with activity against QNS pathogens.

Methods:

- Randomized prospective study
- US adult ambulatory patients with cUTI
- All patients with a positive ambulatory urine culture for an uropathogen
- Retrospective database analysis

Escherichia coli

Klebsiella spp.

E. coli 71.2 152/1,141 (13.3) 157/415 (37.8) 65/1,068 (6.1) 55/384 (14.3)

K. pneumoniae 15.6 72/317 (22.7) 8/24 (33.3) 41/298 (13.8) 4/23 (17.4)

P. mirabilis 5.4 14/96 (14.6) 0/1 (0.0) 12/96 (12.5) 1/1 (100)

E. aerogenes 0.5 0/1 (0.0) 0/1 (0.0) 0/1 (0.0) 0/1 (0.0)

K. oxytoca 7/2 (28) 0/1 (0.0) 3/2 (15) 0/1 (0.0)

S. marcescens 1/1 (100) 0/1 (0.0) 1/1 (100) 0/1 (0.0)

M. morganii 5/12 (42) 0/1 (0.0) 1/12 (8) 1/1 (100)

Table 2: Impact of Quinolones for uncomplicated UTI on Outcomes

Parameter

Suscetteable Non-Susceptible

Antibiotic re-prescription rate*, n (%) 277 (15.9) 177 (37.5)
P value <0.001

Hospitalization*, n (%) 136/1,195 (8.5) 74/440 (16.1)
P value <0.001

With IV/PO antibiotics 108/1,195 (6.8) 59/440 (13.4)
P value <0.001

With IV/PO antibiotics appropriate for QNS pathogens 95/1,195 (6.0) 55/440 (12.5)
P value <0.001

*Based on susceptibility testing performed at the local institution.

- All patients with a positive ambulatory urine culture for an uropathogen.
- Retrospective database analysis

Escherichia coli

Klebsiella spp.

E. coli 71.2 152/1,141 (13.3) 157/415 (37.8) 65/1,068 (6.1) 55/384 (14.3)

K. pneumoniae 15.6 72/317 (22.7) 8/24 (33.3) 41/298 (13.8) 4/23 (17.4)

P. mirabilis 5.4 14/96 (14.6) 0/1 (0.0) 12/96 (12.5) 1/1 (100)

E. aerogenes 0.5 0/1 (0.0) 0/1 (0.0) 0/1 (0.0) 0/1 (0.0)

K. oxytoca 7/2 (28) 0/1 (0.0) 3/2 (15) 0/1 (0.0)

S. marcescens 1/1 (100) 0/1 (0.0) 1/1 (100) 0/1 (0.0)

M. morganii 5/12 (42) 0/1 (0.0) 1/12 (8) 1/1 (100)