



Pathogen Resistance and UTI Prophylaxis

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The topic of UTI prophylaxis is somewhat controversial and there is limited data available regarding the use of prophylaxis and its effects on pathogen resistance. Patients with vesicoureteral reflux (VUR) are commonly initiated on UTI prophylaxis. Historically, infants and children with recurrent febrile UTIs are also started on prophylaxis. However, well-designed randomized controlled trials (RCTs) do not support this use. A cohort study by Patrick Conway, et. al. found that antimicrobial prophylaxis was not associated with decreased recurrent UTIs and was a risk factor for resistance with recurrent UTIs. The most common antibiotics prescribed for UTI prophylaxis include trimethoprim/sulfamethoxazole, nitrofurantoin, cephalexin, and amoxicillin.

Antibiotic use, whether appropriate or not, increases both the individual's risk and the population's risk of acquiring a resistant infection. A meta-analysis by Ceire Costelloe, et. al. reviewed the literature and analyzed studies that evaluated subsequent antibiotic resistance in patients that were prescribed antibiotics in the community setting. Five studies revealed increased odds of having resistant *Escherichia coli* at 2 months (OR 2.5) and 12 months (OR 1.33) post-antibiotic treatment. Simply by treating one UTI with antibiotics increased the likelihood of resistant infections in the future. This further emphasizes the importance of stewardship and treating UTIs according to guidelines and evidence-based medicine.

The prolonged use of antibiotics for prophylaxis has also been found to increase the rate of resistance. Not only does it increase resistance to the medication being used for prophylaxis, but it also increases the rate of multidrug resistance with recurrent infections. This further complicates the empiric selection and treatment of recurrent UTIs and should play a role in the risk-benefit assessment of the use of prophylaxis.

A meta-analysis by Rachel Selekman, et.al. assessed the effect of UTI prophylaxis on the development of a first recurrent UTI that was multidrug resistant. They evaluated RCTs of children with VUR who were and were not treated with continuous antibiotic prophylaxis. Multidrug resistance was defined as any uropathogen that was resistant to any antibiotic in 3 or more classes, excluding those that are intrinsically resistant (e.g. cephalosporins and enterococcus). Six studies fulfilled the inclusion criteria and were evaluated, 3 of which were at a high-risk of bias due to inadequate blinding. Overall, 1,299 children with VUR were included, which led to the evaluation of 224 first recurrent UTIs. Of these, the most common pathogen identified was *Escherichia coli*. They found that among patients receiving continuous antibiotics, they were more likely to develop a multidrug resistant infection compared to those receiving placebo. Those patients were then more likely to receive a broad-spectrum antibiotic to treat the recurrent infection. The use of these more broad-spectrum agents further potentiates the risk of resistance for future infections.

This meta-analysis found that for every 21 patients treated with prophylaxis, 1 additional multidrug resistant recurrent UTI would develop. They also found that for every 10 days of prophylaxis, the odds of a multidrug resistant UTI decreased by 5%. You can conclude from this that continuous antibiotics decreases the risk for developing a UTI, but when recurrence occurs, there is an increased risk of multidrug resistance. This analysis showed that the probability of preventing a recurrent UTI while receiving prophylaxis was equal to the probability of developing a resistant UTI while receiving prophylaxis. In light of this, we as healthcare professionals should use this information and other evidence to facilitate more informed conversations with other practitioners, our patients, and their families when making decisions regarding the use of prophylaxis.

References:

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