

Treatment of simple urinary tract infections in Europe

Different views share the same message: Avoid the use of fluoroquinolones, follow guidelines



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nitrofurantoin and fosfomycin-trometamol. In some cases, only symptomatic relief of symptoms by nonsteroidal anti-inflammatory drugs (NSAIDs) and water intake increase are sufficient. We need to remember that UTI tends to recur, exclude all provocations and be familiar with non-antibiotic prophylaxis. We need to stop overtreatment of uncomplicated UTI and asymptomatic bacteriuria – we are very close to reaching the end of the era of antibiotics, if we aren't already there.

A Georgian view

Almost half of all women suffer from at least one episode of urinary tract infection (UTI) in their lives. Also specific subpopulations are at increased risk of UTI - infants, pregnant women, the elderly, patients with spinal cord injuries and/or catheters, patients with diabetes or multiple sclerosis, patients with acquired immunodeficiency disease syndrome/human immunodeficiency virus, and patients with underlying urological abnormalities.

I would like to share some ideas about the management of uncomplicated UTI by urologists in office practice and emphasise that up to 20% of our patients suffer from this condition. The high frequency of uncomplicated UTI in adults and their overtreatment with antibiotics causes massive antibiotic-resistant bacteria in the population and collateral damage. Resilience of the dominant human faecal microbiotics takes several months after antibiotic treatment. In Georgia, as in many places in world, the most commonly prescribed antibiotics seem to be fluoroquinolones. According to my research in the database of one of the laboratories in Tbilisi, 35% of *E. coli* is resistant to all fluoroquinolones. During empirical treatment of UTI, the growing resistance to cotrimoxazole and ampicillin should be taken into consideration. And I have not even mentioned extended spectrum beta-lactamase producing (ESBLs) and carbapenem-resistant Enterobacteriaceae (CRE).

In 2015, we started implementing the EAU recommendations for uncomplicated UTI management in clinical practice of urologists in office, gynaecologists and primary-care physicians. We met more than one thousand doctors all around Georgia. The central goal of our mission was to switch prescriptions of broad-spectrum antibiotics to



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A Hellenic view

Uncomplicated UTI are among the most common bacterial infections seen in everyday practice. Greek urologists in office take care of a broad spectrum of patients, ranging from low-risk groups such as young adults to vulnerable populations such as elderly patients, spinal cord injury patients as well as patients requiring permanent or intermittent bladder catheterisation.

Within a relatively short period of time, a substantial increase in the non-susceptibility rates of Gram-negative community-acquired uropathogens to most antibiotics, but especially to fluoroquinolones, was noted in Greece (figure 1). Local resistance patterns to antibiotics in Greece are a significant factor in the choice of management of UTI. The vicious circle of further resistance perpetuates and effective options are exhausted. Having that in mind, the antibiotic choice should be considered not only on efficacy and safety but also on the concept that broad-spectrum antibiotics should be used sparsely to safeguard their future effectiveness.

Greece has high antibiotic consumption rates compared to other European countries, both in total and in outpatient clinics. In 2015, 1,242 Daily Defined Doses (DDD) were recorded per 1000 individuals in fluoroquinolones and 3,450 DDD/1,000 individuals for cephalosporins according to The Center for Disease

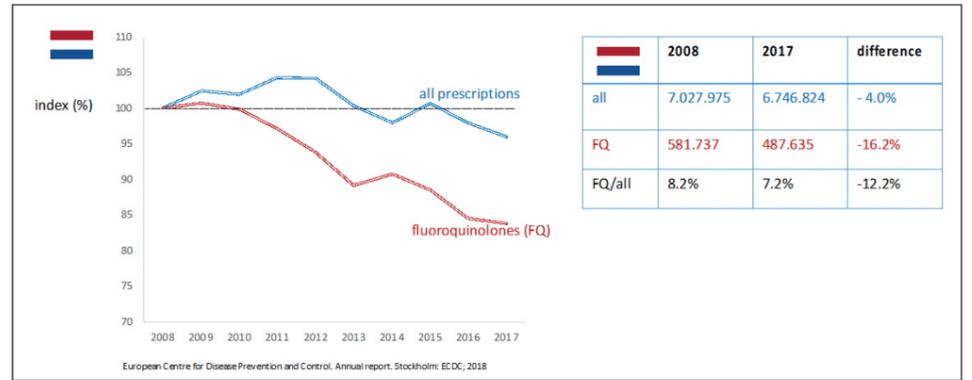


Figure 3: Index of total antibiotic prescriptions in the Netherlands

Dynamics Economics & Policy in our country. Reasons for increased antimicrobial resistance are manifold. Population mobility (immigration and tourism, because of the country's geographic position) can introduce resistant strains. Moreover, the ease of procuring antibiotics without a prescription in Greek pharmacies results in excessive and unreasonable use. Even though the Greek Drug Administration (EOF) requires culture-directed selection of fluoroquinolones for UTIs to prevent their widespread use, some clinicians do not comply with the best practice recommendations and inappropriately circumvent these restrictions.

More information and education for urologists as well as general practitioners are a key measure to promote the rational prescription of antibiotics and should help tackle the rise of antibiotic resistance in Greece.



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A Dutch view

After the introduction and popularisation of the use of oral fluoroquinolones (FQs) in the treatment of UTI, well over half a million prescriptions were written annually in The Netherlands. That was almost 10% of

all antibiotic prescriptions in our country. This generally well-tolerated group of drugs with apparently little side effects was commonly used in the daily offices of general practitioners and urologists.

In recent years, however, two issues have changed our view on prescribing FQs: the growing drug resistance and the knowledge about possible side effects. The European Centre for Disease Prevention and Control publishes the palette of antibiotic resistance for different European countries annually. In Figure 2, the FQ resistance for *E. coli* in the different countries is depicted. There are geographical differences, and note that the general trend is rising resistance.

The relatively rare, but severe side effects of the FQs, such as tendonitis (including spontaneous Achilles tendon rupture), neuropathies, depression, impaired function of smell, taste and vision, have caused the European Medicines Agency to advise against the use of FQs in simple or recurrent lower UTI. In recent years, the prescription of FQs has reduced impressively (figure 3) in The Netherlands. Apart from avoiding these side effects, we could argue that this is one of the reasons why FQ resistance of *E. coli* remained relatively stable in recent years.

In the guidelines of the Dutch general practitioners and urologists, the antibiotic treatment of UTI is nitrofurantoin (first choice), fosfomycin (second) or trimetoprim. In prevention, the focus is on improvement of fluid intake, treatment of constipation, the use of cranberry derivatives in recurrent *E. coli* infections and local treatment with estriol in postmenopausal women. The role of probiotics and other non-antibiotic regimens are frequently debated but failed to get a fixed place in the armamentarium of the office urologists in our country.

Conclusion

In the 2019 edition of the EAU Guidelines on Urological Infections, the recommendation of the management of uncomplicated cystitis is to use antimicrobial therapy that is guided by the spectrum and susceptibility patterns of the aetiological pathogens, efficacy, tolerability, adverse ecological effects, costs and availability. The use of fluoroquinolones is not considered to be first choice and should be kept on the shelf for special occasions, such as treatment of complicated UTI, rare resistance patterns or pyelonephritis. The Guidelines Committee recommends fosfomycin, pivmecillinam and nitrofurantoin as drugs of first choice. With the increasing resistance patterns of different bacteria and the increasing knowledge of the side effects and ecological burden of the antibiotics all over Europe, these guidelines should be followed accurately.

Figure 1

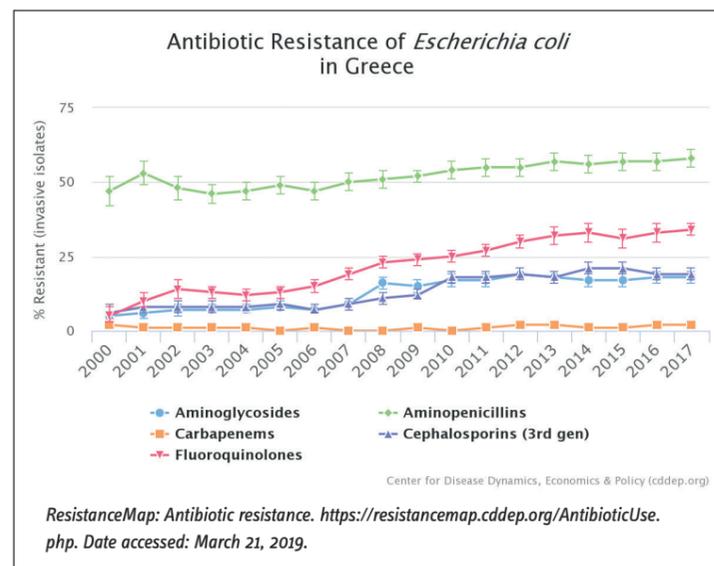
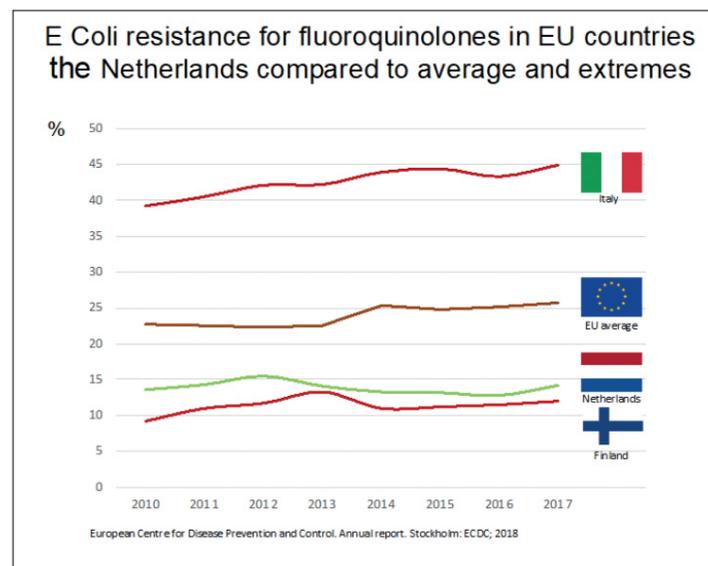


Figure 2



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