S023

2-hour Symposium

Resurrecting old antimicrobial agents

Appropriate usage of nitrofurantoin

A. Huttner[1]

[1]*Geneva University Hospitals, Geneva, Switzerland*

Nitrofurantoin's use has increased exponentially since recent guidelines repositioned it as first-line therapy for uncomplicated lower urinary tract infections (UTI).

Because of its pharmacokinetic profile, nitrofurantoin is approved for use in lower UTI only. Nitrofurantoin was commercialized in an era predating requirements for robust methodology in drug development. Thus, despite the drug's remarkable post-market resurgence and widespread consumption, uncertainties persist regarding its true efficacy and toxicity. We recently performed a structured, systematic review of controlled clinical trials to evaluate nitrofurantoin's efficacy and toxicity when given short-term (≤ 14 days) for the treatment of UTI. This review of 27 trials indicates that nitrofurantoin's clinical and microbiologic efficacy is on par with that of more contemporary antibiotics. Toxicity was minor, reversible, and overall less frequent than that of comparator drugs. Severe adverse drug reactions were not observed. The most feared side effects of nitrofurantoin, pulmonary fibrosis and hepatotoxicity, have been documented overwhelmingly in patients receiving nitrofurantoin prophylaxis for several months or years.

Likely because of nitrofurantoin's multiple modes of action, acquisition or emergence of resistance is relatively infrequent. Indeed, despite several decades of use, much of it prolonged and at lower doses in the context of UTI prophylaxis, nitrofurantoin has generally retained its broad-spectrum activity against Gram-negative and Gram-positive bacteria, including most enterococci, but with the important exception of some Klebsiella strains, *Pseudomonas aeruginosa* and the Proteae (e.g. *Proteus, Morganella* and *Providencia* spp.), which carry intrinsic resistance.

In Western countries, resistance is still rare in *E. coli* and most other extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae. A recent population-based survey of *in vitro* antimicrobial resistance of urinary *E. coli* isolates among U.S. outpatients from 2000 to 2010 showed an increase in nitrofurantoin resistance from 0.8% to 1.6%. The most recent susceptibility data from *E. coli* community-acquired UTI in Europe point to a similarly low resistance prevalence. Nonetheless, nitrofurantoin resistance will likely increase with its recent reintroduction in many countries as first-line therapy for uncomplicated UTI. Indeed, resistance rates among uropathogens in non-Western countries are higher, with recent prevalence documented at 34.3%, 10.1%, and 8.3% in India, Senegal, and South Africa, respectively.