03798 | 03798 Temocillin versus cefotaxime in adults with febrile urinary tract infection, a randomised multicentre clinical trial on effect and collateral damage on intestinal microbiota

02. Bacterial infection & disease

2d. Community-acquired abdominal/gastrointestinal, urinary tract & genital infections

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Background Cefotaxime is widely used in the treatment of febrile urinary tract infection (UTI) including pyelonephritis. The use of cefotaxime is associated with risk for emergence of resistance and infection with Clostridioides difficile. Temocillin is a derivate of ticarcillin and has stability against most ESBLs. The drug has no activity against Gram-positive bacteria. The primary aim of the present study, was to evaluate the ecological impact on the intestinal microbiota of temocillin compared to cefotaxime. Secondary aims were to compare the safety and efficacy of temocillin to cefotaxime in empiric treatment of febrile UTI.

Methods This study was a randomised, controlled, open-label (but blinded for laboratory analysts), superiority multicentre trial on hospitalised patients. Adult women and men with febrile UTI were included at 12 hospitals in Sweden. Patients were randomised to either temocillin 2 g x 3 iv or cefotaxime 1-2 g x 3. The duration of treatment was 7-10 days, of which at least 3 days with study drugs. Rectal swabs were collected at baseline, after the last dose of study drug, prior to any de-escalation therapy, and 7-10 days after discontinuation of treatment. Our superiority endpoint was intestinal colonisation with C. difficile, and/or with Enterobacterales with reduced susceptibility to third generation cephalosporins (3GC). Samples were cultured on non-selective and selective agar media. Statistical analyses were performed using R version 4.0.2 (R Foundation for Statistical Computing). Trial registry: EudraCT Number 2015-003898-15.

Results The modified intention to treat (MITT) population comprised 152 individuals; 77 randomised to temocillin and 75 to cefotaxime. Temocillin generated less ecologic disturbance than cefotaxime, 18/68 (26.5%) vs. 30/62 (48.4%); difference -22.3%, 95% CI: -2.8 to -41.9%, driven by a marked decrease in Enterobacterales with reduced susceptibility to 3GC in the temocillin group, without selection of temocillin-resistant Enterobacterales. Non-inferiority was demonstrated for clinical and bacteriological endpoints. There was no difference in reported adverse events between the treatments.

Conclusions Temocillin resulted in less ecologic disturbance of the intestinal microbiota, while safety and efficacy were non-inferior compared to cefotaxime, indicating that temocillin is an ecologically favourable alternative to cefotaxime in empirical treatment of febrile UTI.

Keyword 1
Forgotten antibiotics
Keyword 2
RCT
Keyword 3
Microbiota

Conflicts of interest

Other support (please specify)
Funded by the Public Health Agency of Sweden.