
Poster

[P25-5] P25-5: Anti-infective drugs (5)

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[P25-5-5] An evaluation of the effectivity of the current treatment of uncomplicated urinary tract infections with fosfomycin based on urinary concentrations in healthy volunteers

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Background

In an era of emerging drug resistance, old antibiotics as fosfomycin, are increasingly being prescribed. Surprisingly, little is known of the urinary concentrations of fosfomycin after a standard dose. We aimed to gain more insight in the pharmacokinetics of fosfomycin to evaluate the effectivity of the treatment of uncomplicated urinary tract infections with fosfomycin. Effectivity is based on urine concentrations in healthy volunteers and the target concentrations to cover the most common uropathogen, *E. coli*.

Methods

3 grams of fosfomycin trometamol was administered to 30 female volunteers. Urine samples were collected during the following 48 hours with every voiding and twice daily up to 7 days. Time, volume, pH and fluid intake were recorded. Urinary fosfomycin concentrations were quantified with ultra-performance liquid chromatography –tandem mass spectrometer (UPLC-MS/MS) system. The creatinine clearance was estimated with the Crockcroft-Gault equation. The time above the MIC' s in urine was calculated based on the concentration-time curves of each volunteer for a range of 0.5 to 128 mg/L.

Results

The following mean values of the pharmacokinetic parameters in urine were calculated, wherein a high inter-individual variability was found: peak concentration 1982.0 ± 1257.4 mg/L; time of the peak 7.5 ± 4.2 h; concentration half-life 12.4 ± 5.7 h and fosfomycin clearance over 48 hours 29.9 ± 7.1 mg/h. An average of 1410.0 ± 311.6 grams was excreted; the urinary recovery was $47.0 \pm 10.4\%$ and 95% of this total amount was excreted within 42 hours of which the main part was excreted during the first 6 hours. Concentrations remained above 64 mg/L for at least 50 hours in all volunteers and >128 mg/L for 39 hours. Covariate analysis indicated that a small reduction in creatinine clearance (80 mL/min compared with a mean of 120 mL/min) and a urination frequency of more than 15 in 48 hours, were associated with a reduced T>MIC.

Conclusions

An exponential relationship was found between the cumulative fosfomycin concentration and time after dose. A considerable inter-individual variability was observed in the pharmacokinetics of fosfomycin indicating potential underexposure in part of the population and the necessity to reevaluate the current dosing regimen of 3 grams.