Poster

[P25-2] P25-2: Anti-infective drugs (2): Beta-lactams

Chair: Veronique Stove, Belgium

Mon. Sep 25, 2017 12:30 PM - 1:30 PM Annex Hall (1F)

(Mon. Sep 25, 2017 12:30 PM - 1:30 PM Annex Hall)

[P25-2-7] Pharmacokinetic and pharmacodynamic characterization of piperacillin-tazobactam, flomoxef and pazufloxacin in prostate tissue and plasma of prostatic hypertrophy patients

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Keywords: pharmacokinetics, phamacodynamics, piperacillin-tazobactam, flomoxef, pazufloxacin

Background

Piperacillin-tazobactam (β-lactam and β-lactamase inhibitor combination), flomoxef (oxacephem) and pazufloxacin (quinolone) are clinically used to treat bacterial prostatitis. However, the prostatic pharmacokinetics and attainment of their pharmacodynamic targets at the site of action had been unclear.

Methods

Piperacillin-tazobactam (2 g-0.25 g, n = 24; 4 g-0.5 g, n = 26), flomoxef (0.5 g, n = 25; 1 g, n = 31), or pazufloxacin (0.5 g, n = 25; 1 g, n = 27) was administered by 0.5-h infusion to patients with benign prostatic hypertrophy prior to transurethral prostatectomy. Drug concentrations in plasma and prostate tissue at 0.5-5 h were measured chromatographically, analyzed noncompartmentally and used to estimate pharmacodynamic attainment of a bactericidal target in prostate tissue (50% of time above the minimum inhibitory concentration [T >MIC] for piperacillin-tazobactam, 70% of T >MIC for flomoxef, and both 8 of maximum concentration [Cmax]/MIC and 100 of area under the concentration-time curve [AUC]/MIC for pazufloxacin).

Results

The mean values for the observed Cmax in prostate tissue and its ratio to plasma were 52.5 and 128.1 mg/kg and 0.33 and 0.39 for piperacillin 2 and 4 g, 17.2 and 32.2 mg/kg and 0.52 and 0.52 for flomoxef 0.5 and 1 g, and 15.7 and 33.7 mg/kg and 0.80 and 0.98 for pazufloxacin 0.5 and 1 g. The corresponding values for AUC were 47.2 and 116.8 mg*h/kg and 0.35 and 0.40 for piperacillin, 14.2 and 29.7 mg*h/kg and 0.50 and 0.50 for flomoxef, and 12.5 and 30.9 mg*h/kg and 0.79 and 0.98 for pazufloxacin, respectively. The highest MIC values at which the usual regimens attained each bactericidal target in prostate tissue were 1 mg/L for piperacillin-tazobactam 4.5 g three times daily (13.5 g/day), 0.5 mg/L for flomoxef 1 g four times daily (4 g/day) and 0.5 mg/L for pazufloxacin 0.5 g twice daily (1 g/day). Despite the different prostatic penetration, the three drugs showed similar site-specific pharmacodynamic profiles.

Conclusions

These comparative results characterize the clinical pharmacokinetics of piperacillin-tazobactam, flomoxef and pazufloxacin in prostate tissue, while also evaluating their dosing regimens for bacterial prostatitis based

on site-specific pharmacodynamic target attainment.