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Clinical pharmacokinetics of beta-lactam and quinolone antibiotics in prostate tissue, and dosing considerations for prostatitis based on site-specific pharmacodynamics

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Introduction & Objectives: Beta-lactam and quinolone antibiotics are clinically used to treat bacterial prostatitis. It is important to understand the pharmacokinetics and pharmacodynamics of antibiotics in prostate tissue to improve treatment efficacy in prostatitis.

Materials & Methods: Piperacillin-tazobactam (2.25 g, n = 24; 4.5 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 intravenously administered to patients with benign prostatic hypertrophy prior to transurethral prostate resection. Blood samples and prostate tissue samples were taken 0.5, 1, 1.5, 3 and 5 h after starting a 0.5-h infusion. Drug concentrations in plasma and prostate tissue were measured chromatographically. The pharmacokinetic data were 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% T > MIC for flomoxef, and both 8 of maximum concentration [Cmax]/MIC and 100 of area under concentration-time curve [AUC]/MIC for pazufloxacin).

Results: The mean values for the observed Cmax in prostate tissue and its ratio to plasma were 52.46–128.07 mg/kg and 0.33–0.39 for piperacillin, 17.24–32.19 mg/kg and 0.52 for flomoxef, and 15.72–33.65 mg/kg and 0.80–0.98 for pazufloxacin. The mean values for AUC in prostate tissue and its ratio to plasma were 47.24–116.78 mg*h/kg and 0.35–0.40 for piperacillin, 14.23–29.65 mg*h/kg and 0.50 for flomoxef, and 12.53–30.88 mg*h/kg and 0.79–0.98 for pazufloxacin. 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). The three drugs showed different prostatic penetration but similar pharmacodynamic profiles.

Conclusions: These comparative results characterize the clinical pharmacokinetics of piperacillin-tazobactam, flomoxef and pazufloxacin in tissue, while also evaluating their dosing regimens for bacterial prostatitis based on site-specific pharmacodynamic target attainment.