Prostatic Penetration of Meropenem in Humans, and Dosage Considerations for Prostatitis Based on Site-Specific Pharmacokinetic-Pharmacodynamic Evaluation

Introduction and Objective: Meropenem is a therapeutic option for the treatment of prostatitis, especially when the patient is refractory to other beta-lactams or intolerant quinolones. However, its prostatic penetration has not been investigated in detail, and its pharmacokinetics-pharmacodynamics (PK-PD) at this site has not been evaluated. The aims of this study were to investigate the penetration of meropenem into human prostate tissue, and to assess to meropenem regimens for prostatitis by performing site-specific PK-PD evaluation.
Materials and Methods: Patients with prostatic hypertrophy (n = 49) prophylactically received a 0.5 h infusion of meropenem (250 or 500 mg) before transurethral resection of the prostate. Meropenem concentrations in plasma (0.5-5h) and prostate tissue (0.5-1.5h) were measured chromatographically. The concentration data were analyzed pharmacokinetically with a three-compartment model, and used to estimate the drug exposure time above the minimum inhibitory concentration for bacteria (T > MIC, % of 24 h) in prostate tissue, an indicator for antibacterial effects at the action site, for six meropenem regimens (250 mg or 500 mg; once daily, twice daily or three times daily; 0.5 h infusions).
Results: The prostate tissue/plasma ratios were 16.6% for the maximum drug concentration and 17.7% for the area under the drug concentration-time curve, and they were irrespective of the dose. Against MIC distributions for clinical isolates of *Escherichia coli*, *Klebsiella species* and *Proteus species*, 500 mg once daily achieved a >90% probability of attaining the bacteriostatic target (20% T > MIC) in prostate tissue, and 500 mg twice daily achieved a >90% probability of attaining the bactericidal target (40% T > MIC) in prostate tissue. However, against *Pseudomonas aeruginosa* isolate, all tested regimens did not achieve a >90% probability of attaining the bacteriostatic and bactericidal targets.
Conclusions: This study investigated the penetration of meropenem into human prostate tissue, and suggested that 500mg regimens were appropriate against the major bacteria causing prostatitis.