

Pharmacokinetic Behavior of Intraperitoneal Teicoplanin during Treatment of Peritonitis Complicating Continuous Ambulatory Peritoneal Dialysis

Continuous ambulatory peritoneal dialysis (CAPD) is an established alternative to hemodialysis for the treatment of end stage renal disease. However, catheter-related infections and peritonitis remain serious disadvantages. The incidence of peritonitis is about one episode per patient per year (9) but has been declining with improved administration systems.

Coagulase-negative staphylococci (CNS) and *Staphylococcus aureus* account for 50 to 80% of peritonitis episodes (9). Current treatment recommendations advise vancomycin plus intraperitoneal ceftazidime or an aminoglycoside as initial empiric therapy (1). Vancomycin is usually given at doses of 15 to 25 mg/liter per bag, sometimes with an intravenous loading dose.

Teicoplanin is a glycopeptide antibiotic with a spectrum of activity similar to that of vancomycin. To date, limited clinical and pharmacokinetic studies of treating CAPD peritonitis have been conducted (2, 3, 5). Following Ethics Committee approval, we have studied the pharmacokinetic behavior of teicoplanin at 20 mg/liter per bag, administered over a 10-day period in 16 patients with clinical and laboratory evidence of peritonitis. Exclusion criteria were age of <18 years, allergy to the study medication, pregnancy or lactation, peritoneal leukocyte count of <100 μ l, effective antibiotic therapy within the previous 48 h, or refusal to give written informed consent.

Teicoplanin at 20 mg/liter and aztreonam at 250 mg/liter per dialysis bag were administered at each exchange (four per day

and continued for up to 10 days, or for 5 days after the dialysate cleared; aztreonam was stopped on the basis of microbiologic culture and sensitivity data.

Samples of early-morning serum and dialysate (7- to 10-h dwell time) were collected and assayed for teicoplanin on days 1, 3, 5, 7, 10, and 20 by a microbiologic assay (6), which was unaffected by the presence of aztreonam. Dialysate drug levels ranged from 4.5 to 6.0 μ g/ml during the dosing period and decreased to <1 μ g/ml by day 20 (Fig. 1). In contrast, the serum drug levels increased to a maximum of ca. 9 μ g/ml by day 10 of the study and decreased to ca. 5 μ g/ml 10 days after stopping of teicoplanin. A two-compartment model was fitted to the serum drug concentration data by using nonlinear regression analysis (PCNONLIN), and this indicated the total clearance (CL_{tot}) to be 0.0025 (standard deviation [SD], 0.0009) liters/h/kg of body weight, the terminal half-life to be 508 (SD, 193) h by using a mean dose of 1.56 mg of teicoplanin per kg per day, and the volume of distribution of the control compartment (V_c) to be 0.48 liters/kg. These data are in keeping with previously published single-dose data (4, 7). An attempt to fit a three-compartment model was made, but no advantage was gained.

The regimen adopted for this study was chosen in order to simplify previous dosage recommendations which adopted a deescalating dosage regimen over a 3-week period (5). The observed maximum concentration of drug in serum (C_{max}) exceeded the MIC for all target gram-positive pathogens. Concerns about drug accumulation were not observed; by day 10, concentrations were well within plasma drug levels achieved by intravenous administration. The washout time (Fig. 1) indicates continued inhibitory dialysate drug concentrations for several days after stopping of treatment. The therapeutic response to this regimen for teicoplanin has also confirmed clinical and microbiologic efficacy (8).

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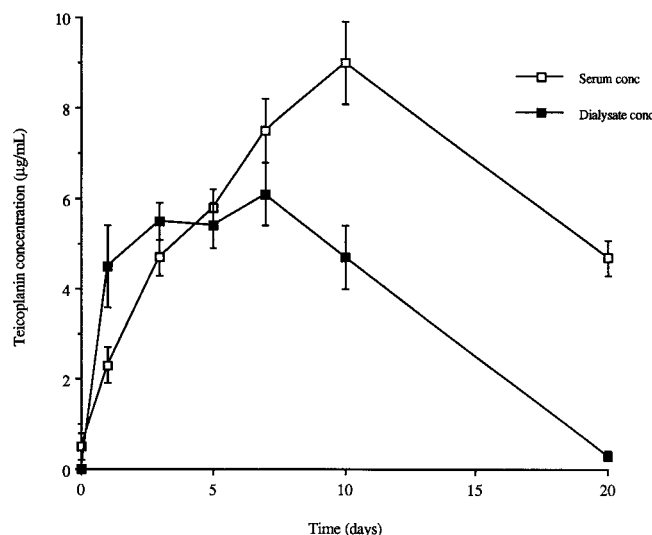


FIG. 1. Mean (\pm SD) (error bars) serum and dialysate teicoplanin concentrations (micrograms per milliliter). The dosage was 20 mg/liter intraperitoneally per exchange.

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