Pharmacokinetics and Pharmacodynamics of Intravenous Daptomycin during Continuous Ambulatory Peritoneal Dialysis

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Summary

Background and objectives This study sought to (1) characterize the pharmacokinetic (PK) profile of intravenous (IV) daptomycin among patients receiving continuous ambulatory peritoneal dialysis (CAPD); (2) identify optimal IV CAPD dosing schemes; and (3) determine extent of daptomycin penetration into the peritoneal space after IV administration.

Design, setting, participants, & measurements A PK study was conducted among eight CAPD patients. Population PK modeling and Monte Carlo simulation (MCS) were used to identify CAPD dosing schemes providing efficacy and toxicity plasma profiles comparable with those obtained from MCS using the daptomycin population PK model derived from patients in the Staphylococcus aureus bacteremia-infective endocarditis (SAB-IE) study. The primary efficacy exposure target was the area under the curve (AUC). For toxicity, the goal was to identify CAPD dosing schemes that minimized plasma trough concentrations in excess of 24.3 mg/L. Finally, peritoneal cavity penetration was determined.

Results Administration of IV daptomycin 4 or 6 mg/kg, depending on indication, every 48 h was identified as the optimal CAPD dosing scheme. This regimen provided cumulative (AUC0–48) and daily partitioned (AUC0–24h and AUC24–48h) plasma AUC values similar to the SAB-IE or “typical patient” simulations. In addition, the proportion of patients likely to experience an elevated trough concentration in excess of 24.3 mg/L was similar between every 48 h CAPD dosing and the referent group. Penetration into the peritoneal cavity was 6% of plasma.

Conclusions Daptomycin 4 or 6 mg/kg, on the basis of indication, IV every 48 h was found to be the optimal IV CAPD dosing scheme.

Introduction

Peritoneal dialysis (PD) is a common renal replacement modality for patients with end-stage kidney disease. Despite advances in PD technology and delivery, infections are still common and represent a significant cause of morbidity and mortality (1). In 2007, the admission rate for bacteremia or sepsis in PD patients was 66.7 per 1000 patient years (1). Treatment of infections in patients on PD has been complicated by the emergence of antibiotic resistance (2), and one of the most problematic pathogens is methicillin-resistant Staphylococcus aureus (MRSA) (3).

Given the rising rates of MRSA infections and emerging efficacy and toxicity concerns with vancomycin (4–7), alternative agents with activity against MRSA are sorely needed. A relatively recent addition to the armamentarium against MRSA is daptomycin. Daptomycin is a lipopeptide antibiotic currently indicated for complicated skin and soft tissue infections and bloodstream infections due to S. aureus including MRSA (8,9). Although the pharmacokinetics (PK) of daptomycin are well described in the general population (primarily renally eliminated, half-life of approximately 8 h, volume of distribution of approximately 0.1 L/kg, and approximately 90 to 93% protein bound), limited information exists regarding the pharmacokinetics and optimal dosing of daptomycin in patients on PD (10,11).

This study had three objectives: (1) characterize the PK profile of daptomycin in plasma and dialysate among patients receiving continuous ambulatory peritoneal dialysis (CAPD); (2) identify an intravenous (IV) daptomycin CAPD dosing scheme for each Food and Drug Administration (FDA)-approved daptomycin regimen that provided efficacy and toxicity plasma profiles comparable with infected, nondialysis patients receiving daptomycin; and (3) determine the...
extent of daptomycin penetration into the peritoneal space after IV administration.

Materials and Methods

Study Design

Eight noninfected adults (≥18 years) on stable PD regimens for ≥1 month were recruited. Nonanuric patients taking medications with the potential to inhibit active tubular secretion were eligible for participation after a 2-week washout. Those patients with peritonitis within the previous 4 weeks were excluded, as were those with clinical signs or symptoms of active infection, elevated white blood cell count, or treatment with any antibiotic during the previous 2 weeks. Patients with serum hemoglobin <11 g/dl, with allergy to daptomycin, or who were pregnant or breastfeeding were also ineligible.

Enrolled patients meeting the study criteria received a standardized CAPD prescription for 1 week before the study day. This standardized regimen consisted of four daily exchanges with 2 L of 2.5% dextrose dialysate having daily dwell periods of 6, 4, 6, and 8 h.

On the study day, patients drained their peritoneal cavities and instilled fresh dialysate via the PD catheter. Patients with residual kidney function provided a urine sample. After drainage, two peripheral venous catheters were placed for drug administration and blood sampling. A single dose of daptomycin 6 mg/kg was administered via 30-minute IV infusion.

A total of 16 blood and 16 dialysate samples were collected from each patient for drug concentration determination. During the first dwell, blood and dialysate samples were collected immediately before daptomycin administration, immediately after completion of the infusion, and 5 minutes, 15 minutes, 1 hour, 2 hours, 4 hours, and 6 hours after completing daptomycin infusion. Four blood and dialysate samples were taken during the second dwell: 30 minutes after the start of fresh dialysate instillation, 30 minutes after dialysate instillation was completed, and then 2 and 4 hours after the end of dialysate instillation. The time to instill fresh dialysate was patient-dependent but generally took 10 minutes. During the third dwell, blood and dialysate samples were collected 30 minutes after the start of dialysate instillation, 30 minutes after dialysate instillation was completed, and then 1 and 2 hours after the end dialysate instillation.

Plasma and dialysate daptomycin concentrations were determined by liquid chromatography tandem mass spectrometry (LC/MS/MS). The analytical reference standard for daptomycin and the internal standard, CB-186,253, were provided by Cubist Pharmaceuticals Inc. The LC/MS/MS instrumentation included an Applied Biosystem API-4000 coupled with an Agilent 1100 Quaternary Pump and a Leap CTC Autosampler. Daptomycin analog CB-183,253 served as the internal standard for both matrix assays. Multiple-ion reactions monitor transitions on mass spectrometer of 811 to 159 and 837 to 365 were used to monitor daptomycin and the internal standard, respectively. Human sodium-heparin plasma was used for plasma assay as a matrix blank. Lactate Ringer solution (Baxter, Deerfield, IL) was used as the matrix blank for analysis of the dialysate samples. The calibration curve was 1.0 to 100 μg/ml for plasma assay and 0.05 to 10.0 μg/ml for dialysate assay. The plasma was extracted via the solid phase method. A Waters HLB (30 mg) 96-well plate was used, and final extracts were analyzed by LC/MS/MS. The dialysate samples were diluted by the internal standard in acetonitrile and centrifuged. The final extracts were reconstituted with 1% formic acid in 90% water to 10% acetonitrile and analyzed by LC/MS/MS. A Waters XBridge column 4.6 × 50 mm, 5 μM was used. The mobile phase A was water, mobile phase B was acetonitrile, and mobile phase C was 10% formic acid in water. The formic acid in the final gradient was 1.0% in a 35 to 50% mobile phase B over a 4.6-minute run.

This study was conducted in agreement with the Declaration of Helsinki, and the protocol was approved by the Institutional Review Board at the Albany College of Pharmacy and Health Sciences. All of the enrolled patients provided informed consent.

Data Analyses

The data were analyzed in a population PK model using the big nonparametric adaptive grid program (BigNPAG) (12). The PK model was parameterized as a three-compartment model with zero-order infusion and first-order intercompartmental transfer and elimination (Figure 1). Our three-compartment model, based partly on work by Janicke et al. (13), is an extension of the standard two-compartment intravenous infusion model with zero-order infusion and first-order elimination and transfer. Additional terms and differential equations were added to the standard two-compartment structural model to account for bidirectional transfer between the central compartment and peritoneal cavity. To properly model the exchanges, each was included as a separate

![Figure 1. Three-compartment pharmacokinetic model with zero-order infusion and first-order intercompartmental transfer and elimination.](image-url)
differential equation in the structural model. Finally, a term was included in the model to account for residual drug from the previous exchange.

The inverse of the estimated assay variance was used as the first estimate of weights. Weighting was accomplished by assuming that total observation variance was proportional to assay variance. Adaptive $\gamma$ was utilized. Upon attaining convergence, Bayesian estimates for each patient were obtained using the “population of one” utility within BigNPAG. For each model, the mean, median, and modal values were used as measurements of the central tendency of the population parameter estimates and were evaluated in the maximum a posteriori probability Bayesian analysis. Goodness of fit was assessed by regression with an observed versus predicted plot, coefficients of determination, and log-likelihood values. Predictive performance was based on the weighted mean bias and bias-adjusted weighted mean precision.

**Monte Carlo Simulation (MCS)**

A series of 9999 subject MCS using ADAPT II (14) were performed to identify intravenous daptomycin CAPD dosing schemes that provided efficacy and toxicity plasma profiles comparable with the “typical” patient receiving daptomycin. The population PK model derived from patients who received daptomycin in the *Staphylococcus aureus* bacteremia-infective endocarditis (SAB-IE) was embedded in the Monte Carlo simulator to estimate the efficacy and toxicity plasma profiles one would expect to observe among infected, nondialysis patients with creatinine clearance ($\text{Cl}_{\text{CR}}$) > 30 ml/min; all of the patients in the SAB-IE study had a $\text{Cl}_{\text{CR}}$ in excess of 30 ml/min. In other words, the population PK model derived from the SAB-IE study was used to simulate the concentration-time profiles of the “referent” or typical nondialysis therapy exposure group. Separate CAPD dosing schemes were developed for each FDA-approved daptomycin dosing regimen (4 and 6 mg/kg IV every 24 hours).

The primary efficacy exposure target of interest was the area under the curve (AUC). Animal model data suggest that the AUC/minimum inhibitory concentration (MIC) ratio is the pharmacodynamic parameter that best describes daptomycin’s activity (15–18). However, the AUC/MIC ratio associated with maximal effect varies. Given the lack of a definitive AUC/MIC threshold associated with antimicrobial effect, especially for patients with bloodstream infections, the distribution of AUC values for any candidate CAPD dosing scheme should at least be comparable with what is typically observed in patients. In this case, the distribution of AUC values from MCS derived from the SAB-IE population PK model served as the referent or “typical patient” AUC exposure distribution (19). For toxicity, the focus was to identify CAPD dosing schemes that minimized the number of MCS instances where trough concentrations exceeded 24.3 mg/L. Animal studies have demonstrated an association between daptomycin trough concentrations and elevations in creatine phosphokinase (CPK) (20,21). More recently, a priori examination of patients from the SAB-IE study substantiated this relationship and demonstrated that elevations in daptomycin troughs, especially above 24.3 mg/L, are associated with an increased probability of a CPK elevation (19).

The concentration-time profiles of daptomycin 4 and 6 mg/kg × 1 in plasma and peritoneal fluid were simulated for 48 and 72 hours. The actual amount (milligrams) of daptomycin used in the MCS was determined by using the distribution of patients’ weights observed in the CAPD study. Concentration-time profiles in plasma and peritoneal fluid were determined for each candidate CAPD regimen. The AUC, concentration immediately before next dose ($\text{Cm}_{\text{in}}$), and concentration 1.5 hours postcompletion of infusion ($\text{Cm}_{\text{ax}}$) were determined in plasma for each candidate CAPD regimen. The AUC was estimated by integrating the appropriate concentration-time curve from $t = 0$ to time $\tau$. For AUC, both cumulative ($\text{AUC}_{0–72h}^\text{cum}$) and noncumulative ($\text{AUC}_{0–24h}^\text{cum}$, $\text{AUC}_{24–48h}^\text{cum}$, and $\text{AUC}_{48–72h}^\text{cum}$) values were simulated. The $\text{Cm}_{\text{in}}$ values simulated were at 48 ($\text{Cm}_{\text{in}}^\text{48h}$) and 72 hours ($\text{Cm}_{\text{in}}^\text{72h}$). These simulated AUC, Cmin, and Cmax values were compared with those obtained from the SAB-IE PK model for 4 and 6 mg/kg IV every 24 hours given as a 30-minute IV infusion.

Monte Carlo simulation was used to calculate the cumulative and noncumulative AUC values in dialsate for daptomycin 4 and 6 mg/kg × 1. The $\text{AUC}_{\text{dialysate}}^\text{dialysate}$, $\text{AUC}_{\text{plasma}}^\text{dialysate}$ mean and median penetration ratios were also determined.

### Results

#### Demographics

Eight patients (seven men) completed the study (Table 1).

#### Population Pharmacokinetic Analysis

The mean (standard deviation [SD]) population parameter estimates for the CAPD population PK model and the previously published “referent” SAB-IE population PK model are provided in Table 2. The observed-predicted

<table>
<thead>
<tr>
<th>Table 1. Demographic information</th>
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<tbody>
<tr>
<td><strong>Age, mean ± SD</strong></td>
<td>58.5 ± 15.1 yr</td>
</tr>
<tr>
<td><strong>Weight, mean ± SD</strong></td>
<td>88.5 ± 16.9 kg</td>
</tr>
<tr>
<td><strong>Body mass index, mean ± SD</strong></td>
<td>28.7 ± 4.8 kg/m²</td>
</tr>
<tr>
<td><strong>Primary cause of ESRD</strong></td>
<td></td>
</tr>
<tr>
<td>Anuric/nonuric, n</td>
<td>2/6</td>
</tr>
<tr>
<td>Dialysis vintage, median (interquartile range)</td>
<td>20.5 (34.75) months</td>
</tr>
</tbody>
</table>
Monte Carlo Simulation

The daptomycin concentrations in plasma (Figure 2, a and b) and peritoneal fluid (Figure 2, c and d) are displayed after a single dose, either 4 or 6 mg/kg, over 72 hours. The results of the AUC distributions for the CAPD and referent model-derived regimens are displayed in Figure 3. At both 4 and 6 mg/kg, the mean cumulative AUC values were similar. The noncumulative AUC values (AUC partitioned into 24-hour increments: AUC0–24h, AUC24–48h, and AUC48–72h) were not as comparable (Figure 3, b and d). Although the candidate CAPD regimen AUC0–24h and AUC24–48h values were higher or similar to the referent regimen, the observed CAPD AUC48–72h values were lower than the referent AUC48–72h values by >50%.

The mean (SD) cumulative AUC0–48h and AUC0–72h values in the peritoneal cavity for 4 mg/kg were 48.4 (33.0) and 56.7 (39.7) mg*h/L, respectively. At 6 mg/kg, the AUC0–48h and AUC0–72h values in the peritoneal cavity were 72.5 (49.5) and 85.0 (59.5) mg*h/L, respectively. The mean (SD) partitioned daily AUC values (AUC0–24h, AUC24–48h, and AUC48–72h) in the peritoneal cavity for 4 mg/kg were 32.9 (21.8), 15.4 (12.3), and 8.3 (8.1) mg*h/L, respectively. For 6 mg/kg, the mean (SD) partitioned daily AUC values (AUC0–24h, AUC24–48h, and AUC48–72h) in the peritoneal cavity were 49.4 (32.7), 23.1 (18.5), and 12.5 (12.0) mg*h/L, respectively. The mean (SD) AUC peritoneal cavity/AUCPlasma penetration ratio was 0.058 (0.033). The median (25th and 75th percentile values) AUCperitoneal cavity/AUCPlasma penetration ratio was 0.050 (0.035 to 0.073).

The results of the Cmax and Cmin MCS analyses are displayed in Table 4. The Cmax values were comparable between the CAPD and referent simulations at both 4 and 6 mg/kg. At both 4 and 6 mg/kg, the mean (SD) Cmin48h values were higher among the CAPD regimens relative to the referent regimen. In contrast, the mean (SD) Cmin72h values were lower for the CAPD regimens relative to the referent regimen. The probabilities of Cmin ≥ 24.3 mg/L were comparable between the CAPD and referent regimen at both 4 and 6 mg/kg (Table 5).

### Table 2. Mean ± standard deviation population pharmacokinetic parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CAPD</th>
<th>SAB-IE (referent)</th>
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<tbody>
<tr>
<td>Vc (L)</td>
<td>6.31 ± 1.19</td>
<td>6.56 ± 3.10</td>
</tr>
<tr>
<td>k12 (h⁻¹)</td>
<td>1.12 ± 1.20</td>
<td>1.67 ± 3.94</td>
</tr>
<tr>
<td>k21 (h⁻¹)</td>
<td>2.55 ± 2.97</td>
<td>1.34 ± 3.40</td>
</tr>
<tr>
<td>CL (L/h)</td>
<td>0.31 ± 0.17</td>
<td>0.96 ± 0.47</td>
</tr>
<tr>
<td>k13 (h⁻¹)</td>
<td>0.007 ± 0.0025</td>
<td>—</td>
</tr>
<tr>
<td>k31 (h⁻¹)</td>
<td>0.12 ± 0.11</td>
<td>—</td>
</tr>
<tr>
<td>VpD (L)</td>
<td>2.64 ± 1.27</td>
<td>—</td>
</tr>
<tr>
<td>Residual amount 1 (mg)</td>
<td>0.47 ± 0.23</td>
<td>—</td>
</tr>
<tr>
<td>Residual amount 2 (mg)</td>
<td>0.49 ± 0.25</td>
<td>—</td>
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Vc, volume of the central compartment; k12: first-order intercompartmental transfer-rate constants from central to peripheral compartment; k21, first-order intercompartmental transfer-rate constants from peripheral to central compartment; CL, nondialytic clearance from central compartment; k13, first-order intercompartmental transfer-rate constants from central to peritoneal compartment; k31, first-order intercompartmental transfer-rate constants from peritoneal to central compartment; VpD, volume of the peritoneal compartment; Residual amount 1, residual daptomycin concentration in peritoneal cavity after first drain; Residual amount 2, residual daptomycin concentration in peritoneal cavity after second drain.

### Table 3. “Goodness of fit” and predictive performances of daptomycin population model in plasma and peritoneal cavity compartment

<table>
<thead>
<tr>
<th></th>
<th>Plasma</th>
<th>Peritoneal Cavity</th>
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<tbody>
<tr>
<td></td>
<td>First Exchange</td>
<td>Second Exchange</td>
</tr>
<tr>
<td>Regression line a</td>
<td>Obs = 1.03 × Pred – 0.87</td>
<td>Obs = 1.06 × Pred + 0.67</td>
</tr>
<tr>
<td>R²</td>
<td>0.88</td>
<td>0.95</td>
</tr>
<tr>
<td>Mean weighted error (mg/L)</td>
<td>–0.07</td>
<td>–0.12</td>
</tr>
<tr>
<td>Bias-adjusted mean weighted square error (mg/L)²</td>
<td>1.7</td>
<td>1.61</td>
</tr>
</tbody>
</table>

aObserved versus predicted plot regression line is the best-fit regression line for the observed-predicted plot after the Bayesian step. Obs, observed; Pred, predicted.

bR² is the coefficient of determination for the best-fit linear regression for the predicted-observed plot after the Bayesian step.
Discussion

To the best of our knowledge, this is the first model-based approach to determine the optimal dosing of an antibiotic in patients receiving CAPD. Rather than relying on noncompartmental PK methods, a three-compartment structural PK model more closely mimicking physiologic conditions during CAPD was devised. The major strength of this population PK model is its application in determining optimal dosing of daptomycin during CAPD. The model can be embedded into an MCS program to estimate exposure profiles in both the central and peritoneal compartment for an infinite number of dosing regimens. The candidate CAPD administration scheme best achieving the exposure target associated with efficacy and minimized toxicity can be selected as the optimal CAPD dosing regimen. These mathematical modeling techniques have an array of other utilities and have become the standard methodologies for assessing the clinical viability and for determining optimal dosage regimens for both experimental and approved antibiotic agents (22).

Overall, the model fit the data extremely well, and the PK parameters were physiologic in nature. Volume in the central compartment was identical to the volume reported in the daptomycin PK model derived from referent (non-dialysis) patients. Mean volume in the peritoneal space was 2.6 L, roughly the amount of fluid administered during each exchange. Clearance was approximately 0.3 L/h, close to previous approximations for patients with minimal kidney function (8, 23–25). Finally, a physiologic amount of residual drug (approximately 0.5 mg) was estimated to remain in the peritoneal cavity after drainage. Because the dialysate concentration at the end of an exchange was between 2 and 6 mg/L for most patients, and the residual volume after drainage is typically between 50 and 100 ml (2 to 6 mg/L × 0.05 to 0.1 L = 0.1 to 0.6 mg), one would expect that 0.5 mg of daptomycin would remain in the peritoneal cavity after drainage before the next instillation.

The results indicate that administration of daptomycin 4 or 6 mg/kg, depending on indication, every 48 hours is an appropriate dosing scheme to treat nonperitoneal systemic infections for patients receiving CAPD. This regimen provided cumulative (AUC_0–48h) values and daily partitioned (AUC_0–24h and AUC_24–48h) values similar to the SAB-IE or “typical patient” simulations. In addition, the proportion of patients likely to experience an elevated trough concentration in excess of 24.3 mg/L was similar between every 48 hours CAPD dosing and the referent group.

At first glance, it appears that dosing every 72 hours is also acceptable. However, when one examines the partitioned daily AUCs out to 72 hours (AUC_0–24h, AUC_24–48h, and AUC_48–72h), the AUC_48–72h in the CAPD group is less than half that of the SAB-IE simulations by day 3. Although dosing every 72 hours has the advantage of lower trough concentrations relative to dosing every 48 hours, a lack of adequate drug exposure on day 3 could lead to treatment failure for infection. Because it is unclear whether the cumulative or partitioned daily AUC is of

Figure 2. | (a) Mean ± SD simulated daptomycin concentrations in plasma after a single 4 mg/kg dose. (b) Mean ± SD simulated daptomycin concentrations in plasma after a single 6 mg/kg dose. (c) Mean ± SD simulated daptomycin concentrations in peritoneal fluid after a single 4 mg/kg dose. (d) Mean ± SD simulated daptomycin concentrations in peritoneal fluid after a single 6 mg/kg dose.
greater import in clinical cure, we err on the conservative side and advocate for dosing every 48 hours.

Approximately 6% of the total AUC observed in plasma was recovered in the peritoneal cavity, which approximates the free concentration observed in patients with normal kidney function. Although only the CAPD modality was studied, we do not anticipate that using a cycler would significantly change the PD dosing recommendations, because very little daptomycin entered the peritoneal cavity. Additionally, this study was performed in patients with minimal peritoneal membrane inflammation; such a condition would most likely facilitate greater drug penetration and subsequently result in higher dialysate concentration. However, the inflammation from peritonitis is expected to resolve relatively quickly once antimicrobial therapy is begun, thus limiting the length of time inflammation would bolster penetration. Although nearly all daptomycin in the peritoneal cavity is unbound, we cannot confidently recommend intravenous daptomycin for peritonitis at this time given the discordance of reported effective AUC/MIC ratios for daptomycin (15,18–20), the lack of a pharmacodynamic target at the tissue level (26), and the lack of data regarding how inflammation would affect concentrations in the peritoneum. Intraperitoneal (IP) administration of daptomycin is a possible alternative to IV.

**Figure 3.** (a) Mean cumulative plasma AUC values for 4 mg/kg daptomycin. (b) Mean partitioned plasma AUC values for 4 mg/kg daptomycin. (c) Mean cumulative plasma AUC values for 6 mg/kg daptomycin. (d) Mean partitioned plasma AUC values for 6 mg/kg daptomycin.
administration (27–29). However, further pharmacokinetic, clinical, and stability studies are necessary before IP administration of daptomycin is adopted as the standard of practice for peritonitis (8).

Several things should be noted when interpreting these results. Although the AUC/MIC is the pharmacodynamic target for daptomycin, the definitive AUC/MIC ratio associated with a high probability of success, especially for MRSA bloodstream infections, has not been identified. In the absence of a well-defined AUC/MIC threshold, it was prudent to design CAPD dosing schemes providing AUC distributions similar to those obtained from the referent population PK model (19). Second, the toxicity target was derived from an *a priori* analysis of the relationship between daptomycin exposure and the probability of CPK elevation among patients from the referent study. Among the 108 evaluable patients, three (50%) of six patients with a Cmin ≥ 24.3 mg/L had elevated CPK values compared with three (2.9%) of 102 patients with a Cmin <24.3 mg/L (P < 0.05). Of the six patients with CPK elevation, CPK levels returned to the normal range during treatment or within the post-treatment follow-up period (19). In the absence of additional exposure-response data, we recommend more intensive CPK monitoring in patients receiving CAPD.

**Conclusions**

In conclusion, we used population pharmacokinetic modeling and Monte Carlo simulation to identify the appropriate intravenous daptomycin-dosing scheme for patients on CAPD. Our results indicated that daptomycin, either 4 or 6 mg/kg on the basis of indication, every 48 hours is an appropriate dosing scheme to treat systemic, nonperitoneal infections for patients receiving CAPD.

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**Disclosures**

Thomas P. Lodise is a consultant for Cubist Pharmaceuticals. This paper benefited from contributions by Lihong Gao, PhD for her assay work and Allison Krug, MPH, for editing. The results were presented in abstract form at the 2010 American Society of Nephrology Renal Week.

**References**

20. Eisenstein BI, Oleson FB, Jr, & Baitz RH: Daptomycin: From the mountain to the clinic, with essential help from Francis Tally, MD. *Clin Infect Dis* 50[Suppl 1]: S10–S15, 2010
22. Lodise TP, Lomaestro BM, Drusano GL: Application of antimicrobial pharmacodynamic concepts into clinical practice: Focus on beta-lactam antibiotics: Insights from the Society of...


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