INTRAPERITONEAL VANCOMYCIN CONCENTRATIONS DURING PERITONEAL DIALYSIS–ASSOCIATED PERITONITIS: CORRELATION WITH SERUM LEVELS

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◆ **Background:** For the treatment of peritoneal dialysis–associated peritonitis (PDP), it has been suggested that serum concentrations of vancomycin be kept above 12 mg/L – 15 mg/L. However, studies correlating vancomycin concentrations in serum and peritoneal dialysate effluent (PDE) during active infection are sparse. We undertook the present study to investigate this issue and to determine whether achieving the recommended serum level of vancomycin results in therapeutic levels intraperitoneally.

◆ **Methods:** We studied patients treated with intraperitoneal (IP) vancomycin for non-gram-negative PDP. We gave a single dose (approximately 30 mg/kg) at presentation, and we subsequently measured vancomycin levels in PDE on day 5; we wanted to determine if efflux of vancomycin from serum to PDE during a 4-hour dwell was consistent and resulted in therapeutic levels.

◆ **Results:** Of the 48 episodes of PDP studied, serum vancomycin concentrations exceeding 12 mg/L were achieved in 98% of patients, but in 11 patients (23%), a PDE vancomycin level below 4 mg/L—the minimal inhibitory concentration (MIC) of many gram-positive organisms—was observed at the end of a 4-hour dwell on day 5. The correlation between the concentrations of vancomycin in serum and PDE (from efflux of antibiotic over 4 hours) was statistically significant, but poor ($R^2 = 0.18$).

◆ **Conclusions:** Our data support the International Society for Peritoneal Dialysis statement that adequate serum vancomycin concentrations can be achieved with intermittent dosing (single dose every 5 days), but cannot guarantee therapeutic PDE levels in the treatment of PDP. Intermittent dosing of vancomycin may not consistently result in PDE concentrations markedly greater than MIC of many important pathogens. Although the clinical significance of this finding remains to be determined, it may be preferable to give smaller but more frequent doses of PDE vancomycin (continuous dosing) for adults with PDP (as is currently recommended for children).

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Peritoneal dialysis–associated peritonitis (PDP) continues to be a major cause of morbidity and technique failure despite wider use of the flush-before-fill and disconnect systems designed to lower the rate of infection. Many peritoneal dialysis (PD) units use the glycopeptide antibiotic vancomycin as a first-line agent for the treatment of PDP, and vancomycin continues to be recommended in the latest guidelines from the International Society for Peritoneal Dialysis (ISPD) (1). Despite widespread use of vancomycin, deficiencies still remain in current knowledge about certain of its aspects, particularly its peritoneal pharmacokinetics during active PDP.

The minimal inhibitory concentration of vancomycin for gram-positive organisms is generally less than 4 mg/L (2,3). A previous study of PDP suggested that serum levels exceeding 12 mg/L may be associated with a better cure rate (4), and the ISPD currently recommends re-dosing when serum concentrations fall below 15 mg/L (1). Unless vancomycin is added to subsequent PD bags, the peritoneal concentration relies on efflux from serum into the peritoneum. However, studies directly examining the efflux of vancomycin from serum into PD effluent (PDE) are limited. Thus, although it is assumed that, when serum levels exceed 12 mg/L, therapeutic PDE concentrations are achieved during PD dwells (approximately 4 hours), this effect has not been proved. Studies examining the pharmacokinetics of vancomycin during PD were not conducted in patients with acute PDP—when peritoneal transport of solutes is known to be altered (5). Moreover, the study populations examined have been small (6–8).

We previously demonstrated that a single large dose of vancomycin given in a long dwell results in rapid

attainment, and maintenance for 5 days, of the ISPD target serum concentration (9). We next wanted to determine whether this dosing regimen, often used around the world, consistently results in therapeutic PDE concentrations. For the present study, we examined PDE concentrations of vancomycin after a 4-hour dwell using fresh PD fluid [representing the average continuous ambulatory PD (CAPD) exchange], on day 5 of PDP. A second aim of our study was to determine if the efflux of vancomycin from serum into the peritoneal cavity was consistent enough to predict the PDE level based on the serum level. Finally, we wanted to determine if low PDE levels of vancomycin might predict treatment failure in PDP episodes.

METHODS

CENTER AND PDP TREATMENT PROTOCOL

This retrospective study was undertaken at the Royal London Hospital, London, UK. During the study period, the center had a PD population of approximately 230 patients and a PDP rate of 1 episode every 27 patient-months. Throughout the study period, no episodes of PDP involving methicillin-resistant *Staphylococcus aureus* or vancomycin-resistant enterococci were observed.

Empiric treatment for PDP in all patients included intraperitoneal (IP) vancomycin, with the dose modified for urine output (anuria defined as a daily urine output of less than 200 mL) and corrected for body weight. That dose was administered on presentation (single dose of 30 mg/kg rounded to the nearest 500 mg for anuric patients, but increased by 25% if not anuric up to a maximum dose of 2.5 g). Patients also received IP gentamicin (0.6 mg/kg once daily for anuric patients, but increased by 25% if not anuric) and oral rifampicin 300 mg twice daily. Daily gentamicin and rifampicin therapy continued until day 5 or until antibiotic therapy could be adapted to the culture results. Patients were told to leave PD bags containing antibiotic *in situ* for a minimum of 6 hours. If patients using automated PD (APD) were normally “dry” during the day, they were instructed to administer antibiotics into a 1-L last fill.

We previously described the effectiveness of the foregoing regimen at achieving therapeutic serum vancomycin concentrations (9). The cohort of patients in the present study represents an entirely new population, unconnected to that earlier study.

SAMPLE AND DATA COLLECTION

We measured the day 5 PDE vancomycin concentration obtained at the end of a 4-hour dwell using antibiotic-free

fluid. We chose a 4-hour dwell time because that duration approximates the length of a standard daytime dwell for a CAPD patient performing 4 daily exchanges.

Subjects were eligible for study enrollment if they presented with a new episode of PDP between August 2005 and August 2008. All diagnoses were confirmed by a high PDE white cell count—exceeding 100/mm³, with more than 50% neutrophils. Users of CAPD and APD were both included. Because the study was examining PDE vancomycin concentrations, we excluded patients with confirmed gram-negative infections. We also excluded patients who failed to attend on day 5 of treatment or within 4 hours of their morning exchange.

On day 5 of treatment (5 days after the initial loading dose of IP vancomycin), patients performed their usual early-morning exchange (without antibiotics in the bag) at home and presented to the PD department 4 hours later. The PDE from this 4-hour dwell was drained, and a sample was collected for measurement of the vancomycin concentration (stored at –70°C until analysis). A serum sample was also taken for measurement of the trough vancomycin concentration.

From the renal unit’s electronic database, we retrospectively obtained patient demographics, the type of organism causing the PDP episode, the associated antibiotic sensitivities, pre-morbid transport status (determined by the result of the most recent peritoneal equilibration test before the peritonitis episode), and outcome of the PDP episode—defined as cleared, relapsed (recurrence of PDP with the same organism within 4 weeks of stopping antibiotic therapy), or non-resolution necessitating removal of the PD catheter.

VANCOMYCIN ASSAYS

Reagents from Roche Diagnostics (Mannheim, Germany) for online therapeutic drug monitoring were used for vancomycin measurements, and the assay was run on the Roche Modular Analytics P module platform. The sampling system uses capacitance liquid level sensing technology. The reagents consisted of 2 ready-to-use bottles: R1 and R2. Bottle R1 contained vancomycin labeled with bacterial glucose-6-phosphate dehydrogenase in buffer (“enzyme reagent”); bottle R2 contained anti-vancomycin antibody (mouse monoclonal), glucose-6-phosphate, and nicotinamide adenine dinucleotide in buffer. This method using monoclonal antibodies diminishes the likelihood of cross-reactivity with vancomycin crystalline degradation products, which has been described when polyclonal antibodies are used (10).

The principle of the test is based on a homogenous enzyme immunoassay technique and relies on competition

between the drug in the sample and the drug labeled with the enzyme reagent for antibody binding sites. Enzyme activity declines upon antibody binding, allowing the drug concentration in the sample to be measured in terms of enzyme activity. The coefficient of variability for the assay is less than 5%.

STATISTICAL ANALYSIS

The relationships between the serum and PDE concentrations of vancomycin, and between transport status and the PDE:serum antibiotic concentration ratio, were assessed using Pearson correlation coefficients because the relationships were approximately linear. Univariate logistic regression analysis was used to assess the impact of PDE and serum vancomycin concentrations on the binary outcome of peritonitis resolved compared with peritonitis relapse or catheter removal. Serum and PDE vancomycin concentrations were also entered, by themselves, into a multivariate logistic regression model to assess their effect on peritonitis recovery, controlling for each other. Values of $p < 0.05$ were considered statistically significant, and the analysis was carried out using the SPSS software package (version 17.0: SPSS, Chicago, IL, USA).

RESULTS

The study included 48 PDP episodes, 29 of which involved patients on CAPD, and 19, patients on APD. Table 1 presents the patient demographics.

Of the 48 episodes of PDP, 38 were caused by gram-positive organisms (27 coagulase-negative staphylococci, 6 *Corynebacterium*, 2 *Enterococcus*, 2 α -hemolytic streptococci, and 1 *Brevibacterium*). The remaining 10 episodes (21%) yielded no growth from the PDE sample. No *Staphylococcus aureus* species were isolated during

the study, and no organism proved to be vancomycin-resistant. In 33 episodes (69%), the PDP cleared; in 11 episodes, the PDP relapsed, with subsequent cure; and in the remaining 4 episodes, the PD catheter was removed.

ANTIBIOTIC CONCENTRATIONS

The mean serum vancomycin concentration among all patients on day 5 was 19.3 mg/L. The mean PDE vancomycin concentration after a 4-hour dwell of fresh PD fluid was 7.2 mg/L (Table 2).

TABLE 1
Patient Demographics

Characteristic	Overall	Value On CAPD	On APD
Patients (<i>n</i>)	48	29	19
Mean age (years)	54.3	56.6	51.1
Men [<i>n</i> (%)]	29 (60)	17 (59)	12 (63)
Women [<i>n</i> (%)]	19 (40)	12 (41)	7 (37)
White [<i>n</i> (%)]	20 (42)	9 (31)	11 (58)
Black [<i>n</i> (%)]	13 (27)	8 (28)	5 (26)
Asian [<i>n</i> (%)]	14 (29)	11 (38)	3 (16)
Diabetic [<i>n</i> (%)]	17 (35)	11 (38)	6 (32)
Mean weight (kg)	75	76	74
Urine output > 200 mL/24 h [<i>n</i> (%)]	29 (60)	17 (59)	12 (63)
Mean vancomycin dose (g)	2.25	2.28	2.21
D/P Cr before PDP	0.651	0.634	0.673
Culture-negative PDP [<i>n</i> (%)]	10 (21)	5 (17)	5 (26)

CAPD = continuous ambulatory peritoneal dialysis; APD = automated peritoneal dialysis; D/P Cr = dialysate-to-plasma ratio of creatinine; PDP = peritoneal dialysis-related peritonitis.

TABLE 2
Correlation Between Vancomycin Concentrations in Serum and Effluent

Variable	Overall	Value On CAPD	On APD
Patients (<i>n</i>)	48	29	19
Vancomycin concentration (mg/L)			
In serum [mean (range)]	19.3 (10.3–30.6)	18.9 (13.1–30.6)	19.8 (10.3–26.4)
In effluent [mean (range)]	7.2 (2.4–17.8)	7.7 (2.4–17.8)	6.5 (2.8–13.6)
Correlation coefficient	0.49	0.35	0.32
R^2	0.18	0.13	0.48
<i>p</i> Value	0.003	0.05	0.001

CAPD = continuous ambulatory peritoneal dialysis; APD = automated peritoneal dialysis.

A PDE vancomycin concentration of less than 4 mg/L was observed in 11 patients (23%), 8 of whom were on CAPD (28% of all CAPD patients), and 3, on APD (16% of all APD patients). Only 1 patient had a day 5 serum vancomycin concentration below 12 mg/L (10.3 mg/L). He was on APD, and his PDE vancomycin concentration after a 4-hour dwell was 3.3 mg/L.

The mean PDE:serum vancomycin concentration ratio was 0.37. Overall, the correlation between serum and PDE concentrations of vancomycin was statistically significant, but poor (correlation coefficient: 0.49; $R^2 = 0.18$; $p = 0.003$; Figure 1).

Of the 11 patients that had a PDE vancomycin concentration below 4 mg/L, 6 were anuric. The correlation between 24-hour urine volume and PDE vancomycin concentration in the study population as a whole was extremely poor ($R^2 = 0.007$). Serum vancomycin concentrations were higher and PDE concentrations were lower in the APD group than in the CAPD group, but the difference did not reach significance ($p = 0.268$).

Figure 1 — Scatter plot and line of best fit showing correlation between serum and effluent vancomycin concentrations in the study patients. Open circles represent continuous ambulatory peritoneal dialysis patients and filled circles represent automated peritoneal dialysis users.

THE INFLUENCE OF TRANSPORT STATUS

The average pre-morbid dialysate-to-plasma ratio of creatinine (D/P Cr) for all patients combined was 0.65 (range: 0.39 – 0.90). For CAPD patients, it was 0.63 (0.39 – 0.90), and for APD patients, it was 0.67 (0.47 – 0.82). Overall, the correlation between D/P Cr and the PDE:serum vancomycin concentration ratio at the end of a 4-hour dwell was extremely poor ($R^2 = 0.0002$).

PREDICTING OUTCOME

In all patients with cleared infection, the mean day 5 trough serum concentration of vancomycin was 18.6 mg/L; in patients who relapsed or underwent PD catheter removal, it was 20.7 mg/L ($p = 0.12$). In patients with cleared infection, the mean day 5 PDE vancomycin concentration after a 4-hour dwell was 7.19 mg/L; in the other patients, it was 7.28 mg/L ($p = 0.94$). Comparing APD with CAPD patients, we observed no differences in the outcome of recovery (74% vs 66%, $p = 0.55$).

We also examined the effect of PDE vancomycin concentration on peritonitis episodes in which the organisms were confirmed to be gram-positive. We compared cure rates for CAPD and APD patients when PDE vancomycin levels were above or below 4 mg/L after a 4-hour dwell on day 5 (Table 3). We observed no statistically significant differences in those cure rates, although we noted a trend toward an improved cure rate in CAPD patients with a higher day 5 PDE vancomycin level: that is, the primary cure rate increased from 57% to 76% if the PDE vancomycin concentration after a 4-hour dwell was greater than 4 mg/L ($p = 0.3$).

We also performed univariate and multivariate logistic regression analyses to examine the effect of serum and PDE vancomycin concentrations on the likelihood of treatment cure (cure without relapse or catheter removal, Tables 4 and 5). Under univariate analysis, (Table 4) increasing concentrations of serum vancomycin were associated with a 10% lesser likelihood of cure (odds

TABLE 3
Effect of Effluent Vancomycin Concentration on Outcomes After Gram-Positive Peritonitis

Effluent vancomycin concentration ^a	On CAPD (n) (% cured)		On APD (n) (% cured)		Overall (n) (% cured)	
>4 mg/L	17	76	11	72	28	75
<4 mg/L	7	57	3	100	10	70

CAPD = continuous ambulatory peritoneal dialysis; APD = automated peritoneal dialysis.

^a After a 4-hour dwell on day 5.

TABLE 4
Univariate Logistic Regression: Effect of Vancomycin
Concentration on Odds of Recovering
from Peritonitis

Adequate vancomycin concentration in	OR	95% CI	<i>p</i> Value
Serum	0.891	0.77 to 1.03	0.127
Effluent	0.993	0.84 to 1.17	0.937

OR = odds ratio; CI = confidence interval.

TABLE 5
Multivariate Logistic Regression: Effect of Vancomycin
Concentrations on Odds of Recovering
from Peritonitis

Adequate vancomycin concentration in	OR	95% CI	<i>p</i> Value
Serum	0.872	0.74 to 1.03	0.102
Effluent	1.06	0.88 to 1.27	0.524

OR = odds ratio; CI = confidence interval.

ratio: 0.891), but that result was not statistically significant. Table 4 also shows that cure was 1% less likely with increasing PDE concentrations of vancomycin, but again, that finding was not statistically significant. A multivariate model that included both the serum and the PDE vancomycin concentration again showed a lesser likelihood of cure with increasing serum concentration and marginally increased odds of recovery with a higher PDE concentration, but again, the results were not statistically significant.

DISCUSSION

The ISPD guidelines contain no specified targets for PDE vancomycin concentration. Such targets are omitted partly because concentrations vary with the type of PD and the duration of dwells. The minimal inhibitory concentration for many gram-positive pathogens is less than 4 mg/L (2,3), and thus, for the present study, we defined an "adequate PDE concentration" to be more than 4 mg/L after a 4-hour dwell (the approximate duration of a CAPD dwell). We found that PDE vancomycin concentration did not reach that target in 23% of patients despite achievement of the ISPD serum target for that antibiotic in almost all patients.

The pharmacokinetics of an intravenous dose of vancomycin in PD patients has been studied (6). At

equilibration, the PDE:serum concentration ratio was found to be approximately 0.33. In our patients, we found that the efflux of vancomycin from serum into the peritoneum during a 4-hour dwell resulted in a similar concentration ratio: 0.37. However, although the PDE vancomycin concentration correlated with the serum concentration ($p = 0.003$), we conclude that serum levels alone should not be used to predict PDE concentration, because the coefficient was only 0.49 ($R^2 = 0.18$).

Our current results are also consistent with our previous study (9) in showing that a single large dose of vancomycin can, at day 5, usually achieve the serum levels suggested by the ISPD (>12 mg/L was almost universally achieved; >15 mg/L was obtained in more than 85% of patients). However, on day 5, 23% of patients had sub-therapeutic PDE concentrations of vancomycin (<4 mg/L) after the equivalent of a standard CAPD dwell. Although we did not measure PDE concentrations after 1 or 2 hours, we can only assume a greater proportion of patients had sub-therapeutic PDE levels during APD sessions.

The variability that we found in the peritoneal transport of vancomycin is consistent with a recent study by Blowey *et al.* (11), who assessed vancomycin pharmacokinetics in 7 healthy children on PD treated with an initial CAPD-like and then an APD-like dialysis regime. Interestingly, even though the peritoneal membrane was not inflamed, dialysate-to-plasma vancomycin ratios varied by a factor of almost 4 between the patients for both dialysis regimes.

Could differences in the small-solute transport status of the peritoneal membrane perhaps predict the variability in the PDE:serum vancomycin ratio between patients? We failed to find a correlation between the D/P Cr from the most recent peritoneal equilibration test in the study patients and the vancomycin ratio. This lack of correlation may be a result of using a pre-morbid D/P Cr, given that an inflamed peritoneum permits greater transfer of vancomycin between the relevant compartments (5,12). Interestingly, our results also showed very poor correlation between residual urine output and the measured PDE vancomycin concentration.

We examined the relationship between PDE vancomycin concentrations and outcomes of the PDP episodes. The PDE vancomycin concentrations in the range we found did not affect the PDP cure rate. That finding held true even when we restricted the analysis to patients with culture-proven gram-positive PDP. Of course, the lack of statistical significance may be a result of the small size of the cohort; the study is open to type II statistical error. Thus, whether the variable transfer of vancomycin from serum into the peritoneum is of clinical relevance remains to be determined. Nonetheless, our results suggest that

targeting a serum vancomycin concentration greater than 12 mg/L or 15 mg/L does not consistently translate into a PDE concentration greater than 4 mg. We therefore concur with the statement in the current ISPD guidelines that serum vancomycin levels should be obtained so as to avoid drug toxicity, but cannot be used to indicate therapeutic concentrations in the peritoneum (1).

The results from the present study suggest that, to ensure consistently high PDE vancomycin concentrations (without toxic serum levels), alternative dosing regimens should be considered. In that respect, perhaps nephrologists treating adults should consider the protocols recommended for pediatric patients, which often use regimes based on continuous dosing. An initial IP loading dose is typically followed by additional small repeated doses in subsequent exchanges.

The efficacy of various dosing regimens has previously been examined. In a randomized study of 51 patients treated with IP vancomycin, Boyce *et al.* found continuous and intermittent dosing regimens to be equally effective (13). However, an interesting point from that small study was that every episode of peritonitis resolved. By contrast, a more recent study by Schaefer *et al.* (14) in children reported eradication of the causative organism from dialysate significantly more frequently with the continuous dosing protocol. Furthermore, Blowey *et al.* commented that a recent review of pediatric data suggested that, compared with continuous regimes, intermittent empiric therapy was associated with a poor early response (11). The continuous form of antibiotic administration does, of course, carry disadvantages from a patient perspective, because patients would likely find an intermittent regime to be far more convenient.

Our study has a number of limitations. First, our center used 200 mL daily as the cut-off for defining anuria (the ISPD suggests 100 mL). However, we do not think that this difference is significant because residual urine output affects serum levels of vancomycin, and 98% of our study patients achieved the target serum vancomycin level of more than 12 mg/L. Second, our study examined the relationship between serum and PDE vancomycin concentrations only after a single 4-hour dwell. A 4-hour dwell is clinically relevant for CAPD patients, but might be too long for APD patients. Future studies should examine PDE vancomycin levels after 1, 2, and 4 hours. Third, although our study is the largest to date to examine the correlation between serum and PDE vancomycin concentrations during active PDP, the number of patients enrolled is still relatively small, and the study is therefore underpowered to determine if the PDE vancomycin concentration on day 5 after a 4-hour dwell is predictive of treatment outcome. In addition, its

retrospective nature means that it is subject to all the limitations common to such studies.

CONCLUSIONS

The present study is, to date, the largest analysis examining the correlation between serum and PDE vancomycin concentrations during active PDP. It supports the ISPD statement that intermittent vancomycin dosing can achieve "adequate" serum levels even after 5 days. Moreover, we concur that measurement of serum vancomycin concentrations safeguards against toxic levels, but cannot be used to ensure therapeutic PDE concentrations. In fact, we demonstrated that the PDE concentration cannot be accurately predicted from the serum concentration.

Despite the shortcomings of the study, we showed that many patients with PDP treated using intermittent vancomycin dosing will experience periods when PDE concentrations are low. On day 5, approximately 25% of CAPD patients will not achieve a PDE vancomycin concentration greater than 4 mg/L during daytime exchanges. For APD patients, in whom dwell times are even shorter (often less than 2 hours), it is likely that an even higher proportion will have "low" PDE vancomycin concentrations for the duration of nighttime treatment. It would therefore be logical to adopt, for adults, the continuous dosing protocol used in children with PDP. However, further studies may be needed to convince nephrologists that the risks and inconvenience of continuous dosing are outweighed by an important potential benefit of improved cure rates.

DISCLOSURES

We confirm that the authors have no conflicting interests that might be construed to bias the results of the present study.

REFERENCES

1. Li PK, Szeto CC, Piraino B, Bernardini J, Figueiredo AE, Gupta A, *et al.* Peritoneal dialysis-related infections recommendations: 2010 update. *Perit Dial Int* 2010; 30:393–423.
2. Schito GC, Auckenthaler R, Marchese A, Bauernfeind A. European survey of glycopeptide susceptibility in *Staphylococcus* spp. *Clin Microbiol Infect* 1999; 5:547–53.
3. Jones RN, Fritsche TR, Sader HS, Ross JE. LEADER surveillance program results for 2006: an activity and spectrum analysis of linezolid using clinical isolates from the United States (50 medical centers). *Diagn Microbiol Infect Dis* 2007; 59:309–17.

4. Mulhern JG, Braden GL, O'Shea MH, Madden RL, Lipkowitz GS, Germain MJ. Trough serum vancomycin levels predict the relapse of gram-positive peritonitis in peritoneal dialysis patients. *Am J Kidney Dis* 1995; 25:611–15.
5. Bastani B, Spyker DA, Westervelt Jr FB. Peritoneal absorption of vancomycin during and after resolution of peritonitis in continuous ambulatory peritoneal dialysis (CAPD) patients. *Perit Dial Int* 1988; 8:135–6.
6. Magera BE, Arroyo JC, Rosansky SJ, Postic B. Vancomycin pharmacokinetics in patients with peritonitis on peritoneal dialysis. *Antimicrob Agents Chemother* 1983; 23:710–14.
7. Obermiller LE, Tzamaloukas AH, Leymon P, Avasthi PS. Intravenous vancomycin as initial treatment for gram-positive peritonitis in patients on chronic peritoneal dialysis. *Clin Nephrol* 1985; 24:256–60.
8. Harford AM, Sica DA, Tartaglione T, Polk RE, Dalton HP, Poynor W. Vancomycin pharmacokinetics in continuous ambulatory peritoneal dialysis patients with peritonitis. *Nephron* 1986; 43:217–22.
9. Blunden M, Zeitlin D, Ashman N, Fan SL. Single UK centre experience on the treatment of PD peritonitis—antibiotic levels and outcomes. *Nephrol Dial Transplant* 2007; 22:1714–19.
10. Smith PF, Morse GD. Accuracy of measured vancomycin serum concentrations in patients with end-stage renal disease. *Ann Pharmacother* 1999; 33:1329–35.
11. Blowey DL, Warady BA, Abdel-Rahman S, Frye RF, Manley HJ. Vancomycin disposition following intraperitoneal administration in children receiving peritoneal dialysis. *Perit Dial Int* 2007; 27:79–85.
12. Rubin J. Vancomycin absorption from the peritoneal cavity during dialysis-related peritonitis. *Perit Dial Int* 1990; 10:283–5.
13. Boyce NW, Wood C, Thomson NM, Kerr P, Atkins RC. Intrapertoneal (IP) vancomycin therapy for CAPD peritonitis—a prospective, randomized comparison of intermittent v continuous therapy. *Am J Kidney Dis* 1988; 12:304–6.
14. Schaefer F, Klaus G, Müller-Wiefel DE, Mehls O. Intermittent versus continuous intraperitoneal glycopeptide/ceftazidime treatment in children with peritoneal dialysis-associated peritonitis. The Mid-European Pediatric Peritoneal Dialysis Study Group (MEPPS). *J Am Soc Nephrol* 1999; 10:136–45.